Common European Standards and Criteria for the Inspection of Blood Establishments

Reflecting European good practice within the area addressing the quality and safety of blood

Editors: E. Seifried and C. Seidl
Frankfurt/Germany, Edition 1.0

ENGLISH
Publication notice:

This manual has been developed by the participants of the EuBIS Project co-funded by the European Commission, Health and Consumer Protection Directorate General, Public Health and Risk Assessment Directorate, DG Sanco Grant Agreement No. 2006202. (2003-2008)

The manual gives valuable information and guidance on common criteria and standards for the inspection of blood establishments based on the requirements set-out in the blood legislation of the European Commission.

Further information on this manual including updated versions, national training courses or seminars organised by the project participants is available from the project Website of EUBIS (European blood inspection system) (www.eubis-europe.eu).

Supported by the European Blood Alliance (EBA)

Disclaimer:

The content of this manual does not necessarily reflect the views of the European Commission. Neither the Commission nor any person acting on its behalf can be held responsible for any use that may be made of the information in this report.

The editors and project participants assume no responsibility for the use to which this manual is made.
Red Cross Blood Donor Service Baden-Württemberg – Hessen, University Hospital Frankfurt am Main, Germany

Editors: Erhard Seifried and Christian Seidl

Edited in cooperation with the Project Participants and Collaborating Partners

Project Coordinators
Erhard Seifried
Christian Seidl

Working Group Leaders
Jan Peter Jansen van Galen
Mark Nightingale
Christian Seidl
Leslie Sobaga

Advisory Board
Patrick Costello
Frances Delaney
Angus Macmillan Douglas
Margarethe Heiden
Wiebke Siegel
Jeroen de Wit

Manual Drafting Group:
Frances Delaney
Jan Peter Jansen van Galen
Helga Marie Huber
Margarethe Heiden
Mark Nightingale
Christian Seidl
Wiebke Siegel
Leslie Sobaga
Fewzi Teskrat
**Project Participants and Collaborating Partners:**

<table>
<thead>
<tr>
<th>Participants</th>
<th>Country</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFSSAPS – France</td>
<td>France</td>
<td>Agence française de sécurité sanitaire des produits de santé (France)</td>
</tr>
<tr>
<td>BSDBH – Germany</td>
<td>Germany</td>
<td>Deutsche Rotes Kreuz Blutspendedienst, Baden-Württemberg, Hessen (German Red Cross Blood Donation Service) (Project Coordinator)</td>
</tr>
<tr>
<td>BTS – Iceland</td>
<td>Iceland</td>
<td>Blóðbankinn, Landspítali (The Blood Bank, Landspitali University Hospital)</td>
</tr>
<tr>
<td>CNS, ISS – Italy</td>
<td>Italy</td>
<td>Centro Nazionale Sangue, Istituto Superiore di Sanita</td>
</tr>
<tr>
<td>DHCSS - Malta</td>
<td>Malta</td>
<td>Directorate of Health Care Services Standards, Government of Malta</td>
</tr>
<tr>
<td>EBS – Estonia</td>
<td>Estonia</td>
<td>Põhja-Eesti Regiinaalhaigla Verekeskus (North-Estonian Regional Hospital Blood Centre)</td>
</tr>
<tr>
<td>EFS – France</td>
<td>France</td>
<td>Etablissement François du Sang (French Blood Establishment)</td>
</tr>
<tr>
<td>FMP – Romania</td>
<td>Romania</td>
<td>Universitatea de Medicina si Farmacie &quot;Victor Babes&quot; Timisoara (University of Medicine and Pharmacy &quot;Victor Babes&quot; Timisoara)</td>
</tr>
<tr>
<td>FOK – Czech Republic</td>
<td>Czech Republic</td>
<td>Fakultni nemocnici Ostrava Krevni centrum (Blood center)</td>
</tr>
<tr>
<td>BRCF – Belgium</td>
<td>Belgium</td>
<td>Rode Kruis Vlaanderen (Belgian Red Cross-Flanders)</td>
</tr>
<tr>
<td>HNBT – Hungary</td>
<td>Hungary</td>
<td>Országos Vérellátó Szolgálat (Hungarian National Blood Transfusion Service)</td>
</tr>
<tr>
<td>IBT – Malta</td>
<td>Malta</td>
<td>Centru Nazzjonali ta't-Trafuzjoni tad-Demm (National Blood Transfusion Service)</td>
</tr>
<tr>
<td>IBTS – Ireland</td>
<td>Ireland</td>
<td>Irish Blood Transfusion Service</td>
</tr>
<tr>
<td>IHT – Poland</td>
<td>Poland</td>
<td>Instytut Hematologii I Transfuzjologii (Institute of Haematology and Blood Transfusion)</td>
</tr>
<tr>
<td>IMB – Ireland</td>
<td>Ireland</td>
<td>Irish Medicines Board - Blood &amp; Tissue Section</td>
</tr>
<tr>
<td>JAZM – Slovenia</td>
<td>Slovenia</td>
<td>Javna agencija RS za zdravila in medicinske pripomočke (Agency for medicinal products and medical devices)</td>
</tr>
<tr>
<td>Acronym</td>
<td>Country</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>MSC</td>
<td>Spain</td>
<td>DG Salud Pública. Ministerio de Sanidad y Consumo (Madrid) represented by Centro Vasco de Transfusion (San Sebastian)</td>
</tr>
<tr>
<td>MSP</td>
<td>Romania</td>
<td>Ministerul Sanatatii Publice (Ministry of Public Health)</td>
</tr>
<tr>
<td>MOH</td>
<td>Cyprus</td>
<td>Υπουργείο Υγείας της Κυπριακής Δημοκρατίας - Ιατρικές Υπηρεσίες και Υπηρεσίες Δημόσιας Υγείας (Ministry of Health of the Republic of Cyprus - Medical and Public Health Services)</td>
</tr>
<tr>
<td>NHS-BT</td>
<td>United Kingdom</td>
<td>National Blood Authority, National Health Service Blood and Transplant (England and North Wales)</td>
</tr>
<tr>
<td>NBT</td>
<td>Bulgaria</td>
<td>НАЦИОНАЛЕН ЦЕНТЪР ПО ХЕМАТОЛОГИЯ И ТРАНСФУЗИОЛОГИЯ (National Centre of Hematology and Transfusiology)</td>
</tr>
<tr>
<td>PEI</td>
<td>Germany</td>
<td>Paul-Ehrlich-Institut (Federal Government Institution)</td>
</tr>
<tr>
<td>RPDA</td>
<td>Germany</td>
<td>Regierungspräsidium Darmstadt (State Governmental Institution)</td>
</tr>
<tr>
<td>SAM</td>
<td>Estonia</td>
<td>State Agency of Medicines, Department of Biologicals</td>
</tr>
<tr>
<td>Sanquin</td>
<td>The Netherlands</td>
<td>Stiching Sanquin Bloedvoorziening (Sanquin Blood Supply Foundation)</td>
</tr>
<tr>
<td>SUKL</td>
<td>Czech Republic</td>
<td>Vedoucí oddělení klinických praxí a dohledu nad zpracováním biologických materiálů. Státní ústav pro kontrolu léčiv (State Institute for Drug Control)</td>
</tr>
<tr>
<td>TILAK</td>
<td>Austria</td>
<td>Zentralinstitut für Bluttransfusion und Immunologische Abteilung, Universitätsklinikum</td>
</tr>
</tbody>
</table>

Supported by the European Blood Alliance (EBA)

Copyright ©
## COOPERATIVE WORKING PARTNERSHIPS

<table>
<thead>
<tr>
<th>CoE – EDQM</th>
<th>Council of Europe - Blood Transfusion &amp; Organ Transplantation activities. European Directorate for the Quality of Medicines and Health Care (EDQM – CD-P-TS), Strasbourg, France</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBA</td>
<td>European Blood Alliance (Executive office in Amsterdam), The Netherlands</td>
</tr>
<tr>
<td>JACIE</td>
<td>JACIE Accreditation Office - EBMT Secretariat, Spain</td>
</tr>
<tr>
<td>KMF</td>
<td>Koch-Metschnikow Forum (KMF), МЕЧНИКОВ-КОХ-ФОРУМ (МКФ). an initiative of the Petersburg Dialogue. (Germany and Russia)</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation (WHO) Regional Office for Europe (Copenhagen), Denmark</td>
</tr>
<tr>
<td>DOMAINE Project</td>
<td>DOMAINE Project, Nijmegen and Amsterdam, The Netherlands</td>
</tr>
<tr>
<td>EUSTITE Project</td>
<td>EUSTITE – Project, Italy</td>
</tr>
<tr>
<td>Optimal Blood Use Project</td>
<td>EU Optimal Use of Blood Project, United Kingdom</td>
</tr>
</tbody>
</table>
AFFILIATED PARTNERS FOR THE INSPECTION SURVEY

AFSSAPS - France  Agence française de sécurité sanitaire des produits de santé (France)
FAGG - Belgium  Federal Agentschap voor Geneesmiddelen en Gezondheidsproducten (Belgium)
ASST - Portugal  Autoridade para os Serviços de Sangue e da Transplantação, (Portugal)
BDA - Bulgaria  Bulgarian Drug Agency (Bulgaria)
DMA - Denmark  Danish Medicines Agency (Denmark)
ITM – Rep. Macedonia  Institute of Transfusion Medicine (Republic of Macedonia)
MoH - Latvia  Ministry of Health, Health Statistics and Medical Technologies State Agency (Latvia)
MoH - Liechtenstein  Amt für Gesundheit (Health Ministry) (Liechtenstein)
SIDC - Slovakia  State Institute for Drug Control (SIDC), Bratislava (Slovakia)
Socialstyrelsen - Sweden  The National Board of Health and Welfare, Socialstyrelsen (Sweden)
Swissmedic - Switzerland  Swiss Agency for Therapeutic Products (Swissmedic), Bern (Switzerland)
Uni-Graz - Austria  Universitätsklinik für Blutgruppenserologie und Transfusionsmedizin (Austria)
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE</td>
<td>Blood Establishment</td>
</tr>
<tr>
<td>CA</td>
<td>Competent Authority</td>
</tr>
<tr>
<td>CAPA</td>
<td>Corrective and preventive actions</td>
</tr>
<tr>
<td>CoE</td>
<td>Council of Europe</td>
</tr>
<tr>
<td>EDQM</td>
<td>European Directorate for the Quality of Medicines and Health Care of the Council of Europe</td>
</tr>
<tr>
<td>EMEA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>EQSTB</td>
<td>European Quality System for Tissue Banking</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
</tr>
<tr>
<td>ICH</td>
<td>International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use</td>
</tr>
<tr>
<td>ISO</td>
<td>International Standards Organisation</td>
</tr>
<tr>
<td>MS</td>
<td>European Union Member State</td>
</tr>
<tr>
<td>PIC/S</td>
<td>Pharmaceutical Inspection Convention / Pharmaceutical Inspection Co-operation Scheme</td>
</tr>
<tr>
<td>QA</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>RP</td>
<td>Responsible Person</td>
</tr>
<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
</tr>
<tr>
<td>SAR</td>
<td>Serious Adverse Reaction</td>
</tr>
<tr>
<td>SMF</td>
<td>Site Master File</td>
</tr>
<tr>
<td>SOP</td>
<td>Standard Operating Procedure</td>
</tr>
</tbody>
</table>
Preface

Ensuring that ‘patients who receive blood transfusion in the European Union are given safe blood’ is a major objective within the framework of public health on the national and European level.

The objective of EuBIS is to set out a methodology for inspecting blood establishments based on the European Commission’s directive requirements related to ensuring the quality and safety of blood.

It is the result of a collaborative effort of representatives from 27 governmental institutions, blood establishments and competent authorities participating in the EuBIS project co-funded by the European Commission.1

In this context, the EuBIS project is the first project that has brought together regulators and manufacturers to jointly develop criteria and standards.

Initiated and coordinated by the Red Cross Blood Donor Service Baden-Württemberg – Hessen in Frankfurt am Main, Germany, this project aimed to develop a manual to assist

• blood establishments in need to optimise their quality system and self-inspection process related to the EU blood directive.

• blood establishments to prepare for regulatory inspections by competent authorities, and

• competent authorities, which wish to use the manual and training guide as a reference for the implementation process of the European blood legislation related to regulatory inspections.

The manual is accompanied by an audit / inspection training guide to assist the inspection process. It also contains master templates of key documents used during the inspection. These documents give examples for the implementation of good practice (GP) as defined by the EU blood directives.

Using commonalities between Member States and the requirements and definitions given by the EU blood legislation, the manual summarises good practice standards. The implementation of these standards will improve the safety of blood. This will reduce the incidence of harm to patients that

---

1 Grant Agreement N°2006202) within the framework of its Public Health Programme (Decision N°1786/2002/EC)
would otherwise arise from citizens travelling around the enlarged EU; and from the movement of blood components within the EU, either through the open-border policy or through crisis-management measures.

The project coordinators herewith express their sincere appreciation to the participating institutions and their representatives, as well as to the team of advisors, in particular to Dr. Jeroen de Wit, Ms. Frances Delaney, Dr. Margarethe Heiden, Dr. Helga Marie Huber, Mrs. Wiebke Siegel and Mr. Angus Macmillan Douglas (OBE) for their continued cooperation, collaboration and support throughout the life of this undertaking. The project coordinators also acknowledge the effort and spirit of Dr. Fewzi Teskrat, Mr. Boudewijn Hinloopen, Dr. Jan Peter Jansen van Galen, Mr. Jan Ceulemans, Dr. Alex Aquilina and Mr. Mark Nightingale in developing educational material for training purposes. Their willingness to share their expertise and experience at the national level on the use of the manual is gratefully appreciated.

The project participants also express their gratitude for the constructive cooperation with the representatives of the European Commission – Mr. Tapani Piha, Mrs. Patricia Brunko and Mr. Thomas Bregeon. Finally, the project participants acknowledge the support given by the European Blood Alliance at present and in sustaining the future dissemination of the Project’s deliverables and the continual development of its ideas.

This 1st Edition of the manual is presented on behalf of the project participants and collaborating partners. An electronic form can be ordered via the Project Website (www.eubis-europe.eu).

Prof. Dr. med. Erhard Seifried
Prof. Dr. med. Christian Seidl

On behalf of the Project Participants
# TABLE OF CONTENTS

COOPERATIVE WORKING PARTNERSHIPS ................................................................. IV  
AFFILIATED PARTNERS FOR THE INSPECTION SURVEY........................................ V  
ABBREVIATIONS.................................................................................................. VII  
PREFACE ........................................................................................................ IX  

1 INTRODUCTION .............................................................................................. 1  
1.1 THE EUBIS PROJECT ................................................................................... 1  
    1.1.1 BACKGROUND .................................................................................... 1  
    1.1.2 OBJECTIVES ...................................................................................... 2  
    1.1.3 METHODOLOGY .................................................................................. 3  
    1.1.4 BACKGROUND SUMMARY .................................................................. 4  

2 AIM AND SCOPE OF THE MANUAL .............................................................. 5  

3 EU LEGISLATIVE REQUIREMENTS FOR QUALITY SYSTEMS OF BLOOD ESTABLISHMENTS .................................................................................. 8  
    3.1 DIRECTIVE 2005/62/EC ..................................................................... 8  
    3.2 RELATED BLOOD LEGISLATION .......................................................... 9  

4 COMMON STANDARDS AND CRITERIA FOR THE INSPECTION OF BLOOD ESTABLISHMENTS ..................................................................... 10  
    4.1 INTRODUCTION ...................................................................................... 10  
    4.2 ACTIVITY PROFILES OF BLOOD ESTABLISHMENTS ......................... 11  
    4.3 COUNCIL OF EUROPE (CD-P-TS) ....................................................... 14  
    4.4 PIC/S .................................................................................................... 16  
    4.5 EU-GMP (EUDRALEX) ....................................................................... 17  
    4.6 ISO STANDARDS .................................................................................. 18  
    4.7 INSPECTION GUIDE AND CROSS REFERENCES ................................. 19  

5 SELF-INSPECTIONS OF BLOOD ESTABLISHMENTS ............................... 23  
    5.1 GENERAL REQUIREMENTS FOR SELF-INSPECTIONS ....................... 23  
    5.2 REQUIREMENTS FOR INTEGRATED SELF-INSPECTIONS ................. 25  
    5.2.1 Responsibilities .................................................................................. 26  
    5.2.2 Education and training of inspectors ............................................... 28  
    5.2.3 Evaluation criteria for deviations and corrective action .................. 29  
    5.2.4 Associated documents ...................................................................... 29
5.3 THE INTEGRATION OF QUALITY RISK MANAGEMENT INTO SELF-INSPECTION .................................................. 33

5.4 THE SELF-INSPECTION PROCESS .......................................................... 35
  5.4.1 Prepare inspection plan and assign inspection team .................. 38
  5.4.2 Agree inspection date and verify inspection details .................. 39
  5.4.3 Perform the inspection and prepare draft report ................. 41
  5.4.4 Prepare final inspection report and agree on corrective action plan ................................................. 43
  5.4.5 Monitor progress against corrective action plan ................ 45
  5.4.6 Close inspection .......................................................................... 46

6 INSPECTIONS BY COMPETENT AUTHORITIES ........................................ 49
  6.1 QUALIFICATION OF INSPECTORS .................................................... 50
    6.1.1 Education .............................................................................. 50
    6.1.2 Experience ......................................................................... 50
    6.1.3 Training .............................................................................. 51
    6.1.4 Responsibilities ................................................................... 53
    6.1.5 Confidential information ..................................................... 54
  6.2 INSPECTION PLANNING AND CAPACITY ASSESSMENT .................. 55
  6.3 CLASSIFICATION OF INSPECTIONS ................................................... 56
    6.3.1 Authorisation inspection ......................................................... 56
    6.3.2 Routine inspection .................................................................. 57
    6.3.3 Product / process related inspection
        (Change control of authorisation) .............................................. 57
    6.3.4 Event-related inspection ......................................................... 58
    6.3.5 Non-routine / unannounced inspections .............................. 58
    6.3.6 Frequency of inspections ....................................................... 58
  6.4 PLANNING FOR AND ASSESSMENT OF AN INSPECTION ............ 59
  6.5 COMPLIANCE VERIFICATION PENDING (OR IN ABSENCE OF) A SITE VISIT ............................................. 59
  6.6 COMPOSITION OF THE INSPECTION TEAM .................................. 60
  6.7 TYPE OF INSPECTION ..................................................................... 61
  6.8 INSPECTION SCHEDULE ..................................................................... 63

7 CONDUCT OF INSPECTION ................................................................. 64
  7.1 INSPECTION PROCEDURES – BEFORE THE INSPECTION ............ 64
    7.1.1 Information provided by blood establishment
        (Site Master File modified for Blood Establishment - SMF-BE) .......... 64
  7.2 INSPECTION PROCEDURES – DURING INSPECTION .................. 65
    7.2.1 Opening meeting ................................................................. 65
    7.2.2 Key elements of the inspection .............................................. 66
    7.2.3 Practical implementation ....................................................... 67
    7.2.4 Donor selection and blood collection .................................... 70
EuBIS Inspection Standards and Criteria, Edition 1.0

7.2.4.1 Donor selection requirements ..............................................70
7.2.5 Inspection of premises and equipment .....................................72
7.2.6 Laboratory Testing .................................................................73
7.2.7 Processing and storage.............................................................74
7.2.8 Transport and distribution ......................................................76
7.2.9 Inspection completion .............................................................76

8 Inspection Procedure – After the Inspection ..........................77
8.1 Official Written Inspection Report ..............................................77
8.2 Conformity Statement .................................................................78
8.3 Blood Establishment’s Response to Inspection Report (CA) .........78
8.4 Scheduling Re-inspection ...........................................................79

9 Evaluation of the Inspection System ........................................79

Annexes

Annex I Site Master File Modified for Blood Establishments (SMF-BE) ........................................................................80
Annex II EuBIS Inspection Report by Competent Authority ..........88
Annex III Documents Consulted in Manual’s Development ..........95
Annex IV Additional References and Project Publications ..........99
Annex V Terminology (Glossary) ......................................................101
Annex VI Participating and Collaborating Institutions and Individuals .................................................................111
Annex VII Associated or Observing Institutions and Participants . 120
1 Introduction

1.1 The EuBIS project

EuBIS, the European Blood Inspection System, is a project funded by the European Commission under its 2006 Call for Proposals and within the framework of its Public Health Programme (2003-2008) addressing the quality and safety of blood. The Project aims to develop pan-European standards and criteria for the inspection of blood establishments. These requirements are intended for use not only by those responsible for the operation of blood establishments but by those in charge of inspecting them, in compliance with relevant European Union (EU) legislation. (www.eubis-europe.eu).

EuBIS is coordinated by the German Red Cross Blood Donation Service with the participation of 27 collaborating partners from 20 Member States, cooperative working partnerships with five organisations and three projects, affiliations with twelve partners involved in conducting its inspection survey, and is supported by the European Blood Alliance. Launched in August 2007, the project has a three-year duration.

1.1.1 Background

The entry into force of European Union legislation on blood, based on Directive 2002/98/EC\(^2\) and its technical requirements, has been accompanied by noteworthy progress towards ensuring the provision of consistently safe blood and blood components across Europe. The significant expansion of the European Union, however, focused attention on the need to have common pan-European standards and criteria for the inspection of blood.

establishments - a key element in the implementation of good practice\(^3\).

Currently such inspections are conducted according to national criteria and standards which differ between Member States. A 1994 report by the European Commission noted that ‘divergent national regulations concerning collection and treatment of blood has contributed to reluctance, if not a refusal, to accept blood and plasma coming from different Member States and even different centres\(^4\). This can lead to risks with respect to consistently safe blood across Europe which, by itself, the Directive cannot help to guarantee.

The 2006 Work Plan of the Public Health Programme (Area 2.2.4) gave impetus to the need for equivalent recognition of inspections of blood establishments among Member States through the development and implementation of commonly accepted criteria and standards. Without them, the levels of risk from having a blood transfusion in the Member States could continue to differ.

### 1.1.2 Project Objectives

The overall objective of the Project is to develop and implement commonly accepted criteria and standards to ensure equivalent recognition of inspection of blood establishments among Member States.

It aims to do this through the development of a manual that will set out:

- common criteria and standards for the inspection of blood establishments
- requirements for the implementation or expansion of quality management systems to be inspected

---


• inspection checklists which closely follow Directive 2002/98/EC and its technical requirements, and
• evaluation criteria for inspections and a benchmark system for deviations and improvements.

It will also serve as the basis of a training programme for inspectors of blood establishments. This will help to ensure common acceptance of the standards and criteria.

1.1.3 Methodology

EuBIS activities got underway in September 2007 with the establishment of an internet platform for communication with the project’s participants. This was followed in October with the development and distribution of a questionnaire to the project’s participants to collect information on current practices related to the inspection of blood establishments in the European Union. It was divided into six sections - the first five were specifically related to blood establishments and addressed: processes covered; Member State establishments; quality systems; inspections and audits; and the inspection process. The sixth section summarised the objectives and deliverables of the EuBIS project itself. The responses were compiled and an EU Inspection survey report prepared.

The first meeting of the Project’s participants was convened in November at which time the results of a comparative analysis of the survey were presented. These results, in combination with Directive 2002/98/EC and its technical requirements, were used to establish the basic structure for the quality systems and pan-European blood inspection standards.

In order to develop the basic structure, the project’s participants were divided into four working groups each with responsibility for a specific subject area. These were: quality management system evaluation; donor recruitment and blood collection; processing and testing; and blood component issuing, storage and logistics. In
continuous work and in individual working group meetings, draft inspection checklists and criteria for the evaluation of inspection results (acceptance or rejection) in the assigned areas were developed.

Recognising that several inspection criteria and programmes in the health care area had already been established, the EuBIS project from the outset consulted these sources and conferred with the responsible authors. These included:

- the Joint Accreditation Committee of the International Society of Cellular Therapy (ISCT) and the European Group for Blood and Marrow Transplantation (EBMT) (jointly referred to as JACIE)
- the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation scheme (jointly referred to as PIC/S)
- the European Medicines Agency (EMA)

Moreover, EuBIS has collaborated and exchanged ideas with the EUSTITE (European Union Standards and Training for the Inspection of Tissues Establishments) project, co-financed under the 2005 Work Plan of the EU’s Public Health Programme. EuBIS has drawn extensively from EUSTITE’s ‘Guidelines for the Inspection of Tissue and Cell Procurement and Tissue Establishments’ and this manual is complementary to it. It has also been in contact with the national competent authorities in the Member States and the International Plasma Fractionation Association (IPFA).

1.1.4 Background Summary

A major aim of the European Commission is to give practical assistance to competent authorities (CA) and blood establishments (BE) in implementing the Directives’ requirements.

---

5 [www.eustite.org](http://www.eustite.org)
However, in a recent Commission survey\(^6\) it was noted that at least five Member States that have transposed the Directive into National law do not perform inspections of BEs. It is hoped that the EuBIS manual will assist them in carrying out this responsibility.

### 2 Aim and Scope of the Manual

The EuBIS manual aims to provide assistance to EU Member States in their implementation of regulatory requirements set out in Directives 2002/98/EC, 2004/33/EC\(^7\), 2005/61/EC\(^8\) and 2005/62/EC\(^9\). These include *inter alia*:

- designation, authorisation, accreditation or licensing of blood establishments (BEs)
- authorisation of the activities which can be undertaken and the applicable conditions for blood collection
- provisions for ensuring the quality and safety of blood and blood components, and
- requirements for imported blood and blood components.

The developed inspection standards and criteria will assist in the independent assessment of quality system structures established

---


by individual blood establishments in compliance with the EU’s legislation.

The manual will assist blood establishments in preparing for inspections. The standards and checklists used for external inspections could be used for internal audits by blood establishments. With respect to the different standards and guidelines that are currently in place, the inspection guide summarizes the most critical aspects to be addressed in order to achieve good practice. For each of these critical points, the Guide provides references to commonly used standards for the inspection of BEs. Common criteria and standards for external inspection of BEs following Article 8 of Directive 2002/98/EC are summarized in the ‘Aide Memoire’ for competent authorities. The ‘Aide Memoire’ gives practical guidance for those, who are less experienced or new in the area of blood and blood components.

Defined principles for the structure of quality systems will assist in implementing or expanding the currently used quality management systems in blood establishments. Moreover, the manual will help to ensure the incorporation of standard operating procedures (SOPs) in a site master file or a quality management handbook reflecting GMP standards.

The manual’s scope reflects that set out in Directive 2002/98/EC, i.e. ‘the collection and testing of human blood and blood components, whatever their intended purpose, and to their processing, storage and distribution when intended for transfusion’.

The work plan of the EuBIS project includes the preparation of a draft of the manual and subsequently a final edition. The draft text, after being circulated to the project participants for their initial comments and contributions, will be discussed at meetings of each of the working groups. Taking into account all relevant

---

10 Directive 2002/98/EC. Article 2.1
remarks and observations, the draft will be revised and a validation process undertaken. The draft will be given to competent authorities or blood establishments that are planning to modify or to set up their inspection system. Potential Member State candidates for the evaluation are Malta, Romania and Slovenia (Malta and Romania would need a start-up, while Slovenia would need to modify their system). Evaluation of the draft manual in a blood establishment could also be undertaken in Romania where their facilities need to introduce quality systems. The draft will be provided to all evaluators in electronic form. It may also be printed for each of the participants and/or collaborating partners depending on financial considerations.

Upon receipt of the evaluations and incorporation of amendments, a final edition of the EuBIS manual will be prepared.

In drafting the manual, EuBIS drew upon the procedures and recommendations that had already been issued in existing documents and guidelines related to inspections. It made a concerted effort to harmonise its guidance and procedures with those of the EUSTITE project as inspectors of the competent authorities frequently have responsibility for inspection of both blood establishments and tissues and cell facilities. The documents consulted are included in Annex III.

The project participants are aware that national legal requirements as indicated by Article 152, Paragraph 4, of the Treaty of Amsterdam will require the use of established standards, i.e. GMP-Eudralex or the ISO-series.

Comments or suggestions from individuals responsible for blood establishments or the Member State competent authorities on the use of the draft manual are welcome. They will be taken into account in the finalisation of the Manual. Comments and suggestions should be sent to: eubis@blutspende.de.
3 EU legislative requirements for quality systems of blood establishments

3.1 Directive 2005/62/EC

Commission Directive 2005/62/EC sets out the technical requirements for blood establishments related to the implementation and maintenance of standards and specifications relating to a quality system. It covers general principles, personnel and organisation, premises, equipment and materials, documentation, blood collection, testing and processing, storage and distribution, contract management, non-compliance and self-inspection, audits and improvements.

As per the EU blood legislation, ‘quality shall be recognised as being the responsibility of all persons involved in the processes of the blood establishment with management ensuring a systematic approach towards quality and the implementation and maintenance of a quality system. The quality system encompasses quality management, quality assurance, continuous quality improvement, personnel, premises and equipment, documentation, collection, testing and processing, storage, distribution, quality control, blood component recall, and external and internal auditing, contract management, non-compliance and self-inspection. The quality system shall ensure that all critical processes are specified in appropriate instructions and are carried out in accordance with the standards and specifications set out in this Annex. Management shall review the system at regular intervals to verify its effectiveness and introduce corrective measures if deemed necessary.

---

All blood establishments and hospital blood banks shall be supported by a quality assurance function, whether internal or related, in fulfilling quality assurance. That function shall be involved in all quality-related matters and review and approve all appropriate quality related documents. All procedures, premises, and equipment that have an influence on the quality and safety of blood and blood components shall be validated prior to introduction and be re-validated at regular intervals determined as a result of these activities.’

3.2 Related blood legislation

The primary piece of EU legislation related to blood is Directive 2002/98/EC. It lays down the general framework for ensuring quality and safety for the collection, testing, processing storage and distribution of blood and blood components. Complementary to it are three European Commission Directives which set out the technical requirements. In addition to Directive 2005/62/EC, Commission Directive 2004/33/EC specifies certain technical requirements for blood and blood components including definitions, information to be provided to and obtained from potential donors, donor eligibility criteria, including temporary and permanent deferral, quality and safety requirements and storage, transport and distribution conditions for blood and blood components. Commission Directive 2005/61/EC deals with requirements for the traceability of blood and blood components and the notification of serious adverse reactions and events. Although adopted prior to Directive 2002/98/EC, elements of the Council’s Recommendation\(^{13}\) of 29 June 1998 on the suitability of blood and plasma donors and the screening of donated blood in the European Union are still applicable unless superseded by the

Directives. Directive 2001/83/EC\textsuperscript{14} on the Community code relating to medicinal products for human use sets out *inter alia* requirements for blood and plasma used for this purpose. However, Commission Directive 2003/63/EC\textsuperscript{15} amends its Article 109 so that determination of the suitability of human blood donors and the testing of donations of starting materials for plasma-derived medicinal products must comply with the requirements of Directive 2002/98/EC.

### 4 Common standards and criteria for the inspection of blood establishments

#### 4.1 Introduction

The ‘vein’ to ‘vein’ activities linked to blood transfusion involve a large variety of processes carried out by blood establishments including the collection, preparation, distribution and issuance of blood and blood components. Regulatory requirements at the European Union level are given by Directives, which differentiate between requirements for plasma-derived medicinal products and blood and blood components. Directive 2001/83/EC applies to all medicinal products, defined as ‘any substance or combination of substances presented for treating or preventing disease in human beings’. By contrast, Directive 2002/98/EC and its current technical annexes - Directive 2004/33/EC, 2005/61/EC and 2005/62/EC - set the legal framework for blood and blood components. For those Member States that classify blood as a medicinal product as defined by the pharmaceutical legislation, requirements related to collection and testing of blood and plasma


still apply\textsuperscript{16}. Similar quality and safety requirements have been introduced for tissues and cells\textsuperscript{17,18,19}.

4.2 Activity profiles of blood establishments

In order to assess the currently used standards and criteria for quality management systems in Europe, an extended survey among the participants of the EU co-funded EUBIS Project was performed (Survey report available on http://www.eubis-europe.eu). Processes were subdivided in section 1 of the survey as follows:

- Blood collection
- Blood component preparation
- Apheresis component preparation
- Related preparations
- Source plasma for fractionation
- Cryoprecipitate
- Autologous blood components
- Blood component testing
- Blood component storage and distribution

\textsuperscript{16} ‘This Directive shall apply to the collection and testing of human blood and blood components, whatever their intended purpose, and to their processing, storage, and distribution when intended for transfusion’. Article 2, Para 1, Directive 2002/98/E


The activity profile obtained from this survey demonstrated that, besides standard blood component preparation, the majority of participating blood establishments are involved in manufacturing processes covered by pharmaceutical regulations; 60% perform the preparation of cryoprecipitate while 80% are involved in the collection of source plasma for fractionation. Autologous blood components are prepared by 88% of blood establishments. In addition, the activities of several blood establishments cover the area of tissues and cells. More than half the participating blood establishments are involved in the preparation of blood component related preparations, such as cord blood, granulocytes and lymphocytes for therapeutic use.

Table 1: EU Directives and activity profile of blood establishments

<table>
<thead>
<tr>
<th>Area and activity</th>
<th>percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood and blood component Directives</strong></td>
<td></td>
</tr>
<tr>
<td>Whole blood preparation</td>
<td></td>
</tr>
<tr>
<td>Cellular (erythrocyte or platelet concentrates)</td>
<td>100</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>94</td>
</tr>
<tr>
<td>Apheresis</td>
<td></td>
</tr>
<tr>
<td>Cellular (erythrocyte or platelet concentrates)</td>
<td>100</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>75</td>
</tr>
<tr>
<td>Autologous blood components</td>
<td>88</td>
</tr>
<tr>
<td><strong>Tissue and cells Directives</strong></td>
<td></td>
</tr>
<tr>
<td>Stem cells</td>
<td>75</td>
</tr>
<tr>
<td>Cord blood</td>
<td>31</td>
</tr>
<tr>
<td>Granulocytes</td>
<td>69</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>50</td>
</tr>
<tr>
<td><strong>Pharmaceutical Directive related preparations</strong></td>
<td></td>
</tr>
<tr>
<td>Source plasma for fractionation</td>
<td>75</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>56</td>
</tr>
</tbody>
</table>
The results of the survey revealed that several standards and guidelines are commonly used by:

- blood establishments for their quality management systems including internal inspections, and
- competent authorities performing external inspections of those blood establishments in European Member States (Table 2). These are the European Good Manufacturing Practice (GMP) standard, the European Good Laboratory Practice (GLP) standard, the technical report series developed by the World Health Organisation (WHO), the Council of Europe (CoE) ‘Guide to the preparation, use and quality assurance of blood components’ and also the International Standard Organisation (ISO) 9000 series of standards and norms.

With respect to the commonly used European or international standards, the EU GMP and CoE standards are the most commonly implemented for routine processes. EU GMP is very often used in combination with EU GLP (Good Laboratory Practice) by blood establishments performing blood component related processes that fall under pharmaceutical legislation. The survey also revealed that the ISO 9000 series standards are widely recognised by blood establishments. One third of blood establishments have already implemented these standards in their quality management systems, being ISO certified and/or accredited. One tenth are in the process of preparing for ISO certification.
Table 2: Commonly used standards and guidelines in Europe

<table>
<thead>
<tr>
<th>Standard/guideline</th>
<th>percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Manufacturing Practice (GMP)</td>
<td>88</td>
</tr>
<tr>
<td>Good Laboratory Practice (GLP)</td>
<td>35</td>
</tr>
<tr>
<td>International Standard Organisation (ISO)</td>
<td>47 *2</td>
</tr>
<tr>
<td>Council of Europe (CD-P-TS)</td>
<td>82</td>
</tr>
<tr>
<td>World Health Organisation (WHO)</td>
<td>12</td>
</tr>
<tr>
<td>National (based on individual Member State)</td>
<td>29</td>
</tr>
<tr>
<td>Good Manufacturing Practice (Eudralex, EU-GMP)</td>
<td>50</td>
</tr>
<tr>
<td>PIC/S guide for blood establishments</td>
<td>50</td>
</tr>
<tr>
<td>WHO GMP standards</td>
<td>25</td>
</tr>
<tr>
<td>International Standard Organisation (ISO)</td>
<td>10</td>
</tr>
<tr>
<td>CoE (EDQM)</td>
<td>65</td>
</tr>
<tr>
<td>National guidelines and standards</td>
<td>40</td>
</tr>
</tbody>
</table>

*1 based on the EuBIS survey including blood establishments and competent authorities from 20 EU Member States
*2 including 12% of blood establishments with ISO accreditation in progress

4.3 Council of Europe (CD-P-TS)

The Council of Europe, which has been involved in issues related to blood transfusion since the early 1950s, has long advocated the principle of voluntary non-remunerated blood donation and promoted mutual assistance, optimal use, and protection of the donor and recipient. Complementary to the GMP guidelines, the
Council of Europe has developed a ‘Guide to the preparation, use and quality assurance of blood components’ [Recommendation No. R (95) 15]. The CoE Guide is commonly used among blood establishments throughout the EU Member States. Only in some Member States, e.g. United Kingdom or Germany, do national recommendations surpass the CoE guide in its application for routine work.

The consultancy process on Recommendation No. (95) 15 started in 1986 leading in 1995 to the adoption of this document as a technical annex by the Committee of Ministers. Recommendation No. R (95) 15 is updated annually by the members of the Committee of Experts on quality assurance in blood transfusion services keeping it in line with scientific progress and EU legislation. The CoE Guide is divided into two Parts: Part A – Principles and Part B – Standards. Principles are regarded as essential requirements that ‘must’ be complied with, while standards are requirements that ‘should be’ considered.

Similar to GMP or ISO standards (see below), the CoE Recommendation explains the contents and background of quality systems for blood establishments, including the activities to be included in these systems and the subjects to be addressed. The proposed quality system of the CoE guide is based on the principles of good practice and quality management, as described in the EU GMP guidelines and the ISO 9000-series standards. Its 2009 version contains recommendations on blood collection, blood components, technical procedures, transfusion practices and quality systems for blood establishments. As of 2009, this appendix – ‘Guide to the preparation, use and quality assurance of blood components’ - is in its 15th edition.

---

20 Guide to the preparation, use and quality assurance of blood components. Council of Europe. Strasbourg
4.4 PIC/S

PIC/S is the acronym for the Pharmaceutical Inspection Convention / Pharmaceutical Inspection Co-operation Scheme. These are ‘instruments’ between countries and pharmaceutical inspection authorities, which together provide active and constructive co-operation in the field of Good Manufacturing Practice (GMP). PIC/S has as its mission ‘to lead the international development, implementation and maintenance of harmonised (GMP) standards and quality systems of inspectorates in the field of medicinal products.’ It aims to do this ‘by developing and promoting harmonised GMP standards and guidance documents; training competent authorities, in particular inspectors; assessing (and reassessing) inspectorates; and facilitating the co-operation and networking for competent authorities and international organisations.’ There are currently 31 participating authorities from around the world in PIC/S. Its expert circle on blood and tissue was founded by the Paul-Ehrlich-Institute (PEI) in 1994 recognizing the need for specialized knowledge on these special issues related to blood and transmissible diseases.

In response to the need for a modification of EU-GMP standards, the expert circle on blood and tissues developed a GMP ‘Guide for blood establishments’. This PIC/S GMP Guide intends to facilitate the introduction of GMP standards for blood and apheresis establishments and is used by PIC/S inspectors in assessing the quality management systems of those establishments. Although the Guide follows the structure of the EU GMP standard, it addresses specific processes to be covered in the collection, preparation and distribution of blood and apheresis components, such as blood donor areas, mobile donor sessions, irradiation of blood components or whole blood collection and component preparation. The PIC/S expert circle on blood and tissues has also developed an ‘aide memoire’ for the inspection of blood establishments, a PIC/S guide to the inspection of source plasma establishments and plasma warehouses, site master files for
source plasma establishments and plasma warehouses and training guidelines for the qualification of inspectors.

4.5 EU-GMP (Eudralex)

The EU-GMP standard (Eudralex) gives detailed and very specific standards for the production of pharmaceutical components. In particular blood establishments that perform cryoprecipitation or the collection of source plasma for fractionation have established quality management systems that relate to these standards. In some Member States, e.g. Germany, where pharmaceutical legislation applies for all blood components, the EU-GMP standard is mandatory. Chapters 1 – 9 of the EU-GMP standard give detailed specifications for quality management, personnel, premise and equipment, documentation, production, quality control, contract manufacturers and analysis, complaints and recall and self inspections. In addition, Annex 2 (biological products) and Annex 14 (blood components) of the EU-GMP standard are used as specifications for plasma fractionation. Both EU-GMP annexes contain requirements and specifications that can be adapted to the production of standard blood components and are used inter-alia by blood establishments. In contrast, several standards defined by EU-GMP are derived from specific production, storage and distribution characteristics of pharmaceutical production processes, such as process monitoring of intermediate and bulk products, batch processing records or ongoing stability programme to monitor the product over its shelf life. These EU-GMP standard requirements are more suited to the manufacturing facilities and production processes for medicinal products by the pharmaceutical industry and are difficult to adapt to standard blood component collection, preparation and distribution as covered by Directive 2002/98/EC.
4.6 ISO Standards

In addition to EU-GMP and the Council of Europe (CD-P-TS) guide, the International Standard Organisation (ISO) 9000 standards are commonly accepted by blood establishments. ISO 9001:2000 specifies requirements for a quality management system where an organisation:

- Needs to demonstrate its ability to consistently provide products that meet customer and applicable regulatory requirements, and
- Aims to enhance customer satisfaction through the effective application of the system, including processes for continual improvement of the system and the assurance of conformity to customer and applicable regulatory requirements.

Blood establishments using ISO 9001:2000 are required to address the effectiveness of their quality management system. In the context of ISO 9001, effectiveness means the extent to which planned activities are realized and planned results achieved. Further requirements specify the need for continual improvements to the quality management system and not for sporadic or irregular evaluations or campaigns. Following ISO 9001, the organisation shall continually improve the effectiveness of the quality management system through the use of

- quality policy
- quality objectives
- audit results
- analysis of data
- corrective and preventive actions, and
- management review.

ISO standards require that the suitability and effectiveness of the quality management system shall be determined. The standards given by ISO 9001 specify requirements for quality management systems that can be used for internal application by organisations,
or for certification, or for contractual purposes. In this context, ISO 9001 focuses on the effectiveness of the quality management system in meeting customer requirements.

4.7 Inspection guide and cross references

The increasing diversity of processes covered by blood establishments, from blood components, pharmaceutical products, to tissue and cells, requires that quality systems need to be flexible in order to adapt to national and European quality requirements. Harmonisation of standards, therefore, would be useful. However, this has to take into account the different legal requirements of the European Union for pharmaceutical products, blood components and tissues and cells. In addition, despite transposition of EU Directives to the Member State level, national laws may require additional modifications for quality management systems. The EuBIS expert group has discussed the importance of those European and national standards in place and has developed a cross-reference guideline for quality management systems of blood establishments based on Directive 2005/62/EC. This cross-reference guideline includes the EU-GMP standards, the PIC/S GMP for blood establishments, the CoE Guide and the ISO 9000 series. By cross-referencing the relevant quality requirements to Directive 2005/62/EC, commonalities between these standards can be identified.
Cross reference guidance to ‘good practice’ following the EU Directives

**Figure 1:** The EuBIS Project expert circle developing a manual for common European standards and criteria for the inspection of blood establishments for good practice (GP) following the EC blood legislation. The manual is supplemented by an audit / inspection – training guide on the relevant aspects to be addressed during the inspection process including cross-references for common European standards and criteria for quality management systems of blood establishments.
The inspection guide is a manual comprising common European standards and criteria used for the process of inspection and self-inspection of blood establishments. There are separate sections on these topics (Chapter 5 ‘Self-inspection’ and Chapter 6 ‘Inspection by competent authority’) including chapters on the conduct of an inspection (Chapter 7), the inspection procedures after the inspection (Chapter 8) and the evaluation of the inspection system (Chapter 9).

The guide is complemented by documents (Annex I and Annex II) that are commonly used during inspections [e.g. modified site-master-file for blood establishments (SMF-BE), inspection summary report]. These documents facilitate the harmonisation of inspection processes and should assist in the documentation of observed deviations. Complementary to this guide, inspection criteria that cover the regulatory standards that apply within the EU based on the EU blood directives have been developed. These include cross-references to commonly used standards. It is anticipated that these criteria will prove useful for trainees involved in regulatory and self-inspections. The criteria, however, are not exhaustive and authorities and blood establishments may wish to supplement this material with additional requirements.

Each section of the guide contains a description of the inspection criterion and example evidence that should be obtained during the inspection to demonstrate compliance. Each criterion is identified by an individual number (criterion no.), a reference to the applicable standard(s) and identifies the sub-process or control point.

The criteria listed in the guide can be used to assist the inspector in preparing the inspection record. For the less experienced inspector it may be suitable to transfer these directly to the inspection record (with any additional criteria identified). Depending on experience, others may prefer to record only the clause and a short description of the area inspected. The guide
may be also used as a reference by inspectors of competent authorities who wish to get assistance in the implementation of inspection criteria and standards based on the EU blood legislation.

**Figure 2**: Inspection Cross reference guide for good practice following the EU blood legislation developed by the EuBIS experts. The cross-reference guide will assist blood establishments in implementing quality system requirements based on EU legislation.

<table>
<thead>
<tr>
<th>Criterion No. and Primary Ref. (EU Dir.)</th>
<th>Sub-process/ control point</th>
<th>Cross-Ref. source</th>
<th>Inspection criterion description</th>
<th>Example evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR 001, 2002/98/EC Art. 5 - Licensing and authorisation</td>
<td>Licensing requirements, PIC/S Chap. 2, EDQM (CoE), Chap. 1</td>
<td>GMP Annex 14</td>
<td>The Blood Establishment has submitted the information listed in Annex I (2002/98/EC) to the Competent Authority. The Competent Authority has verified that the blood establishment complies with the requirements of Directive 2002/98/EC and indicated which activities it may undertake and which conditions apply.</td>
<td>• Manufacturers license and wholesale sale distribution license as appropriate to the activity profile assigned by the Competent Authority. • N.B. For those blood establishments that follow the requirements defined by 2001/83/EC, individual product licenses are required.</td>
</tr>
</tbody>
</table>
5 Self-inspections of blood establishments


5.1 General requirements for self-inspections

There are several equivalent definitions for the expression ‘self-inspection’. Although it is very often used interchangeably with the terms ‘audit’ or ‘internal-audit’, for the purpose of this Manual only the term self-inspection is used.

Self-inspections are an essential part of any quality management system. Section 10 of the Annex to Directive 2005/61/EC clearly defines the need to perform regular self-inspections by blood establishments and to use them for improvements.

‘Self-inspection or audit systems shall be in place for all parts of the operations to verify compliance with the standards set out in this Annex. They shall be carried out regularly by trained and competent persons in an independent way according to approved procedures. All results shall be documented and appropriate corrective and preventive actions shall be taken in a timely and effective manner’. (Directive 2005/62/EC, Annex. Section 10, Para 1 and 2).

A self-inspection should be conducted by trained and competent persons managerially independent of the department concerned. Its purpose is primarily to assess, in practice, if regulations, standards and guidelines defined in the overall quality management system are correctly implemented. These inspections will also offer the chance for personnel at all levels to
discuss processes and quality relevant steps. Self-inspections should include data from trend analysis of non-compliance, deviations and errors to focus on processes in need of improvement. If performed properly and effectively, self-inspections are an ideal tool for optimising processes, implementing preventive measurements and thus supporting continuous improvement of blood safety and component quality. Furthermore, self-inspection will prepare the blood establishment for regulatory inspections carried out by the competent authority or accreditation body.

Regulatory inspections, on the other hand, are formal and objective controls according to adopted standards to assess compliance with European and other relevant blood legislation and to identify problems. It has to be noted, however, that regulatory inspectors cannot examine all areas and documentation during an inspection. They are not responsible if, due to limited time, scope or inability to conduct certain processes, they do not observe a particular non-compliance.

In contrast to the national regulatory or competent bodies, the blood establishment is fully responsible for any blood and blood components manufactured and distributed. It is of vital interest, therefore, for blood establishments to establish solid self-inspection procedures.

Depending on the size of the blood establishment, self-inspections may be organised differently. Large blood establishments or services comprising several blood establishments tend to implement a peer-inspection system. This is carried out by inspectors from different facilities within the same blood establishment. Often, the ‘peer’ inspection is based in a blood service which is comprised of different institutions at different locations that provide experts with equivalent skills and knowledge. Alternatively, ‘peer’ inspections can be organised through cooperation between national or regional blood services.
A self-inspection is carried out by a team comprising several individuals. Very often the team consists of only two inspectors. One will inspect the quality system and in the case of peer inspections a technical specialist may also be involved. The lead inspector is responsible for coordinating the activity of the team and presenting its findings and outcomes. In smaller blood establishments, the self-inspections are frequently carried out by one individual.

5.2 Requirements for integrated self-inspections

The following section gives a general description of an integrated self-inspection system. Blood establishments interested in modifying or adapting their self-inspection system are advised to perform a ‘stage’ / rotation in a service with extensive experience in order to assist in the development of their own implementation plan.21

Definitions22

Critical non-compliance: Any non-compliance in a process or a written procedure which directly affects the safety of the donor or patient.

Major non-compliance: A serious non-compliance in a process or a written procedure but does not on its own affect the safety of the donor or patient.

21 Contacts and references of services willing to assist in these ‘stages’ / rotations are available through the EuBIS Office. (www.eubis-europe.eu)
22 There are similar terms in use for describing deficiencies. In this manual deficiencies and / or non-conformances are defined as non-compliances (see also SMF-BE in Annex) II of this manual.
**Other significant non-compliance:** A non-compliance in a system or process or there is insufficient information to classify it as a major or critical.

**Observation** - an inadequacy in a system or process that is not a failure to comply with a standard.

There could be a combination of several ‘other’ significant non-compliances, none of which, on their own, may be major or critical, but may together represent a major or critical non-compliance. These should be clearly explained and reported as such.

**Responsible Person** - person(s) named on the Blood Establishment licence

**Inspection Master Plan** - This defines the self-inspection frequency for each department / institution including the period (dates), the inspection duration (e.g. half-day or two-day inspection), the scope, and identifies the inspector (or lead inspector, when more than one inspector is involved). The inspection master plan should also include the criteria adopted to formulate the plan (e.g. a plan could envisage one comprehensive inspection and two specific inspections in particular sectors of the blood establishment; the criteria for this choice should be clearly expressed).

### 5.2.1 Responsibilities

**Quality assurance**

The quality assurance will be responsible for preparing a draft annual self-inspection calendar, circulating this calendar to the inspected (e.g. department, etc) and publishing the approved self-inspection calendar. Subsequently, the quality assurance department will allocate the lead inspector and organise self-
inspection teams depending on the scope of the inspection to be performed. In a ‘Peer’ inspection system this will also include organising respective technical experts. Approval of the annual self-inspection calendar is given by the self-inspection stakeholders. In general, these are senior staff members responsible for particular areas of the service (e.g. executive management, institutional director, department heads).

Within blood services comprising several blood establishments, quality management (QM) can comprise local QA departments. These will assist in the co-ordination of the corrective action plan by monitoring its progress, and verifying if appropriate actions are completed and implemented. The local quality assurance office notifies the head of QM when all non-compliances are addressed.

Final approval of the corrective action plan is the responsibility of the head of quality assurance. The QA head will also decide about discussing structural deficiencies or non-compliances (e.g. GMP facility renovations) with the management. In addition, regular briefing sessions (e.g. management review) should be organised with management (e.g. Chief Executive Officer (CEO), Director) at least annually, in order to summarise non-compliance, errors, preventive measurements implemented including trend analysis of component quality and tests performance. This QA management meeting would also define potential steps for continual quality improvement in-line with the design planning for management decision taking for the future (e.g. implementation of new products or test procedures).

**Lead self-inspector**

The lead self-inspector agrees on the date of the inspection with the establishment to be inspected, plans it, and issues inspection documentation. He/she will also manage the inspection team and chair the opening and closing meetings during the self-inspection. The lead self-inspector defines the number and type of non-compliances observed and prepares the inspection report
including a plan for corrective actions. The lead self-inspector will subsequently monitor the transposition (realisation) of this plan, arrange review meetings if appropriate and finally approve the corrective action plan.

**Self-inspector**
The self-inspector performs the inspection and documents non-compliance details.

**The Inspected**
The inspected provides guidance to the inspector and in cooperation with him/her proposes and agrees on corrective actions and timescales. The inspected is responsible for implementing the corrective actions within the agreed timescales and informing quality assurance when the corrective actions are completed.

### 5.2.2 Education and training of inspectors

The education and training of inspectors requires a documented training programme for these personnel. The European blood legislation does not give any restrictions. However, it is generally accepted that regulatory inspectors should have an academic background in the field of biological science or medicine and should have work experience in a blood establishment or hospital blood bank. This will include knowledge of:

- national and international regulations and standards including the European blood legislation.
- structure and organisation of the blood service including differences and commonalities if different locations are used.
- processes of collecting, manufacturing, testing, storage and distribution of blood and blood components.
- principles of issuing and therapeutic use of blood and blood components.
• principles of good laboratory procedures, and
• principles of good manufacturing procedures.

The training of self-inspectors should include detailed knowledge of the quality management system in place and the organisational requirements of the inspection system (e.g. report forms, inspection checklists). The inspector should also be trained in inspection techniques (e.g. risk-based approach, top down or bottom-up system inspections), communication skills (‘open questions’), objectivity (including ethical behaviour) and accurate record keeping for the purpose of documentation. Training of self-inspectors in large blood services will rely on experienced personnel. In contrast, small blood establishments may decide to organise training programmes together with other blood services in their region.

5.2.3 Evaluation criteria for deviations, non-compliances and corrective action

Deviations and non-compliances observed during self-inspections should be classified in order to assess the importance and time scale for correction. There are several schemes used to classify them. Deviations identified during external inspection can be classified as critical, major and other significant non-compliances. The classification of non-compliances interacts with the type of corrective action needed.
5.2.4 Associated documents

5.2.4.1 Self-inspection record Trail

The self-inspection record trail is used to document the different steps performed during an inspection. An inspection trail gives information on the following:

- Date of self-inspection
- Inspection reference (e.g. inspection number)
- Organisation / department involved (this will extend to section and activities)
- Scope of the self-inspection
- Attendance list (those involved in the inspection). These individuals should be referred to in the final inspection report.
- Inspectors (their role, name and signature). With respect to a self-inspection report it should only be signed by the lead inspector on behalf of the team.
- List of clauses / areas examined including notes on details observed during the inspection. This can also include the names of staff present during the self-inspection and / or those with whom there has been an interaction.
- List of non-compliances and/or deviations observed. These non-compliances should give a precise indication as to the topic and the measures for correction.

A template based on the EU-SOP format\textsuperscript{23} can be found in Audit / Inspection - Training guide complementing the EuBIS manual. The self-inspection record trail can serve as or be accompanied by an ‘inspection checklist’.

\textsuperscript{23} The EU-SOP format has been developed by the EU-Q-Blood-SOP Project based on the requirements of the European Union blood legislation (www.eu-q-blood-sop.de)
5.2.4.2 Self-Inspection Guide

The self-inspection guide details those requirements that should be inspected. Although restrictive, it enables the inspector to cover the essential areas. Several aspects are similar to those required by the inspection trail.

- Date of inspection
- Inspection reference (e.g. inspection number)
- Organisation / department involved (this will extend to section and activities)
- Scope of the inspection
- Attendance list (Complete list of all individuals present during the opening and closing meetings as well as those involved in the inspection). These individuals should be referred to in the final inspection report.

*Remark:* Staff interviewed during the inspection are not required to sign. These individuals can be mentioned in the inspection (finding) report.

- Personnel that are essential during the opening and / or closing meetings are:
  - Inspection guide (the person from the organisation responsible for coordination during the self-inspection)
  - Staff involved in the inspection [e.g. Institutional director, department manager, lead technician(s)]

The names and signatures of these personnel should be recorded.

The self-inspection guide will be based on relevant standards for a particular section / activities to be inspected (e.g. blood component testing). This list will use cross-references to existing applicable standards. Several common standards are presented in the EuBIS inspection guide. It would be advisable, therefore, to refer to these standards as a platform for designing a checklist.
The minimum elements for inclusion in the inspection record trail format would consist of the following:

- Criterion Number (e.g. 1, 2, 3, etc.)
- Description of criterion
- Findings / evidence
- Conclusion / outcome (classifications)

An example of such a self-inspection record trail is given in the Audit / Inspection Training guide complementing the EuBIS manual.

5.2.4.3 Self-inspection summary report

The self-inspection summary report can be free-form, completely narrative or follow a set template. However, whichever format used, the following elements must be included:

- Date of inspection
- Inspection reference (e.g. inspection number)
- Organisation / department involved (this will extend to section and activities)
- Scope of the inspection
- Attendance list (names should be listed, however reference should be made to the self-inspection trail and / or self-inspection checklist for their signatures).
- The inspector and his / her role (i.e. lead inspector, expert, etc.). In general the self-inspection report, sections of which may be drafted by different individuals, will be only signed by the lead inspector on behalf of the inspection team.
- Number of non-compliances
- Description of non-compliances including classification
- Corrective action request
- Corrective and preventive action (CAPA) to be completed by:
  - Department
  - Person
• Date
  • Corrective action
    • Taken
    • Not taken
  • Corrective action verified by (name and date)

5.2.4.4 Site-Master-File for blood establishments (SMF-BE)

The site-master-file modified for blood establishments (SMF-BE) comprises information on the activity profile of the blood establishment, including the names of key personnel, facilities, equipment, documentation, contracts / agreements, complaints and product recalls and the quality system.

Information given by the SMF-BE will be used by the competent authorities in preparing and conducting the inspection. It would be advisable for the blood establishment to regularly verify the information in the SMF-BE during self-inspection in order to be prepared for any regulatory / external inspection. Further details are presented in Annex I.

5.3 The integration of quality risk management into self-inspection

Quality risk management, as set out in Volume 4, Annex 20 of the ‘Rules Governing Medicinal Products in the European Union’ is a ‘systematic process for the assessment, control, communication and review of risks to the quality of a product across its lifecycle. It can be applied both proactively and retrospectively.’

---

With respect to self-inspection, integration of a quality risk management system in the process can help to ensure that any assessment of the risk to quality is based on scientific knowledge, experience with the process, and is linked to patient protection.

Annex 20 provides a schematic of a quality risk management process.

**Figure 3:** Overview of a quality risk-management process
Effective quality risk management can help blood establishment administrators to reach better and more informed decisions as well as increase the confidence of regulators in its ability to deal with potential risks. To be effective, however, both blood establishment and regulatory personnel require training in decision-making processes and quality risk management outcomes.

Note: Additional information on the Quality Risk Management process is elaborated in Volume 4, Annex 20.

5.4 The self-inspection process

This section summarises a detailed step-wise description of a self-inspection. In general, it will be essential to set-up a central documentation system in the quality management department. The quality management / assurance together with the key responsible persons will set-up an inspection master plan. It will define the self-inspection frequency for each department / institution including the period (dates), the inspection duration (e.g. half-day or two-day inspection), the scope and the inspector. Based on this inspection master plan the following steps will be pursued.

Before the self-inspection

- Prepare self-inspection plan and assign inspection team (5.4.1)
  - Ensure that up-to-date information is available on the processes carried out in the department to be inspected.
  - Identify significant changes made within the department since the last self-inspection, and any changes to the inspection standards.
  - Review the previous self-inspection and external inspection report for the department.
o Define the detailed scope and assign the inspection team and responsibilities.

- **Agree inspection date and verify inspection details** (5.4.2)
  - Based on the scope, define the inspection agenda (time scale), the staff (inspected) required to be present and inspection date.
  - Inform the inspected department / staff and agree on a date and time scale for the inspection.

- **Prepare the inspection trail based on the self-inspection guide**
  In order to prepare the trail, refer to the EuBIS template given in Annex I of the *Audit / Inspection - Training Guide* complementing the EuBIS manual.

**During the self-inspection**
- **Perform the inspection and prepare draft report** (5.4.3)
  - Open a self-inspection meeting (‘opening meeting’), confirm the audit scope, agenda and audit process.
  - Conduct the inspection following the checklist and agenda. During the inspection, use an inspection trail (refer to the EUBIS self-inspection record / trail template).
  - At the end of the inspection, draft a report of the findings / outcomes including proposed target dates for corrective action (this should be done by the lead inspector, may be hand-written or using the inspection report format based on the EuBIS template).
  - Close the meeting (agree on the findings / outcomes including classification of the findings observed during the inspection). Agree who will respond to the inspection and confirm the target date(s).
After the self-inspection

- **Final inspection report and corrective action plan** (5.4.4)
- **Monitor progress against corrective action plan** (5.4.5)
  - Evaluate and confirm the acceptability of the received response (including action-plan) from the inspected department.
  - Follow-up the action-plan and if necessary plan a follow-up inspection.

- **Close inspection** (5.4.6)

The following sections describe in more detail the step-wise organisation of the self-inspection process.
### 5.4.1 Prepare inspection plan and assign inspection team

<table>
<thead>
<tr>
<th>Step</th>
<th>Responsibility</th>
<th>Description</th>
</tr>
</thead>
</table>
| 1    | Quality assurance (QA) | 1.1 Prepare draft annual inspection calendar based on previous years inspection performance.  
1.2 Define scope of individual inspections (Scope should be officially approved by the BE’s responsible person) |
| 2    | Inspection Stakeholders Group | 2.1 Review draft annual inspection calendar.  
2.2 If required amend annual calendar.  
2.3 Approve annual inspection calendar.  
2.4 Document approval in minutes of meeting.  
Target: 4 weeks before the start of the inspection calendar |
| 3    | Quality assurance (QA) | 3.1 If required by the inspection Stakeholders Group amend annual inspection calendar.  
3.2 ‘Approve’ amended inspection calendar |
<table>
<thead>
<tr>
<th></th>
<th>Allocate Lead Assessors. (in small BE the lead assessor, auditor, head of QA may be the same person)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>4.1 Allocate Lead inspector to each inspection and document the audit scope. Inform Lead inspectors of the inspections allocated to them (e.g. by e-mail) Target: 4 weeks before the start of the inspection calendar</td>
</tr>
<tr>
<td>5</td>
<td>Establish inspection team 5.1 Allocate inspectors to the inspection and document the role. Decide on technical experts needed, either In-House or external. Inform inspectors and/or technical experts of inspection allocated to them.</td>
</tr>
</tbody>
</table>

### 5.4.2 Agree inspection date and verify inspection details

<table>
<thead>
<tr>
<th></th>
<th>Lead Inspector</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Agree date of inspection. 6.1 Contact the site Target: 4 weeks before the month the inspection is scheduled. 6.2 Agree a date for the inspection during the scheduled month. Liaise with site via quality assurance (QA)</td>
</tr>
<tr>
<td>7</td>
<td>Prepare inspection plan.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Verify inspection details via quality management department</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Contact audit team.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 5.4.3 Perform the inspection and prepare draft report

<table>
<thead>
<tr>
<th>Number</th>
<th>Task</th>
<th>Description</th>
</tr>
</thead>
</table>
| **10** | **Inspection Team chaired by lead inspector** | **10.1 Convene opening meeting** with inspected to:  
- Perform introductions  
- Explain purpose of inspection  
- Confirm scope of inspection  
- Explain that the inspection will be conducted against guidelines, policies and procedures  
- Explain how the inspection will be conducted  
- Agree the timetable |
| **11** | **Perform inspection.** | **11.1 Perform inspection.**  
**11.2 Ask inspected to confirm information that may indicate a non-conformity.**  
**11.3 Document findings clearly.**  
**11.4 Decide if findings are:**  
- Critical non-conformity  
- Major non-conformity  
- Other non-conformity  
- Observation  
**11.5 Inform Lead inspector of findings** |
<table>
<thead>
<tr>
<th>12</th>
<th>Prepare draft report.</th>
<th>12.1 Prepare draft inspection report. Co-ordinated by Lead inspector</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.2 Document the following using Inspection Report Template:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Inspection details</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• NC details</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Applicable clause (Guideline, policy, procedure)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Severity of NC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Cause / Reason</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Any observations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Exclusions to inspection scope (e.g. processes not inspected)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Convene closing meeting.</td>
<td>13.1 Convene closing meeting to:</td>
</tr>
<tr>
<td></td>
<td>Chaired by Lead Inspector</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Attended by local staff members, responsible persons and quality assurance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Thank audited and staff</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Review findings</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Correct inaccuracies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Explain reporting arrangements</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Highlight findings which require immediate attention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Mention any activities which were impressive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Invite questions or comments</td>
<td></td>
</tr>
</tbody>
</table>
### 5.4.4 Prepare final inspection report and agree on corrective action plan

<table>
<thead>
<tr>
<th>Lead inspector</th>
<th>14</th>
<th>Prepare final inspection report.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14.1</td>
<td>Prepare final inspection report using inspection report template.</td>
</tr>
<tr>
<td></td>
<td>14.2</td>
<td>Post and/or E-mail final report to: QA at inspected site</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Target: within 10 working days of closing meeting</td>
</tr>
</tbody>
</table>

| Document inspection and non-compliance details | 15 | Document inspection date and performance in annual inspection plan. |
|                                               |    | 15.2 Document inspection and non-compliance details in 'central' inspection system. |
|                                               |    | 15.3 Attach an electronic copy of the inspection report to the inspection record in your quality system. |
|                                               |    | 15.4 Inform ‘centre’ QA that the inspection report has been documented. |

<table>
<thead>
<tr>
<th>QA at Inspected Site</th>
<th>16</th>
<th>Receive inspection report from Lead inspector.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16.1</td>
<td>Receive inspection report to inspected. (e.g. via e-mail)</td>
</tr>
<tr>
<td>17</td>
<td>Convene meeting(s).</td>
<td>17.1 Convene meeting(s) with inspected to review inspection report and prepare corrective action plan.</td>
</tr>
<tr>
<td>----</td>
<td>-------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| 18 | Prepare corrective action plan. | 18.1 Review inspection report.  
18.2 Agree the following with QA at audit site:  
- Underlying problem  
- Corrective action(s)  
- Target completion date  
- Person responsible for corrective action  
18.3 Cause / reason  
If required refer non-compliance to a National Officer / Strategic Head if issue cannot be resolved locally. |
| QA at Inspected Site | Document corrective actions | 19.1 Document corrective actions by preparing  
- required documents  
- Changes in procedures (e.g. validation data)  
19.2 Define individual ‘Supporting Actions’ if corrective action is required by more than one department. |
| Lead Inspector, Head of QA and Site QA | Review corrective action plan. | 20.1 Schedule meeting to review corrective action plan.  
20.2 Review corrective action plan  
20.3 Review corrective action plan |
Are proposed corrective actions and target dates acceptable?
- List number of acceptable and not-acceptable items
- Sent summary of these items to inspected
- Agree on revised corrective action plan
  Target: within 30 working days of the closing meeting

21 Approve corrective action plan.
   21.1 Approve corrective action plan and document agreed corrective action plan in the QA-system.

22 Perform corrective actions.
   22.1 Perform corrective actions as agreed in corrective action plan.
   22.2 Inform QA at inspected site when individual corrective actions have been completed.
   22.3 Inform QA at inspected site if the corrective action cannot be completed by the target date and the reason why.

5.4.5 Monitor progress against corrective action plan

23 QA at Inspected Site
   Monitor progress against corrective action plan.
   23.1 Monitor completion of corrective actions against
EuBIS Inspection Standards and Criteria, Edition 1.0

23.2 corrective action plan. Receive notification that corrective action has been completed.
23.3 Verify that corrective action has been completed and is effective.
23.4 If required amend target corrective action date and note reason why. Reason for change must be justified.
23.5 Communicate amended audit plan and time scale to inspected.
23.6 Document the actual corrective / supporting action details.
23.7 Close the individual non-compliance list.

24 Notify Head of QA. 24.1 Notify Head of QA that all Corrective Actions have been completed.

5.4.6 Close inspection

<table>
<thead>
<tr>
<th>Step</th>
<th>Responsibility</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>Close inspection.</td>
<td>28.1 Receive notification from QA at inspected site that all corrective actions have been completed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>28.2 Review corrective actions.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>28.3 Document that inspection is closed.</td>
</tr>
</tbody>
</table>
Figure 4A: Example flow-chart for an integrated self-inspection / audit system (NHS-BT)\textsuperscript{25}

\textsuperscript{25} The flow-chart represents the self-inspection process used by the National Health Service Blood and Transplant (UK) in performing peer-audits (© NHS-BT).
Figure 4B: Example flow-chart for an integrated self-inspection / audit system (NHS-BT)\textsuperscript{26}

\textsuperscript{26} The flow-chart represents the self-inspection process used by the National Health Service Blood and Transplant (UK) in performing peer-audits (© NHS-BT).
Specific requirements exist for the inspection of blood establishments by national regulators [competent authorities (CA)]. Directive 2002/98/EC (Article 8 para. 1) requires that Member States organise inspection and control measures to ensure that blood establishments comply with its provisions. These procedures, which are conducted by officials representing the CA, involve blood establishments and facilities of third parties entrusted to carry out evaluation and testing procedures. They include the collection of samples for examination and analysis, and require the examination of documents relating to the inspection (para. 3).

The regulatory inspection process serves as a formal and objective method, according to adopted standards, for assessing a blood establishment’s compliance with the European Union’s blood legislation and other relevant requirements and identifying problems and deficiencies or non-compliances. For a better understanding of this process, the following chapters provide background on several aspects related to the implementation of this legislative requirement. Although it focuses on the EU blood legislation, it has taken into account the inspection criteria and standards developed by the EUSTITE project consortium for tissues and cells.
General requirements

6.1 Qualifications of Inspectors

6.1.1 Education

Although no specific requirements related to the education and experience of inspectors of blood establishments are set out in the European Union’s legislation, it is generally accepted that they possess a diploma, certificate or other evidence of formal qualification in the field of medicine, pharmacy or other life-science disciplines.

These requirements reflect to a large extent those required by Directive 2002/98/EC (Article 9, para. 2a) for the ‘responsible person’ (RP) of a blood establishment.27

6.1.2 Experience

Practical experience in operational areas of blood or tissue and cell establishments has been of significant benefit for someone interested in becoming an inspector. Knowledge of hospital procedures, manufacturing aspects in the pharmaceutical industry, or regulatory requirements has also proven to be ‘beneficial’. A valuable trait is the ability to communicate effectively and with discretion and tact. Once recruited, inspectors are usually given basic / induction training (e.g. quality systems) before receiving specialised training in selected areas (e.g. blood components). Their competence is assessed periodically.

27 NOTE: The EUSTITE guidelines for the inspection of tissue and cell procurement and tissue establishments suggests, that ‘at least one member of the inspector team should have the same level of qualification as the responsible person of the institute to be inspected or have the necessary education and experience to inspect such a site’.
6.1.3 Training

In general, there are no specific requirements given by the EU legislation for an inspectorate training programme.

However, Member State inspectors have qualifications and experience that are needed to carry out the functions of this position. Nevertheless, however well-qualified and experienced the individual may be, basic training and orientation may have been required due to the specialised nature and responsibilities of the job. This is normally provided by the national inspectorate.

*Basic training* covers general topics essential for the inspector, including principles of inspection techniques (e.g. risk-based approach). It also includes:

- a number of site inspections with a certified inspector initially as an observer,
- at least two site inspections as a trainee,
- followed by two site-inspections as an inspector supervised by an experienced (lead) inspector.

Qualification of an inspector by the competent authority, which includes the evaluation of the individual’s performance, enables the trainee to become a lead inspector.

Depending on the education and experience of the candidate inspector, the basic training programme may be omitted and *specialised training* initiated directly. It focuses on topics essential for the optimal qualification of the inspector. This specialised training includes a familiarisation visit to a blood establishment in order for the candidate to become acquainted with its overall processes, functions and operations. These visits are preferably arranged with a BE, that is not audited by the same CA.

In order to keep the inspectors up to date, the specialised training programme is normally repeated at regular intervals. In addition on-going training is normally organised.
The following topics are normally covered by the training programmes.

**Basic training programme**
- European blood legislation (Directives)
- European legislation for medicinal products
- European and International Quality management standards in place for blood establishments [e.g. GxP regulations (GMP, GDP, GLP), Council of Europe (CD-P-TS), PIC/S, WHO]
- Accreditation, designation, authorisation or licensing systems in the Member State
- National legislation in place in the Member State
- National health systems and organizational structures for human blood and blood components in the Member State
- Organisation of national / international regulatory authorities and inspectorates
- Organisation of the national blood supply.
- Inspection techniques (e.g. risk-based approach, top-down or bottom-up system inspection)
- Communication skills (including ‘open questions’)
- Objectivity including ethical behaviour
- Accurate record keeping for the purpose of documented evidence

**Specialised training programme**
- Principles of quality management (e.g. risk and error management, change control)
- Knowledge of the processes and equipment to be audited by theoretical and practical training (collection, testing, processing, storage and distribution). The practical training may comprise familiarisation visits to blood establishments
- Data processing and protection systems
- Diseases transmissible by blood
• Laboratory techniques / In-vitro diagnostic tests (screening tests)
• General hygiene
• Detailed design, validation and maintenance of environments
• Haemovigilance (including look-back procedures)
• Risk and error management

On-going training
• Standards, guidelines and legislation
• New techniques
• State-of-the-art related to blood and blood components

6.1.4 Responsibilities

The inspector’s responsibility is to verify that the information provided by the blood establishment is accurate and that all procedures in place are in compliance with the European blood legislation.

As a representative of the competent authority he / she has a written mandate to carry out inspections and control measures\(^{28}\). This includes the compilation of a detailed report about the blood establishment, enabling the competent authority to accredit, designate, authorise, or license it. The inspector also assesses the suitability of the processes in use for the preparation of blood and blood components.

Inspectors, however, cannot examine all areas and documentation during an inspection. Consequently, they are not responsible if, due to limited time, scope or inability to conduct certain processes, they do not observe a particular non-compliance.\(^{29}\)

---


\(^{29}\) Eustite inspection guidelines, Chapter 2
In carrying out the inspection, an inspector, as a rule, is aware of the particular situation (e.g. nervous tension?) created by external audits. The inspection style attempts to create a positive and open atmosphere with indications that the inspection will not be limited to the disclosure of deficiencies or non-compliances. With respect to the category of deviation observed, the inspector gives clear causative explanations (refer to Chapter 7.2.9 - Inspection completion). If, however, he/she have the impression that the inspected does not consider or respect his/her observations, the inspector provides clear indications on the regulatory and legal background and the respective clause.

6.1.5 Confidential information

Confidentiality is an essential aspect of the inspection process. Therefore, the national inspectorate and inspectors advice the blood establishment to be inspected that confidential information obtained in oral, written or observed form before, during or after the inspection process, will be handled in compliance with legal requirements for the protection of confidentiality and those for disclosure for the protection of public health.

Respecting confidentiality requirements is of particular importance in situations where a blood establishment holds an individual license or patent for a particular test or manufacturing procedure or where a third party has given a licensing agreement for certain procedures.

The inspection of personnel files (dossiers) for evidence of qualifications requires a sensitive approach, in that these data are highly confidential and access for the inspector may be limited by national regulations.

In order to overcome strict confidentiality requirements related to personnel, a summary dossier, which covers the key education
and qualifications of the staff with respect to their functions, may be used. This would include, in particular, the continuing internal or external education of the staff member.

6.2 Inspection planning and capacity assessment

An important and critical first step in attaining a successful inspection is correct planning and documentation at the national level. The competent authority (inspectorate) is responsible for setting up an inspection plan, in order to fulfil the minimum requirements of Directive 2002/98/EC that ‘inspections have to be performed at least every two years’.

The planning, therefore, first requires an overview of the exact number and activity profiles of the blood establishment(s) in the Member State, taking into account observations / deviations of previous inspections. This includes reported changes of the activity profile (e.g. registration profile of blood components) or incidents / events (e.g. serious adverse events) reported by the institution or third party.

Depending on the activity profile, the competent authority decides on the qualification and the number of inspector(s) required to conduct the inspection. In general, the relationship between qualified inspectors per blood establishment varies between Member States depending on their size and activity profile (Table 3).

A newly formed inspectorate in a Member State may find it useful to draft an annual inspection master plan. These master plans will require assigning inspection teams and prospective dates for inspections and thus assessing the capacity.
Table 3: Relation between trained inspectors and blood establishments in various Member States (EuBIS survey 1.0, 2008)

<table>
<thead>
<tr>
<th>Member State</th>
<th>Inspectors (N)</th>
<th>Blood establishments – BE (N)</th>
<th>Population (Mio)</th>
<th>Relation BE / Inspector</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>12</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>78</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>159</td>
<td>82</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>17</td>
<td>62</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>64</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>45</td>
<td>324</td>
<td>58</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>5</td>
<td>60</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>4</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

6.3 Classification of inspections

Inspections can be classified according to the time frame in which they are carried out.

6.3.1 Authorisation inspection

Authorisation inspections take place in order to assess a particular situation (e.g. prior to the opening of a new blood establishment / a new facility / new activity in order to confer a processing license). Generally, these inspections require a larger time frame to be carried out and therefore extra time has to be included in the
planning process to allow for flexibility. Assessment of the
inspection scope and the composition of the inspection team,
however, relies on comparable experience from similar profiled
inspections.

6.3.2 Routine inspection
Routine inspection implies a visit to the blood establishment at
least every two years in accordance with Directive 2002/98/EC,
Article 8. The scheduling of these inspections takes into account
the risk-assessment findings of the individual blood establishment
from previous inspection reports.

6.3.3 Product / process related inspection (Change control
of authorisation)
In addition to routine inspections, situations arise when an
inspector is required to look at a particular product / process
related change. This may be a new or modified process which
may affect product specifications. The inspection of limited areas
of a particular blood establishment may be appropriate such as in
cases where the blood establishment has given notification of
process changes affecting the product specifications and / or
previously given authorisation of these processes by the
competent authority. The scheduling for and complexity of these
inspections depends on the risk assessment by the inspectorate
and is based on information provided by the blood establishment.
In cases where the risk assessment indicates only minor
modifications, written evidence based on validation data may be
accepted by the inspectorate and the inspection postponed until
the next routine re-inspection.
6.3.4 Event-related inspection
This classification of inspections is scheduled at short notice in cases where serious adverse events or reactions have been reported by the blood establishment or third party. Event-related inspections require a specific risk assessment of the process by the competent authority. In cases where product quality is affected by equipment, material or substances provided by suppliers, the inspection process may also include evidence presented by these suppliers.

6.3.5 Non-routine / unannounced inspections
In contrast to the aforementioned, these inspections are conducted at very short notice or are unannounced. An unannounced inspection is usually as a consequence of a suspected 'illegal or fraudulent activity or serious breach of legal requirements which might expose donors or recipients to risk'\(^{30}\). Such inspections may also be as a result of a request from a competent authority in another Member State or another official authority in the Member State itself to investigate specific issues. In such serious cases, the inspection team may include representatives from the legal authorities (e.g. public prosecutor).

6.3.6 Frequency of inspections
The elaboration of an inspection programme and the scheduling of visits to individual blood establishments are prepared by the competent authority. In order to adhere to a planned inspection schedule, sufficient resources need to be available and allocated so that the inspections can be conducted successfully.

Although the interval between two inspections and control measures must not exceed two years, other types of inspections could be carried out during this period. These could focus on a

\(^{30}\) EUSTITE manual, chapter 3
specific area or process (e.g. a non-compliance issue or new procedures) or they could be an office-based review of an updated SMF-BE (see Annex I for proposed standard format).

6.4 Planning for and assessment of an inspection

In planning for an inspection, the competent authority carries out a thorough assessment of the blood establishment. With respect to routine inspections, the following criteria may be used:

- Activity profile of the blood establishment
  - number of blood components produced
  - different production areas or facilities
  - CE certified test systems and / or in-house test systems
  - Type of blood collection (on-site or external) using either mobile units or fixed facilities
- Type and specification of blood and blood components prepared by the blood establishment
  - standard blood components alone, or
  - in combination with related components (e.g. granulocytes, lymphocytes)
  - pharmaceutical production (plasma for fractionation, cryoprecipitation)
- Compliance with the SMF-BE
- Number and severity of non-conformities in a previous inspection
- Number of adverse events / reactions or recalls conducted.

6.5 Compliance verification pending (or in absence of) a site visit

Situations may arise when a site inspection cannot be carried out. On such occasions, another course of action may be taken in
order to ensure that the BE’s activities comply both with EU legislation and national requirements. Taking fully into account a risk assessment, a review of an updated SMF-BE may provide the CA with an alternative regulatory approach (e.g. Product / process related inspection instead of routine inspection).

In order to implement this approach, first it is necessary for the CA to receive from the blood establishment an updated SMF-BE. This should be accompanied by documentation on any non-compliance issues and how they have been successfully addressed. The responsible person's signature confirming the accuracy of the information in the SMF-BE should also be included. The file then can be evaluated by an inspector to ensure compliance with regulatory requirements. If a specific technical issue arises, the opinion of an expert, not affiliated with the blood establishment, could be sought.

Information on any modification to an existing process in the blood establishment or the introduction of a new one, however, must be incorporated into the SMF-BE and submitted to the competent authority for approval.

6.6 Composition of the inspection team

The right composition of the inspection team is essential for an efficient inspection. As a rule, the team consists of two inspectors, each with specific experience. Inspections by a single inspector are avoided.

Lead inspector

A lead inspector, with responsibility for coordinating the activities of the inspection and presenting its findings and outcomes, is assigned.
Trainee inspectors
A trainee inspector may accompany the inspection team in order to observe the procedures and gain practical experience. In general, there is only one trainee in the inspection team. Trainee inspectors perform their inspection under the supervision of an experienced inspector.

Technical experts\textsuperscript{31}
Technical experts may be invited by the lead inspector to take part in the inspection in order to assist the team when a specific area of technical knowledge is required (e.g. GMP clean room facilities). The technical expert has no inspection mandate. His / her role is to advise the inspection team He / she must comply with any confidentiality agreement and avoid any conflict of interest.

6.7 Type of Inspection
Inspections are of three types according to the area to be looked at.

1) **General system evaluation:** This inspection focuses on the quality management system or site-master file including the overall quality policy in place that ensures the quality and safety of the blood and blood components. Inspection of the quality policy can be carried out through documented evidence. This can be, for example, external proficiency testing results, error and risk management, or document change control.

2) **Technical and process evaluation:** This part of the inspection concentrates on assessing practical performance during working hours. The focus is on monitoring the handling procedures and the qualification of the staff involved at different levels during the collection,
testing or processing for blood and blood components. Technical and process evaluation also comprises the verification of process quality results. This type of inspection is highly important where an innovative process or a very significant change to an authorised process has to be evaluated. Inspections may also focus on quality control or donor testing laboratories or third parties.

3) **Subcontractor or third party evaluation:** The inspection of subcontractors on a Member State’s own territory depends on the activity profile of the BE.

In cases where the testing or processing of blood or blood components is subcontracted fully or in part to an external organisation clear evidence is obtained on compliance with the quality and safety regulations in place. Examples for this procedure are e.g. external NAT testing for viral markers or supply of blood components derived from / processed by another blood establishment.

This is done through documentation provided by the subcontractor (e.g. ‘conformity statements’ given by competent authorities on this subcontractor, lot verification and / or CE conformity statement) or by an inspection of this external site.

It is the responsibility of the BE to verify the compliance of the subcontractor and/or third party supplier for critical goods (e.g. medical devices, IVD) with the appropriate requirements by the EU legislation and/or any other related regulation(s).

---

32 Directive 2002/98, Art 8, Para 3, ‘...inspect blood establishments as well as facilities of any third parties on its own territory entrusted by the holder of the designation, authorisation, accreditation or licence referred to in Article 5 with the task of carrying out evaluation and testing procedures pursuant to Article 18’. 
6.8 Inspection schedule

Preparation of an inspection schedule prior to the visit to a blood establishment greatly facilitates the work to be carried out. It identifies issues that require attention, particularly if they have been identified during a review of the SMF-BE, outlines concerns that may have been identified during a prior inspection, and notes any other matters that may need to be addressed.

The inspection is also facilitated if the blood establishment is made aware in advance of:

- the objectives and scope of the inspection
- the date and time of the inspection
- the inspection team members and their respective roles
- the blood establishment staff whose presence is required during the inspection
- the expected time and duration for each major inspection activity (premises, processes, etc.)
- the time table for the opening and final meetings, and
- the approximate time frame for the transmission of the written inspection report.
7 Conduct of Inspection

7.1 Inspection Procedures – before the inspection

Prior to the inspection of a blood establishment, the team familiarises itself with the organisation. They
- examine the contents of the SMF-BE particularly its adherence to the EU Blood Directives and any relevant national regulations
- review what blood components are prepared and the processes applied
- review the reports from previous inspections
- review follow-up actions (if any) arising from previous inspections
- review any blood or blood component recalls initiated since the previous inspection
- take note of any Serious Adverse Events or Reactions (SAE and SAR) notified since the previous inspection, and
- take note of any national standards or guidelines associated with the site to be inspected.

7.1.1 Information provided by blood establishment (Site Master File for Blood Establishment - SMF-BE)

The blood establishment to be inspected provides the following prior to the inspection.
- SMF-BE (refer to Annex I)
- blood establishment registration and licence
- important changes since the last inspection
- examples of SOPs and other types of documents on request.
7.2 Inspection procedures – during inspection

7.2.1 Opening meeting

The inspection starts with an opening meeting comprising the senior management of the blood establishment, the responsible person (RP) and the quality assurance,

The purpose of this meeting is to
- introduce the inspection team and the BE personnel participating in the inspection outlining their responsibilities
- summarize the purpose and scope of the inspection
- discuss the timetable of the inspection agenda.
- review the management structure of the blood establishment
- identify documentation that may be required during the inspection
- reiterate the confidential nature of the visit

In order to have an overview of the blood establishment site to be inspected, the inspection team requests information on:
- its quality management system
- the organisation's quality policy
- significant changes in facilities, equipment, processes and personnel since the last inspection, and
- how non-compliances have been resolved, if this information has not already been forwarded to the CA.

In cases where there is a team conducting the inspection, a separate room is required for debriefing meetings.

When the inspection is the first visit to the BE, the inspection team may make a short site tour for familiarisation following the opening meeting.
7.2.2 Key elements of the inspection

The essentials covered during the inspection of the blood establishment are:

- **Quality management**
  - quality system and quality assurance
  - risk management system

- **Personnel and organisation**
  - organizational structure (personnel, training and qualifications)

- **Premises** (areas for donor selection, blood collection, testing, processing, storage, waste disposal)
  - e.g. SOPs for decontamination cleaning, cross contamination prevention, etc.

- **Equipment and materials**
  - e.g. reviewing of process change control [installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ)]

- **Haemovigilance**
  - traceability (e.g. coding system used)
  - adverse reactions or events.

- **Blood collection, testing and processing**
  - donor requirements (e.g. donor records including donor consent)
  - collection procedures (e.g. SOPs, records)
  - mobile units or external collection facilities (if applicable)
  - laboratory procedures (e.g. handling of samples)
  - testing (e.g. validation records)
  - packaging and labelling
• Storage and distribution (e.g. compliance with Good Distribution Practice)
• Contract management
• Non-Compliance: deviations, complaints, recall, corrective and preventive actions.
• Self-Inspection, audits and improvement
• Quality control
• Questions raised relating to the assessment of licensing application (e.g. authorization inspections)
• Other specific issues identified (e.g. relevant future changes announced by company)
• Assessment of the SMF-BE (e.g. all changes are updated)

The key elements are further addressed in the EuBIS Audit / Inspection –Training Guide including cross-references to common inspection standards used.

7.2.3 Practical implementation

Implementation of the inspection focuses on verifying information included in the SMF-BE through the assessment of documents on-site, the questioning of staff to determine their competence, visiting facilities and observing / surveying the actual performance of collection, testing, processing, storage and distribution of blood and blood components.

In order to implement the inspection process, it can be divided into the following:
• **System-related inspection**
• **Process/Product-related inspection**

The general system evaluation, which is a static process, focuses on the evaluation of documents that are part of quality management.

In contrast, the process evaluation is an active process, which requires the presence of the inspector at any site of the blood establishment while in operation. This also allows the direct contact with different levels of staff.

Both types of inspections include the identification of critical elements giving proof for the overall quality of the blood establishment.

• The **system-related inspection** will include examples of
  • job descriptions and the role of the Responsible Person
  • training of staff
  • maintenance (e.g. change control) of standard operating procedures (SOPs)
  • validation (processes)
  • qualification (equipment, facilities)
  • purchases
  • subcontractor or third party contracting (if applicable)
  • internal auditing system / self-inspection procedure
  • quality control (e.g. results of random sampling analysis)
  • donor selection criteria
  • testing
  • management of complaints, non-conformities, recalls, etc.

33 The system for performing self-inspections in the organisation is examined, although the reports themselves are not normally read by the inspector.
- management of adverse events and reactions
- look-back procedures
- retention of donation samples for re-testing
- data handling, confidentiality

The **process / product - related inspection** is an active process on-site, which may follow part of the ‘vein-to-vein’ chain from the blood donor to the distribution of the blood components. This inspection includes examples of

- the donor management system (e.g. donor registration)
- traceability of each individual unit of blood or blood component from the donor to its final destination\(^{34}\) (e.g. donor identification, labelling)
- specific standard operating procedures (SOPs) related to the particular process being inspected
- documentation including relevant records, print-outs or electronic data handling
- hygiene and cleaning procedures
- environmental monitoring (e.g. waste, particular measurements for classified production rooms)
- equipment maintenance (e.g. log-book)
- quality control data, starting materials, intermediates and finished components
- relevant quality control measurements to safeguard the product specifications
- release procedures
- storage and distribution.

\(^{34}\) Directive 2005/61/EC, Art 1: ‘Final destination whether this is a recipient, a manufacturer of medicinal products or disposal, and vice versa’.
7.2.4 Donor selection and blood collection

7.2.4.1 Donor selection requirements

Directive 2004/33/EC (Annex II Part B) requires every blood donor to provide to the blood establishment not only personal data that uniquely distinguishes them but also their medical history. Therefore, every blood establishment must have donor registers that contain the provided information as well as any clinical data emanating from that donation. The donor register contains:

- Identification of the donor (first name, family name, sex, date of birth)
- Contact details (e.g. address)
- Health and medical history of the donor
- Donor questionnaire
- Informed consent
- Self-exclusion form (if applicable by national regulations).

Maintenance of these records must comply with Directive 95/46/EC on the protection of individuals with regard to the processing of personal data as well as the data protection and confidentiality measures set out in Article 24 of Directive 2002/98/EC. These records must be legible and permanent.

It is recommended that the identity of blood donors is verified by a photo-document (e.g. passport, identity card, drivers licence).

In accordance with Directive 2002/98/EC and/or equivalent national requirements, the inspector checks that the donor screening procedures and their records comply with the requirements regarding donor identity, list of donor selection/deferral criteria, completion of a donor questionnaire, donor consent, medical history, and the identification of behavioural risks that would lead to donor deferral.
He / she checks to ensure that SOPs exist for the donor selection process and that evaluation is assessed by trained personnel and the outcome documented.

Donor register requirements are inspected by examining examples (documents) of the following from at least two donors:

- Completed donor questionnaires
- Self-exclusion form (if applicable by national regulations)
- Donor consent form
- Donor history (e.g. donation frequency, health and medical history)

The process-related inspection is carried out while the relevant activities are operational. This includes:

- Donor identification
- Health examination
- Pre-donation testing (e.g. haemoglobin, blood pressure, temperature)
- Donor history review and acceptance / deferral

### 7.2.4.2 Blood collection requirements

With respect to the actual collection of blood and blood components, the inspector verifies that it is carried out under conditions that protect the health of the donor and the safety of the donations, is performed by trained personnel, and is in accordance with SOPs.

The process-related inspection is carried out while the relevant activities are operational. This includes verification of:

- donor identity
- use of sterile single-use needles and collection bags / apheresis sets
7.2.4.3 Traceability requirements

For each blood or component collected, there must be sufficient data to ensure traceability. This includes:

- identification of the blood establishment
- identification of the donor
- identification / description of collected blood and blood components

In addition, the inspection covers

- reports of any serious adverse event or reaction and the associated corrective action(s).
- Product recall procedures
- Look-back procedures

7.2.5 Inspection of premises and equipment

Inspection includes an intensive visit to all premises of the blood establishment relevant for the collection, testing, processing, storage and distribution of blood and blood components. This includes

- Blood collection and processing areas
- Mobile units or external facilities (if applicable)
- Blood testing area
- Blood and blood component storage areas (released and non-released)
- Relevant equipment for transportation of blood components (including mobile units and/or external facilities)
- Relevant equipment for transportation of issued blood components
- Storage area for disposable materials (e.g. blood bags, test kits, labels)
- Waste disposal areas
- Engineering support (e.g. temperature control system, air conditioning / heating systems)

The inspection also includes equipment such as balances, apheresis machines, cell counters, centrifuges, separators, sterile connecting devices, tubing sealers, freezers, irradiators and the specialised equipment for blood group and infectious-marker testing.

The inspection effort may concentrate in one department (area) of the blood establishment if there are special problems or requirements.

Observations by the inspector are announced immediately to the relevant blood establishment personnel during the premises tour.

7.2.6 Laboratory Testing

Prior to the inspection, the inspector reviews the SMF-BE to determine if the testing is carried out only internally or if there are tests that are subcontracted.

The inspector verifies compliance with the testing requirements of Directive 2002/98/EC (Annex IV) by:
- Following a number of donations through the testing procedure
- Confirming the certification / accreditation for each test used.
- Checking that tests are used according to the manufacturers instructions. In the event, tests are
modified, sufficient validation must be available by the laboratory to prove its performance.

- Checking pre-acceptance procedures prior to the use of new batches of kits.
- Examining the records to prove verification of the test kit performance by internal quality control using
  - reference standards for accuracy of equipment (calibration)
  - working standards (or reference material) tested at intervals for determination of drift occurring during testing.
- Examining equipment log-books and maintenance records
- Checking the results of external proficiency testing

If the blood establishment has subcontracted an external laboratory to perform the testing, the inspector verifies that;

- the blood establishment has a contract with the external laboratory,
- the external laboratory is authorised by the competent authority for the contracted activities,
- the external laboratory is regularly audited either by the BE or an appropriate third party,
- the BE checks its compliance with testing requirements and its regular and successful participation in external proficiency testing.

### 7.2.7 Processing and storage

The inspector verifies compliance with the legislative requirements by:

- following a donation through the processing steps for standard blood component preparation including the relevant process records.
reviewing the documentation for special manufacture steps (e.g. washing, splitting, volume-reduction, leukocyte filtration, irradiation)

- examining quality assurance results based on statistical process control in order to monitor blood component specifications (including microbiology testing)
- reviewing the reception procedure for supplies used by the blood establishment (e.g. blood bags including stabilising and additive solutions, solutions for washing cellular components)
- examining equipment log-books and maintenance records
- examining the release process of blood components from the production area
- reviewing non-conformities during processing recorded and the corrective and preventive actions taken

With respect to storage, the inspector visits storage areas and examines:

- Temperature records and if applicable humidity records
- Separate storage of quarantined blood or blood components and those 'released for distribution'
- Procedures for authorising and transferring blood or blood components from quarantine to 'released for distribution'
- One maintenance and calibration record of a critical piece of storage equipment selected by the inspection team.
- Procedures to ensure restricted access and prevent cross-contamination
- Requirements for storing and disposing of biohazard waste
7.2.8 Transport and distribution
With respect to the transportation of blood and blood components, the inspector verifies that there are written procedures to check that transport and distribution conditions are met. Several packaging containers and their labels are examined and a determination made as to their suitability for the distribution of the released blood and blood components so that their sterility and integrity are maintained. The inspector also reviews procedures in place to ensure traceability.

7.2.9 Inspection completion
Upon completion of the inspection, the lead inspector convenes a meeting with representatives of the blood establishment to summarize the team’s findings. Meeting participants include the responsible person, quality manager, any other personnel invited by the responsible person as well as members of the inspection team. Discussions focus on issues related to non-compliance that were observed during the inspection with supportive facts and observations presented. The seriousness of any non-compliance, which may be classified as critical, major or other, is emphasised by the inspector. All relevant observations are discussed so that the blood establishment can undertake corrective actions as soon as possible. In the event of any non-compliance that may put at risk the quality and safety of the blood or blood components, the inspector may request the quarantine and/or cessation of supply of specific components.

A provisional summary statement can be prepared that reflects the inspection’s findings. All non-compliances would be listed and reference to the EU Directives and other relevant EU Guidelines and national regulations and standards mentioned. All non-compliances found are listed even if corrective actions have taken place straight away.
Non-compliances or deficiencies can be classified as:

**Critical non-compliance:** Any non-compliance in a process or a written procedure which directly affects the safety of the donor or patient.

**Major non-compliance:** A serious non-compliance in a process or a written procedure but does not on its own affect the safety of the donor or patient.

**Other significant non-compliance:** A non-compliance in a system or process or there is insufficient information to classify it as a major or critical.

**Observation:** An inadequacy in a system or process that is not a failure to comply with a standard.

It is to be noted that there could be a combination of several “other” significant non-compliances, none of which on their own may be major or critical, but may together represent a major or critical non-compliance. These should be clearly explained and reported as such.

Observations (suggestions) obtained during the inspection, where action can be taken by the blood establishment, are listed.

### 8 Inspection procedures – after the inspection

#### 8.1 Official written inspection report

Following the inspection, the lead inspector prepares an official inspection report within a fixed time frame – ideally no later than four weeks post inspection. A sample template for this report is given in Annex II. It covers *inter alia* the scope of the inspection and its findings.
The conclusions clearly identify non-compliances, classified as critical, major or other according to the preceding definitions. The inspector provides a clear statement about the outcome of the inspection and whether the BE is in compliance with EU legislation and national requirements on blood.

The report includes a date by which the BE must submit proposals and a time schedule for rectifying the non-compliances (an action plan).

8.2 Conformity statement

Upon request, the CA can prepare a conformity statement related to the activities of the SMF-BE. This statement indicates that the BE complies with the EU legislation and relevant national regulations.

8.3 Blood establishment’s response to inspection report

The inspected blood establishment must notify the competent authority in writing and within certain time limits, in accordance with the classified non-compliances, of the actions proposed.

In case of critical non-compliances corrective actions must be taken by the BE without delay. It is generally accepted that for major non-compliances the BE must respond within 14 days; in case of ‘other’ significant non-compliances within 30 days of receipt of the inspection report. The response includes the specific steps (action plan) which have been or will be taken to correct the failures mentioned above and to prevent their recurrence.

If corrective actions cannot be completed within 30 days, the inspected blood establishment should state the reason for the delay and the time within which the corrections will be completed (the authority will decide upon the acceptability of the given time period). After this the blood establishment has to report about the final corrections.
The inspector evaluates the proposed action plan submitted by the BE. Based on the evaluation, the inspector recommends to the CA that

i) it accredits / designates / authorises / licenses the BE,  

ii) that it authorises a second site visit by the inspection team, or  

iii) that it requests additional information regarding corrective actions from the BE before an authorisation recommendation can be made.

8.4 Scheduling re-inspection of the blood establishment

Depending on the overall performance, the type of non-compliances observed during the previous inspection and the blood establishment’s response to the inspection report (CA), a re-inspection may be scheduled.

9 Evaluation of the inspection system

In order to ensure that a national inspection system is functioning efficiently and effectively, the CA undertakes periodical reviews of its procedures and practices related to blood establishments. Performance indicators, such as presented below, are used in this review.

- number and type of inspections conducted per year
- number of blood establishments certified/authorised/licensed per year

Performance of inspectors is reviewed periodically. Their training needs are addressed and they are provided with updated training possibilities by the CA.

Whenever possible, the composition of the inspection team varies. This is beneficial for the inspectors who gain knowledge from the experience of others.
Annex I Site master file modified for blood establishments (SMF-BE)

Following the requirements given by Directive 2002/98/EC, the following information must be provided by the blood establishment to the competent authority for the purpose of designation, authorisation, accreditation or licensing in accordance with Article (29)\textsuperscript{35}

General information:
- identification of the blood establishment
- name, qualification and contact details of responsible persons
- activity profile
- a list of blood components manufactured.

A description of the quality system, to include:
- documentation, such as an organisation chart, including responsibilities of responsible persons and reporting relationships
- documentation such as site master file or quality manual describing the quality system in accordance with Article 11(1)
- number and qualifications of personnel
- hygiene provisions
- premises and equipment
- list of standard operating procedures for recruitment, retention and assessment of donors, for processing and testing, distribution and recall of blood and blood components and for the reporting and recording of serious adverse reactions and events.

\textsuperscript{35} Directive 2002/98/EC
Report of the blood establishment's preceding year’s activity. This annual report will include:

- total number of donors who give blood and blood components
- total number of donations
- an updated list of the hospital blood banks which it supplies
- total number of whole donations not used
- number of each component produced and distributed
- incidence and prevalence of transfusion transmissible infectious markers in donors of blood and blood components
- number of product recalls
- number of serious adverse events and reactions reported.
Site-Master-File for Blood Establishments (SMF-BE)

Section A. General Information

Full name of the establishment
Establishment postal address and street address if different
Telephone number
Fax Number
Email address
Contact telephone Number

Activity summary

Please tick the relevant boxes or indicate the activities carried out on site

<table>
<thead>
<tr>
<th>Activity</th>
<th>Blood and Cells</th>
<th>Processes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collection</td>
<td>Whole blood</td>
<td>Whole blood donation</td>
</tr>
<tr>
<td>Testing</td>
<td>Erythrocytes</td>
<td>Apheresis</td>
</tr>
<tr>
<td>Processing</td>
<td>Thrombocytes</td>
<td>Washing</td>
</tr>
<tr>
<td>Storage</td>
<td>Fresh Frozen Plasma</td>
<td>Splitting</td>
</tr>
<tr>
<td>Distribution</td>
<td>Plasma for fractionation</td>
<td>Cryo preservation</td>
</tr>
<tr>
<td>Importation</td>
<td>Cryoprecipitates</td>
<td>Cell selection</td>
</tr>
</tbody>
</table>
Section B. Activity–Details

Does the establishment conduct donor testing? Yes ☐ No ☐
(If no, indicate which organization conducts testing)

Types of Blood* collected by the establishment:
* Whole blood, autologous or allogeneic
* Blood components, received by apheresis

Types of blood components, processed by the BE

Processing methods
(please add here the room numbers)

Number of donors in the previous year

Number of produced blood components in the previous year

Quality control testing methods
Section C. Personnel
Name of the Responsible person as defined in Directive
(Please attach a brief curriculum vitae)
Name of Establishment Director
Name of Medical Director
Name of the head of quality control
Name of the quality Manager
Name(s) of other relevant key personnel
Total number of the staff

Section C - This should include the following:

- Qualification, experience and responsibilities of key personnel
- Outline of arrangements for basic and in-service training and how records are maintained
- Personnel hygiene requirements, including clothing
- Functional organization chart which identifies roles and reporting relationships
- Organization chart indicating how many people are working in collection, processing, quality control, quality assurance, administration, storage and transport.

Section D. Facilities

- Short description of the site (size, location and adjacent environment)
- Number of outside collection sites, number of mobile sites (busses)
- Description of the processing and storage facilities indicating the number of rooms, their dimensions and
environmental classification, where relevant. Simple floor plan of collection, production and laboratory areas.
- Description of preventive maintenance programs and recording system

Section E. Equipment
- Brief description of major production and control laboratory equipment,
- Qualification and calibration including recording system,
- Arrangements for computerized systems validation.

Section F. Documentation
- Arrangements for the preparation, revision and distribution of necessary documentation for collection of blood and manufacture of blood products
- Standard operation procedures (SOP)
- Donor questionnaire
- Manufacturing records
- Analytical methods
- Product specifications
- Release procedures including the release for sale of finished products.

Section G. Contracts / Agreements with other organizations
Are there any activities carried out by a third party (e.g. testing, cleaning, storage, transport)?
Yes ☐ No ☐

If yes, indicate which steps and name the organization that acts as the third party. Add a copy of the contract, if available.

Section H. Haemovigilance system
SAE / SAR investigation and reporting system and management of look-back procedures.
Section I. Complaints and product recall
Describe the arrangements for the handling of complaints and product recalls.

Section J. Risk management system

Section K. Quality System
Give a short description of the quality system applied at the blood establishment including the self inspection program.

Has the BE been certified by any external body e.g. ISO? Yes  □  No  □
If yes, add the certification number and institution

Section L. Signature and Date

Date (DD/MM/YYYY):

_________________________________________________________________________
Signature of the Responsible Person
Section M. Instructions for the submission of form

The form should be submitted as an initial application for accreditation/ designation/ authorization/ licensing by the Competent Authority for blood. It should be re-submitted prior to any following re-inspection or whenever significant changes in activity, staffing or processes applied have taken place.

Each CA to insert relevant instructions:
## Blood Inspection Report

### Inspected site(s)

*Name and full address of the Inspected site*

### Activities carried out

**Collection:**
- In-house
- External stationary sites
- Mobile units

**Processing:**
- from whole blood
- by apheresis

**Laboratory testing:**

**Storage and transportation**

**Distribution**

**Source plasma for fractionation**

**Cryoprecipitate**

**Other:**
- (please define)

### Inspection date

*Day, month, year*
## Inspector(s)

*Name of inspector(s)*

*Name of expert / assessor (if applicable)*

*Name of the Competent Authority*

## References

*Accreditation / designation / authorisation / licensing number or date*

### 1. Introduction

#### 1.1 Short description of the blood establishment and the activities performed

#### 1.2 Issuing Date / Version of Site-Master-File or Quality Manual

#### 1.3 Date of previous inspection

#### 1.4 Names of Inspector(s) involved in the previous inspection

#### 1.5 Major changes since the previous inspection
2. Brief report of the inspection activities undertaken

<table>
<thead>
<tr>
<th>2.1 Scope of Inspection</th>
<th>Short description of the inspection: Classification (e.g. Authorisation or routine inspection) and the type of inspection (e.g. system related, product / process-related)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2 Inspected area(s)</td>
<td>(Each inspected area should be specified)</td>
</tr>
<tr>
<td>2.3 Activities not inspected</td>
<td>(Where necessary attention should be drawn to areas or activities not subject to inspection on this occasion)</td>
</tr>
<tr>
<td>2.4 Personnel met during the inspection</td>
<td>(The names and titles of key personnel met, should be specified &lt; listed in annex &gt;)</td>
</tr>
</tbody>
</table>

3. Inspection Team’s findings and observations relevant to the inspection

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2 Personnel and organisation</td>
<td></td>
</tr>
<tr>
<td>3.3 Premises including mobile sites</td>
<td></td>
</tr>
<tr>
<td>3.4 Equipment and materials</td>
<td></td>
</tr>
</tbody>
</table>
3.5 Documentation

3.6 Blood collection, testing and processing

3.6.1 Donor eligibility

3.6.2 Collection of blood and blood components

3.6.3 Laboratory testing

3.6.4 Processing and validation

3.6.5 Labelling

3.6.6 Release of blood and blood components

3.7 Storage and distribution

3.8 Contract management

3.9 Non-compliance Management of deviations, complaints, recalls, corrective and preventive actions

3.10 Self-Inspections, audits and improvements
3.11 Traceability and notification of serious adverse reactions (SAR) and events (SAE)

3.12 Information technology (IT)

3.13 Other specific issues identified (e.g. relevant future changes announced by company)

4. Miscellaneous

4.1 Distribution of Report

4.2 Other

(List attached)

5. Annexes

•

•

•
Section 6: All non-compliances should be listed and the relevant reference to the EU Directives and other relevant EU Guidelines and relevant national regulations and standards should be mentioned. All non-compliances found should be listed even if corrective actions have taken place straight away. If the non-compliances are related to the assessment of the marketing application it should be clearly stated.

Definition of significant non-compliances

**Critical non-compliances**: Any non-compliance in a process or a written procedure which directly affects the safety of the donor or patient.

**Major non-compliances**: A serious non-compliance in a process or a written procedure but does not on its own affect the safety of the donor or patient.

**Other significant non-compliances**: A non-compliance in a system or process or there is insufficient information to classify it as a major or critical.

Note: There could be a combination of several “other” significant non-compliances, none of which on their own may be major or critical, but may together represent a major or critical non-compliance. These should be clearly explained and reported as such.

6. List of non-compliances classified into critical, major and other significant

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Subsection</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1</td>
<td>Critical non-compliances</td>
<td></td>
</tr>
<tr>
<td>6.1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.2</td>
<td>Major non-compliances</td>
<td></td>
</tr>
<tr>
<td>6.2.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.3</td>
<td>Other significant non-compliances</td>
<td></td>
</tr>
<tr>
<td>6.3.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.3.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Section 7: List non-compliances type observations obtained during the inspection, where action to be taken by the blood establishment is suggested

7. Suggestions (observations)

The company should be asked to inform the Inspectorate about the progress of the corrected actions and a proposed time schedule for corrections.

8. Summary and conclusions

8.1

8.2

This should include a time line for response by the BE (see chapter 7.3 response from BE)

Final statement

Compliance or non-compliance with GP/GMP standards, EU or national laws

The Inspection Report should be signed and dated by the Inspector(s) / Assessors who participated in the inspection

Name(s) and signature(s)

1. Competent authority or regulatory Institution that has performed the inspection

2. If applicable national regulatory office

Organisations

Date
Annex III  Documents consulted in Manual’s development

EU Legislation


**European Commission Documents**


**European or International Regulators**


EudraLex, The rules governing medicinal products in the European Union, Annex 14 – Manufacture of medicinal products derived from

ISO Guidelines for quality and/or environmental management systems auditing (ISO 19011).

**Council of Europe**

Recommendation No. R(95) 15 of the Committee of Ministers to Member States on the Preparation, Use and Quality Assurance of Blood Components.


**World Health Organisation**


**Professional Societies or Projects in the field of blood, tissue and cells**


PIC/S Standard Operating Procedure (pi 026-1 October 2006) Qualification and training of inspectors in the field of human blood, tissues and cells.

## Annex IV

**Additional references and Project publications**

Minimum Requirements for Blood Bank Compliance with Article 14 (Traceability) and Article 15 (Notification of Serious Adverse Reactions and Events) of EU Directive 2002/98/EC. Published by the Irish Medicines Board and the Irish National Accreditation Board. Edited by IMB/INAB Expert Group on Blood and Blood Components and should be used in conjunction with the ISO15189 Standard (available via the IMB homepage)

Guide of Recommendations for Tissue Banking. Edited by SANCO-EQSTB Project participants. Recommendations have been developed as a result of a European project entitled *European Quality System for Tissue Banking* (EQSTB) co-funded by DG Sanco. [http://sanco-eqstb.hospitalclinic.org/sanco/index.html](http://sanco-eqstb.hospitalclinic.org/sanco/index.html)

Guidelines for the inspection of cell and tissue procurement and tissue establishments (Eustite). These Guidelines have been produced as part of an EU funded project entitled ‘European Union Standards and Training for the Inspection of Tissue Establishments’ (see www.eustite.org)


<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audit</td>
<td>Documented review of procedures, records, personnel functions, equipment, materials, facilities, and/or vendors in order to evaluate adherence to written SOPs, standards, or government laws and regulations, conducted by professional peers, internal quality system auditors or certification body auditors.</td>
<td>Adapted from the Council of Europe Guide for Safety and Quality Assurance for Organs, Tissue and Cells for Transplantation, 3rd Edition, 2007</td>
</tr>
<tr>
<td>Audit programme</td>
<td>A systematic and independent examination to determine whether quality activities and related results comply with planned arrangements and whether these arrangements are implemented effectively and are suitable to achieve objectives.</td>
<td>Council of Europe: EDQM, Guide. 14th edition, 2008</td>
</tr>
<tr>
<td>Audit Trail</td>
<td>see Self-Inspection Record</td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>Whole blood collected from a donor and processed either for transfusion or for further manufacturing</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td>Blood component</td>
<td>A therapeutic constituent of blood (red cells, white cells, platelets, plasma) that can be prepared by various methods</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td>Blood establishment</td>
<td>Any structure or body that is responsible for any aspect of the collection and testing of human blood or blood components, whatever their intended purpose, and their processing, storage, and distribution when intended for transfusion. This does not include hospital blood banks.</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Calibration</td>
<td>The set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure, and the corresponding known values of a reference standard.</td>
<td>EudraLex</td>
</tr>
<tr>
<td>Clean area</td>
<td>An area with defined environmental control of particulate and microbial contamination constructed and used in such a way as to reduce the introduction, generation and retention of contaminants within the area. Note The different degrees of environmental control are defined in the Supplementary Guidelines for the Manufacture of sterile medicinal products.</td>
<td>EudraLex</td>
</tr>
<tr>
<td>Clean / contained area</td>
<td>An area constructed and operated in such a manner that will achieve the aims of both a clean area and a contained area at the same time.</td>
<td>EudraLex</td>
</tr>
<tr>
<td>Deficiencies, critical</td>
<td>See non-compliance</td>
<td>EMEA</td>
</tr>
<tr>
<td>Deficiencies, major</td>
<td>See non-compliance</td>
<td>EMEA</td>
</tr>
<tr>
<td>Deficiencies, other significant</td>
<td>see non-compliance</td>
<td>EMEA</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Distribution</td>
<td>The act of delivery of blood and blood components to other blood establishments, hospital blood banks and manufacturers of blood and plasma derived products. It does not include the issuing of blood or blood components for transfusion.</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td>Donation</td>
<td>Blood and blood components collected from an individual and intended for transfusion to another individual (allogeneic) or to the same (autologous).</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Donor</td>
<td>A person in normal health with good medical history who voluntarily gives blood or plasma for therapeutic use.</td>
<td>Council Recommendation 98/463/EC</td>
</tr>
<tr>
<td>Donor, first time</td>
<td>Someone who has never donated either blood or plasma</td>
<td>Council of Europe: EDQM, Guide.</td>
</tr>
</tbody>
</table>
| Donor, regular    | Someone who routinely donates their blood or plasma (i.e. within the last two years), in accordance with minimum time intervals, in the same donation centre. | Council of Europe: EDQM, Guide.  
|                   |                                                                           | PIC/S GMP Guide         |
| Donor, repeat     | Someone who has donated before but not within the last two years in the same donation centre. | Council of Europe: EDQM, Guide.  
<p>|                   |                                                                           | PIC/S GMP Guide         |
| Expert            | Individual with appropriate qualifications and experience to provide technical advice to a CA inspector | EUSTITE Guidelines     |</p>
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Familiarisation visit</strong></td>
<td>An activity, that includes a visit to a blood establishment in order for a candidate inspector to become familiar with its overall processes, functions and operations.</td>
<td>EuBIS</td>
</tr>
<tr>
<td><strong>Good practice</strong></td>
<td>All elements in established practice that collectively will lead to final blood or blood components that consistently meet predefined specifications and compliance with defined regulations</td>
<td>Directive 2005/62/EC</td>
</tr>
<tr>
<td><strong>Good Manufacturing Practice</strong></td>
<td>All elements in the established practice that will collectively lead to final products or services that consistently meet appropriate specifications and compliance with national and international regulations.</td>
<td>PIC/S GMP for blood establishments, PE 005-3, 25 September 2007</td>
</tr>
<tr>
<td><strong>Inspection</strong></td>
<td>Formal and objective control according to adopted standards to assess compliance with this Directive and other relevant legislation and to identify problems</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td><strong>Inspection schedule</strong></td>
<td>A schedule prepared by the competent authority for an specific inspection. The schedule comprises the inspection content (based on the scope) and the time frame</td>
<td>EuBIS</td>
</tr>
<tr>
<td><strong>Inspection team</strong></td>
<td>A team comprising several individuals that perform an inspection. Very often an inspection team consists of two inspectors. One inspector will inspect the quality system and in the case of ‘peer’ inspections a technical specialist inspector may also be available.</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Inspection, external (regulatory)</td>
<td>An inspection carried out by the Competent Authority or accreditation body. Formal and objective control according to adopted standards to assess compliance with the European blood legislation and other relevant legislation and to identify problems. (This definition expands on the definitions given by the Directive 2002/98/EC and the CoE Guide).</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Inspection, peer</td>
<td>A ‘peer’ inspection is carried out by inspectors from different facilities within the same blood establishment. The ‘peer’ inspection will require a multi-centre structure of the same blood establishment that provides experts with equivalent skills and knowledge based at different locations. Alternatively, ‘peer’ inspections can be organised through the cooperation between national or regional blood services.</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Inspection, self-</td>
<td>An inspection conducted by trained and competent representatives of the organisation but managerially independent of the department concerned</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Note:</td>
<td>There are several equivalent definitions for this term. The word self-inspection is very often used inter-alia with the terms ‘audit’ or ‘internal-audit’.</td>
<td></td>
</tr>
<tr>
<td>Inspector, lead</td>
<td>The lead inspector is responsible for coordinating the activity of the inspection ‘team’ and presenting the findings and outcomes of the self-inspection. In smaller BE very often the</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>inspections are carried out by a single inspector.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inspectorate training programme</td>
<td>An inspectorate training programme covers general topics essential for the inspector, including principles of inspection techniques as well as specific and on-going training.</td>
<td>EuBIS</td>
</tr>
<tr>
<td>Non-Compliance</td>
<td>Deficiency observed during an inspection. This term is used similar to the term non-conformance defined by EMEA</td>
<td>GMP</td>
</tr>
<tr>
<td>Critical non-compliance</td>
<td><em>Any non-compliance in a process or a written procedure which directly affects the safety of the donor or patient.</em></td>
<td>GMP</td>
</tr>
<tr>
<td>Major non-compliance</td>
<td><em>A serious non-compliance in a process or a written procedure but does not on its own affect the safety of the donor or patient.</em></td>
<td>GMP</td>
</tr>
<tr>
<td>Other significant non-compliance</td>
<td><em>A non-compliance in a system or process or there is insufficient information to classify it as a major or critical.</em></td>
<td>GMP</td>
</tr>
<tr>
<td></td>
<td><em>Note: There could be a combination of several “other” significant non-compliances, none of which on their own may be major or critical, but may together represent a major or critical non-compliance. These should be clearly explained and reported as such.</em></td>
<td></td>
</tr>
<tr>
<td>Observation (suggestion)</td>
<td>An inadequacy in a system or process that is not a failure to comply with a standard.</td>
<td>GMP</td>
</tr>
<tr>
<td></td>
<td>Observations obtained during the inspection, are 'non-compliances' where action to be taken by the blood establishment is suggested</td>
<td></td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td><strong>Pathogen Reduction</strong></td>
<td>Procedures that alter pathogen surface structures and/or penetrate into pathogens irreversibly impeding proliferation of pathogens</td>
<td>Council of Europe: EDQM, Guide.</td>
</tr>
<tr>
<td><strong>Technologies (PRT)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Processing</strong></td>
<td>Any step in the preparation of a blood component that is carried out between the collection of blood and the issuing of a blood component.</td>
<td>Directive 2005/62/EC</td>
</tr>
<tr>
<td><strong>Qualification</strong></td>
<td>As part of validation means the action of verifying that any personnel, premises, equipment or material works correctly and delivers expected results.</td>
<td>Council of Europe: EDQM, Guide.</td>
</tr>
<tr>
<td><strong>Quality system</strong></td>
<td>The organisational structure, responsibilities, procedures, processes, and resources for implementing quality management.</td>
<td>Directive 2005/62/EC</td>
</tr>
<tr>
<td><strong>Quarantine</strong></td>
<td>The physical isolation of blood components or incoming materials/reagents over a variable period of time while awaiting acceptance, issuance or rejection of the blood components or incoming materials/reagents.</td>
<td>Directive 2005/62/EC</td>
</tr>
<tr>
<td><strong>Responsible person</strong></td>
<td>A person responsible for - ensuring that every unit of blood or blood components has been collected and tested, whatever its intended purpose, and processed, stored, and distributed, when intended for transfusion, in compliance with the laws in force in the Member State,</td>
<td>Directive 2002/98/EC Article 9</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>Risk assessment</td>
<td>Method to assess and characterise the critical parameters in the functionality of an equipment, system or process.</td>
<td>Council of Europe: EDQM, Guide.</td>
</tr>
<tr>
<td>Self-Inspection Record</td>
<td>see also audit trail</td>
<td></td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>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 which results in, or prolongs, hospitalisation or morbidity.</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td>Serious adverse reaction</td>
<td>An unintended response in donor or in patient associated with the collection or transfusion of blood or blood components that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity.</td>
<td>Directive 2002/98/EC</td>
</tr>
<tr>
<td>Specification</td>
<td>A description of the criteria that must be fulfilled in order to achieve the required quality standard.</td>
<td>2005/62/EC</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>Standard</td>
<td>The requirements that serve as the basis for comparison.</td>
<td>Directive 2005/62/EC</td>
</tr>
<tr>
<td>Standard operating procedures</td>
<td>A document describing a regularly recurring operation that affects the quality of the process. Its purpose is to ensure that the operations are carried out correctly and in a consistent way.</td>
<td>EU-Blood-SOP Manual</td>
</tr>
<tr>
<td>Statistical process control</td>
<td>Method of quality control of a product or a process that relies on a system of analysis of an adequate sample size without the need to measure every product of the process.</td>
<td>Council of Europe: EDQM, Guide</td>
</tr>
<tr>
<td>Third country</td>
<td>Any country that is not a Member State of the European Union.</td>
<td>European Commission ec.europa.eu</td>
</tr>
<tr>
<td>Third party / Subcontractor</td>
<td>Any organisation that provides a service to a procurement organisation or a BE on the basis of a contract or written agreement. Includes donor or blood testing laboratories, contract sterilisers and user hospitals which store blood components pending human application.</td>
<td>European Quality System for Tissue Banking (EQSTB), Guide for auditing tissue establishments,</td>
</tr>
<tr>
<td>Traceability</td>
<td>The ability to trace each individual unit of blood or blood component derived thereof from the donor to its final destination, whether this is a recipient, a manufacturer of medicinal products or disposal, and vice versa;</td>
<td>Directive 2005/61/EC</td>
</tr>
<tr>
<td>Validation</td>
<td>The establishment of documented and objective evidence that the pre-defined requirements for a specific procedure or</td>
<td>Directive 2005/62/EC</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
<td>Source</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------------------------------------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Validation</td>
<td>A description of the validation activities, responsibilities and procedures. It describes specifically how a certain validation is to be done.</td>
<td>Council of Europe: EDQM, Guide.</td>
</tr>
</tbody>
</table>
## Annex VI

### Participating and collaborating institutions and individuals

<table>
<thead>
<tr>
<th>Country</th>
<th>Participants</th>
<th>Working Group members</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AT</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| AUSTRIA | Zentrallnstitut für Bluttransfusion und Immunologische Abteilung *(Central Institute for Blood Transfusion and Department of Immunology)*
University Clinics Innsbruck
Anichstrasse 35
A - 6020 INNSBRUCK |
|         | Prof. Dr. Harald Schennach, Director |
| **BE**  |
| BELGIQUE / BELGIË | Het Belgische Rode Kruis Dienst voor het Bloed, Rode Kruis-Vlaanderen
Vieurgatsesteenweg 98
1050 BRUSSEL |
|         | Prof. Dr. Philippe Vandekerckhove, CEO, Director |
|         | Jan Ceulemans, QA Manager |
|         | Dr. Matine Baeten, Medical Director |
| **BG**  |
| BULGARIA | НАЦИОНАЛЕН ЦЕНТЪР ПО ХЕМАТОЛОГИЯ И ТРАНСФУЗИОЛОГИЯ
*National Center of Hematology and Transfusionology*
Plovdivsko Pole Str. 6
1756 SOFIA |
|         | Prof. Andrey Andreev, MD, PhD, Director |
|         | Svetla Bakalova, MD, PhD |
|         | Quality Assurance Department |
### EuBIS Inspection Standards and Criteria, Edition 1.0

<table>
<thead>
<tr>
<th>Country</th>
<th>Participants</th>
<th>Working Group members</th>
</tr>
</thead>
<tbody>
<tr>
<td>CZ ČESKÁ REPUBLIKA</td>
<td>Fakultní nemocnici Ostrava (Faculty Hospital Ostrava) Krevní centrum (Blood center) 17. Listopadu 1790 CZ 708 52 OSTRAVA</td>
<td>Prim. MuDr. Zuzana Cermáková Director Member of the Project Advisory Board Ing. Roman Nemec Quality Assurance Manager</td>
</tr>
<tr>
<td>CY KYPROS</td>
<td>Υπουργείο Υγείας της Κυπριακής Δημοκρατίας - Ιατρικές Υπηρεσίες και Υπηρεσίες Δημόσιας Υγείας (Ministry of Health of the Republic of Cyprus - Medical and Public Health Services) Medical Services and Public Health Services 10 Marcou Drakou, Pallouriotissa 1449 LEFKOSIA (Nicosia)</td>
<td>Dr. Stala Kioupi Agrotou, Acting Director Zoe Sideras</td>
</tr>
<tr>
<td>Country</td>
<td>Participants</td>
<td>Working Group members</td>
</tr>
<tr>
<td>---------</td>
<td>--------------</td>
<td>-----------------------</td>
</tr>
</tbody>
</table>
| DE      | *Red Cross Blood Donation Service Baden-Württemberg-Hessen*  
Institut für Transfusionsmedizin und Immunhämatologie  
Sandhofstrasse 1  
60528 FRANKFURT AM MAIN  

Prof. Dr. med.  
Dr. h.c. Erhard Seifried  
Medical Director and CEO  
Project Leader and Member of the Project Advisory Board  
Roger Fleck  
Head Administration and Finances – Frankfurt  
Dr. Thea Müller-Kuller  
Project Management  
Dr. Petra Skrablin  
Project Management |
|         |              | Prof. Dr. med.  
Christian Seidl  
Vice Medical Director, GRCBDS Frankfurt  
Project Coordinator  
Working Group 1 Leader  
MUDr. Walid Sireis  
Division Director – Quality Management  
Project Management |
|         | *Regierungspräsidium Darmstadt*  
*State Governmental Institution - Hessia*  
Dezernat VI 65.2 - Pharmazie  
Louisenplatz 2  
(Kollegiengebäude)  
DE - 64283 DARMSTADT  
Wiebke Siegel  
Member of the Project Advisory Board |
<p>| | |
|         |              |</p>
<table>
<thead>
<tr>
<th>Country</th>
<th>Participants</th>
<th>Working Group members</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paul-Ehrlich-Institut eine Einrichtung im Geschäftsbereich des Bundesministeriums für Gesundheit Paul-Ehrlich Straße 51-59 DE - 63225 LANGEN</td>
<td>Prof. Dr. Rainer Seitz, Director Division Hematology and Transfusion Medicine Dr. Magarethe Heiden</td>
</tr>
<tr>
<td>EE EESTI</td>
<td>Põhja-Eesti Regionaalhaigla Verekeskus Blood Centre North Estonia Regional Hospital J. Sültiste tee 19 13419 TALLINN</td>
<td>Dr. Riin Kullaste, MD, Director Dr. Tatjana Plahhova, MD Quality Manager Svetlana Orlova, Specialist</td>
</tr>
<tr>
<td></td>
<td>State Agency of Medicines Department of Biologicals 1, Nooruse str, 50411Tartu, Estonia</td>
<td></td>
</tr>
<tr>
<td>ES SPAIN</td>
<td>Centro Vasco de Transfusion Av. Zuatzu, 4 ES - 20018 SAN SEBASTIAN</td>
<td>Dr. Jose Manuel Cardenas, MD Technical Director</td>
</tr>
<tr>
<td></td>
<td>DG Salud Pública, Ministerio de Sanidad y Consumo Pº del Prado 18-20. ES - MADRID 28047</td>
<td>Dr. Elena Moro</td>
</tr>
<tr>
<td>Country</td>
<td>Participants</td>
<td>Working Group members</td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>FR</strong></td>
<td>Etablissement Français du Sang (EFS)</td>
<td>Leslie Sobaga</td>
</tr>
<tr>
<td><strong>FRANCE</strong></td>
<td>20 avenue du stade de France</td>
<td>Direction des Affaires Internationnes</td>
</tr>
<tr>
<td></td>
<td>93218 LA PLAINE SAINT-DENIS Cedex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prof. Dr. Jacques Hardy Director</td>
<td>Direction Qualité Nationale, Gestion des Inspections - Analyse de Risque</td>
</tr>
<tr>
<td></td>
<td>Dr. Alain Beauplet</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Direction Qualité Nationale</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leslie Sobaga</td>
<td>Working Group 4 Leader</td>
</tr>
<tr>
<td></td>
<td>Dr. Chantal Guiol, Ph.D.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dr. Fewzi Teskrat, PhD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Conseiller Spécial pour les produits issus du corps humain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Affaires européennes et internationales</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Direction de l'inspection et des Etablissements</td>
<td></td>
</tr>
<tr>
<td><strong>HU</strong></td>
<td>Agence française de sécurité sanitaire des produits de santé (AFSSAPS)</td>
<td>Dr. Eszter Miskovits, MD</td>
</tr>
<tr>
<td><strong>MAGYARORSZÁG</strong></td>
<td>Inspectorate and Companies Department</td>
<td>Director QA-QC</td>
</tr>
<tr>
<td></td>
<td>143, 147 boulevard Anatole</td>
<td></td>
</tr>
<tr>
<td></td>
<td>93285 SAINT-DENIS Cedex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dr. Chantal Guiol, Ph.D.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dr. Fewzi Teskrat, PhD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Conseiller Spécial pour les produits issus du corps humain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Affaires européennes et internationales</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Direction de l'inspection et des Etablissements</td>
<td></td>
</tr>
</tbody>
</table>

**Country Participants**

**FRANCE**

Etablissement Français du Sang (EFS)
20 avenue du stade de France
93218 LA PLAINE SAINT-DENIS Cedex

Prof. Dr. Jacques Hardy
Director
Dr. Alain Beauplet
Direction Qualité Nationale

Leslie Sobaga
Direction des Affaires Internationales
Direction Qualité Nationale, Gestion des Inspections - Analyse de Risque

Working Group 4 Leader

**FRANCE**

Agence française de sécurité sanitaire des produits de santé (AFSSAPS)
Inspectorate and Companies Department
143, 147 boulevard Anatole
93285 SAINT-DENIS Cedex

Dr. Chantal Guiol, Ph.D.

Dr. Fewzi Teskrat, PhD
Conseiller Spécial pour les produits issus du corps humain
Affaires européennes et internationales
Direction de l'inspection et des Etablissements

**MAGYARORSZÁG**

Országos Vérrellátó Szolgálat
Hungarian National Blood Transfusion Service
Karonlina str. 19 – 21
1113 BUDAPEST

Dr. Eszter Miskovits, MD
Director

Dr. Klára Baróti-Tóth, Ph.D.
Director QA-QC
<table>
<thead>
<tr>
<th>Country</th>
<th>Participants</th>
<th>Working Group members</th>
</tr>
</thead>
<tbody>
<tr>
<td>IE</td>
<td>The Irish Blood Transfusion Service Board (IMB)</td>
<td>Dr. William Murphy</td>
</tr>
<tr>
<td></td>
<td>Irish Blood Transfusion Service</td>
<td>National Medical Director</td>
</tr>
<tr>
<td></td>
<td>National Blood Centre</td>
<td></td>
</tr>
<tr>
<td></td>
<td>James’s Street</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IE - DUBLIN 8</td>
<td></td>
</tr>
<tr>
<td>IRELAND</td>
<td>Irish Medicines Board</td>
<td>Dr. Patrick Costello</td>
</tr>
<tr>
<td></td>
<td>Blood &amp; Tissue Section</td>
<td>Blood &amp; Tissues Manager, Compliance</td>
</tr>
<tr>
<td></td>
<td>Earlsfort Centre</td>
<td>Department</td>
</tr>
<tr>
<td></td>
<td>Earlsfort Terrace</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IE - DUBLIN 2I</td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td>Blóðbankinn, Landspitali (The Blood Bank, Landspitali University Hospital),</td>
<td>Dr. Sveinn Guðmundsson, MD.</td>
</tr>
<tr>
<td>ICELAND</td>
<td>Snorрабraut 60</td>
<td>Director and CEO</td>
</tr>
<tr>
<td></td>
<td>IS-105 Reykjavík</td>
<td></td>
</tr>
<tr>
<td>IT</td>
<td>Centro Nazionale Sangue (CNS) (Italian National Blood Centre)</td>
<td>Prof. Dr. Giuliano Grazzini</td>
</tr>
<tr>
<td>ITALIA</td>
<td>Istituto Superiore di Sanità National Institute of Health</td>
<td>General Director - CNS</td>
</tr>
<tr>
<td></td>
<td>Via Giano della Bella, 27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>00162 Rome</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>Participants</td>
<td>Working Group members</td>
</tr>
<tr>
<td>------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>LU</td>
<td>11 rue Batty Weber L-7259 Bereldange Luxembourg</td>
<td>Frances Delaney Project Consultant Member of the Project Advisory Board</td>
</tr>
<tr>
<td>LUXEMBOURG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MT</td>
<td>Centru Nazzjonali ta't-Trafuzjoni tad-Demm National Blood Transfusion Service</td>
<td>Dr. Alex Aquilina Director</td>
</tr>
<tr>
<td>MALTA</td>
<td>St. Luke’s Square MSD 07 G’MANGIA</td>
<td>Dr. Richard Zammit</td>
</tr>
<tr>
<td></td>
<td>Government of Malta Directorate of Health Care Services Standards Palazzo Castellania 15 Merchants’ Str. VALETTA VLT 2000</td>
<td>Dr. Miriam C. Vella</td>
</tr>
<tr>
<td>NL</td>
<td>Stiching Sanquin Bloedvoorziening Sanquin Blood Supply Foundation Plesmanlaan 125 1066 CX AMSTERDAM</td>
<td>Dr. Jeroen De Wit CEO Member of the Project Advisory Board</td>
</tr>
<tr>
<td>NEDERLAND</td>
<td></td>
<td>Dr. Jan Peter Jansen van Galen Division Director Sanquin North Working Group 2 Leader</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Boudewijn Hinloopen, BEd, BSc. Head Production Department Sanquin Region Northeast</td>
</tr>
<tr>
<td>Country</td>
<td>Participants</td>
<td>Working Group members</td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>PL POLSKA</td>
<td>Instytut Hematologii i Transfuzjologii (Institute of Haematology and Transfusion Medicine) I. Gandhi St.14 02-776 Warszawa</td>
<td>PhD MSc. Elzbieta Lachert</td>
</tr>
<tr>
<td></td>
<td>Prof. Dr. Krzysztof Warzocha, Director</td>
<td>PhD MSc. Jolanta Antoiewicz-Papis</td>
</tr>
<tr>
<td></td>
<td>MD PhD Magdalena Letowska, Deputy Director</td>
<td></td>
</tr>
<tr>
<td>RO ROMANIA</td>
<td>Universitatea de Medicina si Farmacie &quot;Victor Babes&quot; Physiology and Immunology Uta Ioan Colonel Martir No.2 300041 TIMISOARA</td>
<td>Dr. Carmen Tatu, Ph.D. Blood Transfusion Center Timisoara</td>
</tr>
<tr>
<td></td>
<td>Prof. Dr. Virgil Paunescu Director</td>
<td>Dr. Antoaneta Dragoescu</td>
</tr>
<tr>
<td></td>
<td>Ministerul Sanatatii Publice (Ministry of Public Health) 1-3 Cristian Popisteanu Street 010024 BUCHAREST</td>
<td>Dr. Gabriela Uifalean</td>
</tr>
<tr>
<td></td>
<td>Transfusion Department University Emergency Hospital Bucharest, Bucharest,</td>
<td>Dr. Corina Posea, MD Ministry of Health Medical Expert</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SO SLOVENIA</td>
<td>Zavod Republike Slovenije za transfuzijsko medicino (Blood Transfusion Centre of Slovenia) Slajmerjeva 6 SI-1000 LJUBLJANA</td>
<td>Dr. Dragoslav Domanovic, Director</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dr. Irena Razborsek, MD</td>
</tr>
<tr>
<td>Country</td>
<td>Participants</td>
<td>Working Group members</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>UK</strong></td>
<td><strong>ENGLAND</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The National Blood Authority - Blood and Transplant (NHS-BT) (England and North Wales) Oak House Reeds Crescent WD24 4QN WATFORD, HERTS</td>
<td>Dr. Lorna Williams Medical Director NHSBT Dr. Alan Slopecki Head of Quality Assurance Crescent Drive Brentwood Essex, CM15 8DP Steve Morgan NHSBT International 2440 The Quadrant Aztec West Bristol BS32 4AQ</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mark Nightingale Quality Officer Southampton Facilities Working Group 3 Leader Sarah Raymond Quality Officer</td>
</tr>
<tr>
<td><strong>UK</strong></td>
<td><strong>SCOTLAND</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The Martin Gorham Douglas Gorham Partnership Consulting Brighton Douglastown, Forfar SCOTLAND, DD8 1TP</td>
<td>Angus Macmillan Douglas, OBE Project Consultant Member of the Project Advisory Board</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Annex VII  
**Associated or observing institutions and participants**

<table>
<thead>
<tr>
<th>Country</th>
<th>Collaborating Partners</th>
<th>Collaborating members</th>
</tr>
</thead>
</table>
| AT Austria  | Universitätsklinik für Blutgruppenserologie und Transfusionsmedizin  
Auenbruggerplatz 3  
8036 Graz  
Abteilung III/4 - Strategische Angelegenheiten, Blut, Gewebe und Transplantationswesen  
Bundesministerium für Gesundheit  
Radetzkystraße 2  
1031 Wien  | Prof. Dr. Gerhard Lanzer  
Min.-Rat. Dr. Johann Kurz |
| BE Belgique / België  | Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten  
Eurostation  
Bloc 2  
Place Victor Horta 40 bte 40  
Brussels  | Walter Bontez |
| BK Bulgaria  | Bulgarian Drug Agency, Sofia  
26, Yanko Sakazov Blvd.  
1504 Sofia  | Lyubina Gaydarova |
| DK Denmark  | Danish Medicines Agency  
Axel Heides Gade 1  
DK-2300 København S  | Christina Palvad,  
MSc Pharm |
| FYROM Republic of Macedonia  | Institute Of Transfusion Medicine  
Vodnjanska 17, Skopje  
Republic of Macedonia  | Dr. Risto Dukovski  
Dr. Olga Todorovsca |
<table>
<thead>
<tr>
<th>Country</th>
<th>Collaborating Partners</th>
<th>Collaborating members</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV Latvia</td>
<td>Health statistics and medical Technologies State Agency</td>
<td>Anita Daugavvanaga Head of System of Standards for Biomedicine Health Statistics and Medical Technologies</td>
</tr>
<tr>
<td></td>
<td>Duntes 12/22, Riga, LV-1005</td>
<td></td>
</tr>
<tr>
<td>PT Portugal</td>
<td>Autoridade para os Serviços de Sangue e da Transplantação Ministério da Saúde, Av. João Crisostomo, 9 1000 Lisboa</td>
<td>Alice Lopes Cordeiro</td>
</tr>
<tr>
<td>SE Sweden</td>
<td>The National Board of Health and Welfare (Socialstyrelsen) Socialstyrelsen 106 30 Stockholm</td>
<td>Monica Axelsson and Torsten Mossberg</td>
</tr>
<tr>
<td>SK Slovakia</td>
<td>State Institute for Drug Control (SIDC) Kvetná 11 825 08 Btaislava 26a</td>
<td>Renáta Ovádeková, Ph.D.</td>
</tr>
<tr>
<td>UK United Kingdom</td>
<td>Medicines and Healthcare products Regulatory Agency (MHRA) 18-105 Market Towers 1 Nine Elms Lane London SW8 5NQ</td>
<td>Ian Rees</td>
</tr>
<tr>
<td>Liechtenstein</td>
<td>Amt für Gesundheit (Health Ministry) Amt für Gesundheit Äulestrasse 512, 9490 Vaduz</td>
<td>Brigitte Batliner</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Swissmedic, Swiss Agency for Therapeutic Products Hallerstr.7 CH-3000 Bern 9</td>
<td>Dorit Schmidkunz-Eggler</td>
</tr>
</tbody>
</table>
Common European Standards and Criteria for the Inspection of Blood Establishments

Reflecting European good practice within the area addressing the quality and safety of blood

Editors: E. Seifried and C. Seidl
Frankfurt/Germany, Edition 1.0

ENGLISH