DEPARTMENT OF BIOLOGICAL STANDARDISATION, OMCL
NETWORK & HEALTHCARE (DBO)

RFO/nko

English / Anglais

PA/PH/TS (22) 16

Strasbourg, June 2022

EUROPEAN COMMITTEE (PARTIAL AGREEMENT) ON BLOOD TRANSFUSION (CD-P-TS)

21st Edition of the Guide to the preparation, use and quality assurance of blood components ("the Blood Guide") – Change Log

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21st Edition of Blood Guide – Change Log

A log of all changes made to the standards and supporting non-standard text in the 21st Edition of the Blood Guide ("the *Guide"*) are included in the table below.

Note: Where necessary, changes have been made throughout *the Guide* updating the terms "must" and "should" in accordance with the process defined in Chapter 1 "General Notices".

The changes made in this regard are not included in the change log.

Good Practice Guidelines (GPG)

Section / Subsection	Standard	Change
1. General principles	1.1.7	New standard included to clarify that the requirements in implementing a quality system also apply to hospital blood banks.
2. Personnel and organisation	2.11	Updated standard to remove redundancy in the text regarding the assessment of training programmes. **Note**: text of standard 4.7.2.5, from the previous edition of the GPG, was incorporated here.
3. Premises	3.1.6	Updated standard on the requirements for defining temperature and humidity of the preparation areas.
3.3. Blood collection area	3.3.2.3	Updated standard to refer to ancillary facilities for consistency of terms.
3.6 Ancillary areas	3.6.2	Updated standard to refer to preparation areas for consistency of terms.
4. Equipment and materials	4.1.9	Updated standard to include reference to Regulation (EU) 2017/745 on Medical Devices and Regulation (EU) 2017/746 on In Vitro Diagnostic Medical Devices.
4.2 Data processing systems	4.2.1 – 4.2.26	New and updated standards on data processing systems in order to integrate the text of appendix 3 of the Guide and to align the text with basic requirements on computerised systems as defined in the EU GMP Guide.
4.3 Qualification and validation	4.3.1.2	Updated standard for consistency of terms to remove "collection" and "testing" as both activities are included under the term "preparation"
4.7 Control of equipment and materials	4.7.1.3	Updated standard to improve consistency in terminology regarding qualification and requalification of equipment in supplier contracts.
	4.7.1.4	Updated standard with new wording relating to the discovery of a fault or non-conformance with potential impact on the quality, safety and efficacy of blood components.
6.1 Donor eligibility	6.1.12	Updated standard to clarify that donors should be instructed to inform the blood establishment about any relevant information that was not previously disclosed to them.

6.4 Testing for infectious markers	6.4.3	Updated standard to clarify that additional testing for other agents or markers may be required, taking into account the individual risk of transmitting infection diseases.
6.5 Blood group serological testing of donors and donations	6.5.7	Updated standard to include reference to the classification of reagents in Regulation (EU) 2017/746 on In Vitro Diagnostic Medical Devices
6.6 Processing and validation	6.6.3	Updated standard to clarify text regarding use of open systems
8. Outsourced activities management	8.4.6	New standard included on the need to define the interaction of contracts of different levels.

Chapter 1 – General Notices

Section / Subsection	Standard	Change
1.2.2 Standards	n/a	Updated text defining the process by which the terms "must" and "should" are used within *the Guide* Updated text defining the process by which new or modified standards are updated and referenced within the *Guide*

Chapter 2 – Donor Selection

Section / Subsection	Standard	Change
2.1.2 Sex and gender	2.1.2.1	New section relating to the sex and gender of donors and patients including a new standard (2.1.2.1) and supporting non-standard text **(see Background Document 1)**
2.2.1 Donor eligibility	2.2.1.2	New standard relating to the requirement to have an area for confidential interviews aligned with EU Directive 2005/62/EC Annex 3.2
	2.2.1.7	New standard relating to procedures for any abnormal findings arising from the donor selection process aligned with GPG
2.2.2 Donor age	n/a	Standard removed: "Where allowed by national legislation, blood donation may be considered from donors aged 17"
2.2.3 Donor haemoglobin	2.2.3.2.	Hb-requirements for plasma and apheresis donations removed from Table 2-1 and included as specific standards **(**2.4.2.11, 2.4.2.16 and 2.4.2.18) in subsection 2.4.2 "Apheresis Donation"
2.2.4 Iron stores	2.2.4.1	Updated non standard text on measures to prevent iron depletion and to protect donor health **(see Background Document 2)**
2.2.5 Questionnaire and interview	2.2.5.1.	Updated standard to align with GPG
	2.2.5.4	Updated standard relating to the evaluation of donors for physical attributes that may suggest an underlying condition.
2.3.2 Non-infectious medical conditions	2.3.2.2 2.3.2.3	New standard and non-standard text relating to allergy and anaphylaxis **(see Background Document 3)**

	2.3.2.4	Updated standard to align with EU Directive 2004/33/EC Annex III. New and updated non-standard text relating to cancer and malignant diseases **(see Background Document 4)**
	2.3.2.5 2.3.2.6	New and updated standards relating to cardiovascular disease
2.3.4 Interventions and treatments	2.3.4.1	New non-standard text on accepting modified standards based on risk assessment for acupuncture, tattooing, body piercing and aesthetic medical procedures **(see Background Document 5)**
	2.3.4.7 2.3.4.8	Updated standard and new non-standard text on accepting modified standards based on risk assessment for surgery **(see Background Document 6)**
	2.3.4.9 2.3.4.10	Updated standard and new non-standard text on accepting a modified standard based on risk assessment for dental care / oral healthcare **(see Background Document 7)**
	2.3.4.11	New non-standard text relating to donors who have received blood and blood components for treatment other than for transfusion **(see Background Document 8)**
2.4 Specific standards for donors of different types of components	Table 2-3	A new table included providing the interval between donations. **Note:** intervals presented in hours and weeks and updated throughout the text where required.
2.4.2 Apheresis donation	2.4.2.6 – 2.4.2.14	Updated standards and non-standard text relating to donors undergoing plasmapheresis **(see Background Document 9)** **Note:** Hb-requirements for plasma and apheresis donations removed from Table 2-1 and included as specific standards 2.4.2.11, 2.4.2.16 and 2.4.2.18.
2.5.1 Donor instruction	2.5.1.1.	Updated standard relating to post donation information to align with the GPG.

Chapter 3 – Collection of Blood and Blood Components

Section /Subsection	Standard	Change
3.2 Premises for blood and blood Component Collection	3.2.1.6	Updated standard to refer to ancillary areas to ensure consistency of terms and align with GPG.
3.6.2 Venepuncture and mixing of donation during collection	3.6.2.5	Updated standard to extend the accepted bleeding time from 12 minutes to 15 minutes for whole blood donations where used in the preparation of platelets. This standard has also been clarified such that it only applies to whole blood collections. **(see Background Document 10)**
	3.6.2.6	Updated standard to extend the accepted bleeding time from 12 minutes to 15 minutes from whole blood collections where the plasma is used for direct transfusion or the preparation of coagulation factors. **(see Background Document 10)**

Chapter 4 – Processing, Storage and Distribution of Blood and Blood Components

Section / Subsection	Standard	Change
4.0 Overview	n/a	Updated non-standard text on platelet storage conditions that while optimal, agitated at room temperature, refrigerated is also possible.
4.1 Processing	4.1.1.3	Updated standard relating to the minimisation of microbial contamination load by validated cleaning and/or monitoring procedures.
4.1.2 Choice of bag system	n/a	Updated non-standard text relating to the leaching of plasticizers and regulation under the medical devices legislative framework Change to 2, 3 DPG (dipohsphocglycerate) as a parameter to be considered for studies of component preparation
4.1.3 Red cell and platelet preservation	n/a	Updated non-standard text on red cell and platelet preservation. This section was reorganised according to component type to align with component monographs. Clarification that a mix of citric acid and sodium citrate is used to adjust pH of anticoagulant below pH 6 to prevent caramelisation of glucose during heat sterilisation. New non-standard text relating to platelet additive solution and the rationale for glucose being a preferred quality marker over pH for platelets stored in additive solution **(see Background Document 11)** Updated non-standard text on microaggregates in red cells components
4.1.4 Centrifugation of whole blood derived blood components	n/a	Updated non-standard text relating to centrifugation of whole blood derived blood components to add the mean density of whole blood for ease of reference.
4.1.6 Freezing and thawing of plasma for direct transfusion	n/a	Updated non-standard text relating to the thawing and refreezing of plasma
4.1.8 Open and closed systems and sterile connection devices	n/a	Updated non-standard text relating to the use of open and closed systems incorporating GPG standards
4.2. Storage and distribution	n/a	Subsection 4.2.2 Equipment. Updated non-standard text relating to equipment clarifying that the number of temperature sensors to be used should be determined by temperature mapping Subsections 4.2.3 – 4.2.6 reorganised according to component type to align with the component monographs. Subsection 4.2.7 – 4.2.10. Restructuring of text to include all subsections and standards related to transportation under section 4.2. “Storage and Distribution”
4.3.2 Bacterial safety	n/a	Updated non-standard text relating to bacterial safety to recommend considering a quarantine period after sampling and inoculation to decrease the risk of transfusion of contaminated blood components

4.3.4 Pathogen Inactivation Technologies	n/a	Updated non-standard text related to pathogen inactivation technologies (PIT) to remove reference to “cost effectiveness “and for assessing the value of PIT in conjunction with current and alternative methods for risk reduction.

Chapter 5 – Blood Component Monographs

Note: Reference to the term “per final unit” was standardised throughout the chapter. The changes made in this regard are not included in the change log.

Section	Monograph	Change
5.0 Overview	n/a	Updated non-standard text to include a reference to current and future developments in blood component processing
Part A. Whole blood components	A-1 and A-2	A lower limit is defined for temperatures during transport
Part B. Red cell components	B-4	Haemoglobin content for red cells (buffy coat removed) was lowered from 45 to 43 (g per unit)
Part C. Platelet components	C-2 to C-6	Updated technical information to remove specification of the number of buffy coats required for producing pooled components. The number is to be determined by national regulations and the system used. **Note:** Associated text updated in the component monograph E2 where relevant for white cell components The unit for determining platelet content was standardised to 10^11 platelets throughout the relevant monographs. Updated text relating to preparation of platelets by single centrifugation method introduced and referenced throughout component monographs, where relevant. Updated text to clarify that the second processing step can either be done manually (separation of buffy coat pool by centrifugation, transfer, semi-automated expression) or automated (separation and expression of buffy coat pool during centrifugation).
Part C. Platelet components	C-4, C-5, C-9, C-10 and C-11	Updated technical information to recommend glucose as the preferred marker and replacement of pH for quality control monitoring of platelets in additive solution **(see Background Document 11)**
Part C. Platelet components Part D. Plasma components	C-6 and C-11 D-2 and D-4	Residual content of photosensitisers to be considered as part of the validation for pathogen reduced components.
Part D. Plasma components	D-2	Updated technical information for fibrinogen to be checked after processing

Chapter 6 – Component Monographs for Intrauterine, Neonatal and Infant Use

Section / Subsection	Standard	Change
6.0 Overview	n/a	Updated non-standard text clarifying that pathogen inactivation technologies are an alternative to irradiation for the prevention of Transfusion Associated Graft Versus Host Disease.

Chapter 7 – Pre-Deposit Autologous Donation

Section / Subsection	Standard	Change
7.1.2 Role of the blood establishment physician	7.1.2.3	Updated standard with clarifying text on information to be provided to the patient by the physician in charge

Chapter 8 - Immunohaematology

Section / Subsection	Standard	Change
8.2 Selection of reagents and validation of methods	8.2.1.4	Updated standard to reflect change from EU directive 98/79/EC to Regulation (EU) 2017/746. Standard updated to include a list of reagents classified as class D in Annex VIII of the Regulation.
	8.2.1.6	Updated standard changing the requirement from “all validation data for lots of reagents” to a requirement for a “Certificate of Analysis that reagent lots meet defined acceptance criteria”.
8.3 Quality control and quality assurance	8.3.1.1	Updated non-standard text on the use of a risk based assessment to inform the frequency of control
8.4 Blood group testing	n/a	Subsection 8.4.1. Updated non-standard text. Antenatal testing to identify pregnancies/foetuses at risk of haemolytic disease of the foetus and newborn (HDFN) has been added as an indication for molecular testing.
	8.4.2.6	Updated non-standard text on selection of patients based on unconfirmed phenotyping results. Clarification that unconfirmed results may be printed on a product label but should be differentiated from confirmed results
	8.4.2.7	Updated standard providing a clarification that verification of ABO and RhD blood group does not need to be verified on each subsequent donation of plasma intended only for fractionation.
	8.4.2.9	Updated non-standard text on handling of antibody-screen positive results in donors.
8.5 Pretransfusion testing	n/a	Subsection 8.5.1. Updated non-standard text to include a description of antiglobulin crossmatch.

	8.5.1.3	Updated non-standard text to introduce a reduced frequency for antibody investigation in patients with autoantibodies or patients undergoing treatments that might interfere with pre-transfusion testing, based on an individual patient assessment.
8.5.2 Type and screen procedure	8.5.2	Updated non-standard text to introduce a recommendation for antiglobulin crossmatching to be undertaken in patients with clinically significant antibodies.
8.5.3 Electronic release	8.5.3.1	Updated standard to clarify where a type and screen procedure may be used as a replacement for antiglobulin cross match testing
8.5.5 Additional considerations	n/a	Updated non-standard text on the use of extended red cell antigen matching to avoid allo-immunication. A reference to Intrauterine Transfusion (IUT) has been introduced.
	8.5.5.1	Updated standard to clarify the transfusion of RhD-positive blood to RhD-negative patients reflective of current practice.

Chapter 9 – Screening for markers of TTI

Note: There was a standardisation of terminology throughout the chapter to refer to "reactive sample" where required. The "sample" was also linked to the "donation" throughout the text.

The changes made in this regard are not included in the change log.

Section / Subsection	Standard	Change
9.0 Overview	n/a	Updated non-standard text to include clarifications on screening tests, supplementary tests, confirmatory tests and confirmed positive results.
9.1 Selection of infectious marker kits and validation of test methods	9.1.1.1	Updated standard to include reference to the In Vitro Diagnostics Regulation EU 2017/746 Note: Standard removed. 9.1.1.2 Previously read "EU Directive 98/79/EC classifies the HIV, HTLV, hepatitis B and hepatitis C screening tests in list A, Appendix II. The manufacturer must have a full quality system certified by an authorised body and must submit batch release certificates for each lot" Reference to EU Directive 98/79/EC, replaced by Regulation (EU) 2017/746. The updated standard 9.1.1.1 negates the need for the previous standard 9.1.1.2.
	9.1.1.4.	Updated standard to align with GPG
9.2 Requirements for samples	9.2.2.2	Updated non-standard text on donor archive samples.
9.3 Quality control and quality assurance	n/a	Structural changes to this section to align with Chapter 8. Section now divided into quality control, internal quality control and external quality assurance. Updated non-standard text as an introduction to the section.
	9.3.2.1	Updated standard and non-standard text on quality control testing.

		Note: Tables 9-1, 9-2 and 9-3 removed. All information within tables merged and included in the standard and non-standard text.
9.5.1 Mandatory testing requirements	9.5.1.2	Updated standard to remove reference to the analytical sensitivity limits for HBsAg testing
9.5.2 Nucleic acid amplification techniques	9.5.2.1	Updated standard to remove the lower detection limits for the validation of NAT assays.
9.5.3 Additional screening	n/a	Addition of Malaria and West Nile Virus as examples of additional testing that may be required taking into account the epidemiological situation in the region or country.

Chapter 10 - Haemovigilance

No notable changes were made to Chapter 10 in the 21st Edition of *the Guide*.

Chapter 11 – Elements for a Quality System on the Clinical Use of Blood

Section / Subsection	Standard	Change
11.7.2 Storage of blood components in hospital clinical areas	11.7.2.1	Updated standard and non-standard text relating to the storage of blood components in hospital clinical areas including a recommendation that blood should not remain out of controlled storage for more than 60 minutes if not transfused.

Appendices

The appendix on data processing systems (previously Appendix 3) was removed and relevant text was integrated into the new and updated standards on data processing systems in the GPG.

No changes were made to the other appendices.