REG-60 version 2 Requirements for marketing authorisations of medicinal products in the manufacture of which substances derived from human blood or its constituents have been used

This guideline supersedes guideline REG-60 version 1 with effect from 26th June 2026.

The guideline is issued on the basis of and in accordance with the provisions of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Certain Related Acts (the Pharmaceuticals Act), as amended, Decree No. 228/2008 Coll., on the Marketing Authorisation of Medicinal Products, as amended, and Decree No. 143/2008 Coll., on the Establishment of Detailed Requirements for Ensuring the Quality and Safety of Human Blood and Its Constituents (Decree on Human Blood), as amended.

The guideline is legally binding.

The provisions of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Certain Related Acts, as amended (hereinafter referred to as the "Act"), the provisions of Decree No. 228/2008 Coll., on the Marketing Authorisation of Medicinal Products, as amended (hereinafter referred to as the "Decree"), apply to the authorisation of industrially manufactured medicinal products in the production of which substances derived from human blood or its components have been used. The specified guidelines of the State Institute for Drug Control (SÚKL, hereinafter referred to as the "Institute") generally applicable to the marketing authorisation of medicinal products, and the provisions of Decree No. 143/2008 Coll., on the establishment of detailed requirements for ensuring the quality and safety of human blood and its components (the Decree on Human Blood), as amended.

This guideline focuses only on requirements specific to the above-mentioned group of medicinal products, which are not described in sufficient detail in the generally applicable guidelines of the Institute. The Annex contains a list of guidelines and warnings of the European Medicines Agency (EMA, hereinafter referred to as the "Agency") that are also binding for medicinal products derived from human blood or its components authorised in the Czech Republic. An up-to-date overview can be found on the http://www.ema.europa.eu website.

The requirements of this guideline apply to all applications for marketing authorisations for a medicinal product. For marketing authorisation holders in the Czech Republic, the general requirements to take into account available scientific knowledge and the obligation to minimise the adverse consequences of the effects of medicinal products on humans make it necessary to ensure the safety of all their medicinal products with regard to the risk of transmission of foreign agents derived from human blood or its components. The relevant data needed to prove safety must be included in the documentation submitted as part of the registration procedure. In view of the rapidly evolving situation, new knowledge and facts concerning the issue of quality assurance and safety of medicinal products of human and/or animal origin, it is necessary to apply the requirements of this Guideline (including all guidelines and regulations to which reference is made) not only to new applications for marketing authorisations for medicinal products, but also to all medicinal products already authorised (regular updating of the relevant documents, requirements for annual updates of the "Plasma Master File"). These requirements apply to all raw materials derived from human blood and its constituents used in the manufacture of any medicinal product (i.e. all excipients, e.g. albumin used as a vaccine stabiliser, antithrombin used in factor IX concentrate or substances derived from human blood and its constituents used in the manufacture of radiopharmaceuticals, etc.). This guideline does not affect the requirements of guideline REG-59, in its current version, '*Requirements for registration of products in relation to the risk of transmission of animal spongiform encephalopathies*'. Where both substances from the organs and tissues of ruminants and substances derived from human blood or its components have been used in the manufacture of a medicinal product, the provisions of both Guidelines apply to it.

The specific requirements for the marketing authorisation of medicinal products in the manufacture of

which substances derived from human blood or its components have been used are as follows:

Module 1

- Administrative information

  Sections 2.6.2 and 2.6.3 of the application for marketing authorisation (eAF, 'electronic application form', in its updated version) shall be completed, including the submission of the relevant documents.
- Summary of Product Characteristics, SPC/SmPC. It is required to provide information in the SPC in accordance with the corresponding instructions (see Annex).

Module 3 - CHEMICAL, PHARMACEUTICAL AND BIOLOGICAL INFORMATION ON PREPARATIONS CONTAINING CHEMICAL AND/OR BIOLOGICAL ACTIVE SUBSTANCES

In this Part, the requirements of the documents set out in the Annex apply. These requirements apply to all raw materials derived from human blood and its constituents used in the manufacture of any medicinal product (i.e. all excipients, e.g. albumin used as a vaccine stabiliser, antithrombin used in factor IX concentrate or substances derived from human blood and its constituents used in the manufacture of radiopharmaceuticals, etc.).

- Manufacturing process

  A detailed description of the manufacture, validation of the manufacturing process and a manufacturing diagram shall be provided, including all sub-stages of manufacturing included in the manufacturing process for the purpose of inactivating or removing viruses monitored for the risk of transmission of infection from the blood donor or component thereof to the recipient of the medicinal product (see virological documentation for more information).
- Control of the starting materials

  Specific requirements for plasma-derived medicinal products: For products derived from human blood or plasma, by way of derogation from the provisions of Module 3, the documentation requirements for starting materials derived from human blood or plasma specified in the 'Control of starting materials and raw materials' may be replaced by the “Basic document on plasma” (i.e. Plasma Master File, hereinafter referred to as the “PMF”). The PMF may have a certificate issued by the Agency according to this part (see Annex for valid guidelines). If the source of the active substance/excipient derived from human blood or its components is starting material other than human plasma, the same requirements apply to those starting materials derived from other human blood components (e.g. leukocytes, erythrocytes). Corresponding documentation for raw materials "Basic document on ... (name of the source material)' for any starting material derived from human blood or its components should contain the same data as the Plasma Master File (PMF).

- The Plasma Master File (hereinafter referred to as the "PMF") means a separate document, independent from the registration dossier, which provides all detailed information on the properties of all human plasma used as a starting material and/or raw material for the production of subfractions or intermediate fractions, components of excipients and active substances or active substances that are part of medicinal products or medical devices.
- Each human plasma fractionation/treatment facility shall prepare and maintain an updated set of relevant detailed information specified in the PMF.
- The PMF shall be submitted by the marketing authorisation (hereinafter referred to as the “MA”) applicant or MA holder to the Agency or the Institute. If the MA applicant or MA holder is not the same as the PMF holder, the MA applicant/holder shall ensure that the PMF is made available to him for submission to the Institute/Agency. In cases where PMF certification by the Agency is requested, the Institute will wait for the Agency to issue a certificate before deciding on the application.
- Any registration dossier containing a component derived from human plasma shall refer to the PMF corresponding to the plasma used as starting material or raw material.

The PMF shall contain information on the plasma used as starting material or raw material, in particular

(for more see the instructions in the Annex):

1. Origin of plasma

- Information on the centres or establishments where blood/plasma collection is carried out, including inspections and approvals and epidemiological data on blood-borne infections.
- Information on centres or installations where testing of plasma samples and mixtures is carried out, including information on inspections and approvals.
- Criteria for the selection and exclusion of blood/plasma donors.
- An established system that allows you to trace the path of each donation from the blood/plasma collection device to the finished products and vice versa.

2. Plasma quality and safety

- Compliance with the monographs of the European Pharmacopoeia.
- Testing of blood/plasma sampling and mixtures for infectious agents, including information on test methods and, in the case of plasma mixtures, validation data of the tests used.
- Technical characteristics of blood and plasma collection bags, including information on the anticoagulant solutions used.
- Conditions of storage and transport of plasma.
- Procedures for quarantine warehouse and/or quarantine period.
- Characterization of plasma mixtures.

3. A system established between the manufacturer of a product derived from plasma and/or a unit which processes or fractionates plasma, on the one hand, and the centres or establishments which collect and test blood/plasma, on the other hand, defining the conditions of their cooperation and the approved specifications.

4. Furthermore, the PMF must contain a list of products for which the PMF is applicable, whether they are registered or in the registration procedure, including the investigational products.

Assessment and certification:

- For products that have not yet been registered, the applicant for marketing authorisation shall submit a complete documentation to the Institute with a separate PMF attached, if this document has not already been previously evaluated by the Institute.
- The PMF is subject to scientific and technical assessment carried out by the Institute or the Agency.
- If the PMF holder applies for PMF certification to the Agency, the result of the Agency's positive evaluation is a certificate of compliance of the PMF with European Union (EU) legislation, to which an evaluation report is attached. The issued certificate is applicable throughout the EU.
- The PMF must be updated every year, and if the PMF is certified, recertification must be requested annually.
- Changes subsequently made in the PMF must be evaluated according to the conditions and procedure set out in the relevant EU regulation on the assessment of marketing authorisation variations.
- When assessing a product, the Institute will take into account the PMF certificate, the renewed PMF certificate or the change in the PMF for the given product or products.
- In cases where the PMF concerns only products derived from blood or plasma, the registration of which is limited to the Czech Republic, the scientific and technical assessment of the PMF will be carried out by the Institute.

In most cases covered by this guideline, the same plasma is the starting material for the manufacture of different dosage forms of different preparations. Under these conditions, the Institute does not insist on

the repeated submission of extensive documentation for the same raw material. The applicant may submit the PMF as an independent part of the registration dossier common to all products that are based on the same starting/raw material. The condition for this simplification is:

- ensure a clear assignment of PMF to the marketing authorisation dossier of the product whose starting material is described by the PMF data (provide a clear reference to the relevant PMF if it has already been submitted for the same data),
- submit an updated PMF once a year (complete PMF highlighting all changes that have occurred during the last year) or a statement confirming that there have been no changes. In the case of a certified PMF, the PMF update is done in accordance with the "Second Step" instruction for PMF.
- Submission of an updated PMF does not replace making changes to the registration.

For excipients derived from blood or its components (most often albumin), the shelf life should be synchronised with the shelf life of the finished medicinal product (for further clarification, we recommend you refer to the requirements of paragraph 10.3 of EMA/CHMP/BWP/706271/2010, as they are also related to the provision of information on any additional risk data on the use of the donation).

- Safety assessment in terms of foreign agents, both viral and non-viral

  With regard to foreign agents, information assessing the risk of potential contamination by foreign agents, whether non-viral or viral, shall be submitted, as provided for in the relevant guidelines, as well as in the relevant general monographs and general chapters of the European Pharmacopoeia. If the presence of potentially pathogenic foreign agents is unavoidable, the material concerned may only be used if further processing ensures their removal and/or inactivation, which shall be supported by validation in the section dedicated to viral safety evaluation. In the case of products derived from human blood or plasma, the origin and the criteria and procedures for the collection, transport and storage of the starting material must be described and documented in accordance with the provisions of Decree No 228/2008.

  Detailed information is provided on (for more information, see the guidelines in the Annex):

  - methods of inactivation/removal of foreign agents, both viral and non-viral, their inclusion in the manufacturing process, including the designation of steps carried out under 'virus-free zone' conditions (exclusion of virus contamination),
  - validation of inactivation/removal of foreign agents, both viral and non-viral, precise description of the design, date and workplace at which the validation was performed, selection of model viruses (at least 4 viruses, e.g. models representing HIV 1, HAV, HCV, lipid DNA virus, non-lipid virus, parvovirus B19) and non-viral agents, measurement results, kinetics, calculations and final evaluation of the validation result; model validation studies shall be appropriate to the manufacturing conditions (the permissible range of all parameters determining the course of inactivation/removal of foreign agents, both viral and non-viral, and the robustness of the procedure, shall be indicated); validation shall be performed separately for each product-type and for each step of inactivation/removal of foreign agents, both viral and non-viral.

Notification of new legislation – preparation of entities/establishments

On 7 August 2027, Regulation (EU) 2024/1938 of the European Parliament and of the Council of 13 June 2024 on quality and safety standards for SoHOs intended for human use will enter into force. It will also replace Directives 2002/98/EC and 2004/23/EC. The national legislation, i.e. the SoHO Act/Decree, will be updated to implement the corresponding provisions of the new Regulation (2024/1938). **For more information, see Information on the new SoHO Regulation – SÚKL.**

List of documents

Below are European documents that set out specific requirements for the marketing authorisation of

medicinal products in the manufacture of which substances derived from human blood or its components have been used. For current guidance and requirements, see http://www.ema.europa.eu and Information on the new SoHO Regulation – SÚKL (https://sukl.gov.cz/soho/informace-k-novemu-narizeni-o-latkach-lidskeho-puvodu-soho/).

Title of the European Medicines Agency guideline (see for more http://www.ema.europa.eu)	**Guideline no.**
Guideline on Plasma-Derived Medicinal Products	EMA/CHMP/BWP/706271/2010
Guideline on the scientific Data Requirements for a Plasma Master File (PMF) revision 1	EMEA/CHMP/BWP/3794/03 Rev.1
Annexes to Guideline on the Scientific Data Requirements for a Plasma Master File (PMF) revision 1	EMEA/CHMP/BWP/3794/03 Rev.1 Annexes
Concept paper on the revision of the Guideline on the Scientific Data Requirements for a Plasma Master File (PMF) Revision 1 and Annexes (draft)	EMA/CHMP/BWP/91140/2025
Plasma Master File (PMF) requirements. Questions and Answers for PMF Holders	EMA/CHMP/BWP/153612/2025. Rev 1
Procedural Announcement: Temporary derogations to certain eligibility criteria for whole blood and blood components donors in the context of a risk of shortage caused by the Influenza A(H1N1) pandemic	EMA/715726/2009
Guideline on Epidemiological Data on Blood Transmissible Infections – revision 1	EMA/CHMP/BWP/548524/2008 rev 1
Appendices to Guideline on epidemiological data on blood transmissible infections	EMA/735037/2015 Rev.1
Guideline on validation of Immunoassay for the Detection of Antibody to Human Immunodeficiency Virus (anti-HIV) in Plasma Pools	EMEA/CHMP/BWP/298388/05
Guideline on validation of Immunoassay for the Detection of Hepatitis B Virus Surface Antigen (HBsAg) in Plasma Pools	EMEA/CHMP/BWP/298390/2005
Guideline on requirements for Plasma Master File (PMF) Certification	CPMP/BWP/4663/03
CHMP position statement on quality and safety assessment for the Plasma Master File (PMF) certification with regard to donor deferral criteria for sexual risk behaviour	EMA/CHMP/BWP/76987/2021
Guideline on the Investigation of Manufacturing Processes for Plasma-Derived Medicinal Products with Regard to variant Creutzfeldt-Jakob disease (VCJD) risk	CPMP/BWP/CPMP/5136/03
REPORT OF PMF EPIDEMIOLOGY WORKSHOP with INDUSTRY	EMEA/CHMP/BWP/233408/2009
CHMP Reflection Paper on Creutzfeldt-Jacob Disease and Plasma-Derived and Urine-Derived Medicinal Products	EMA/CHMP/BWP/303353/2010 Rev 3
CPMP Position Statement on West-Nile Virus and Plasma-Derived Medicinal Products	EMEA/CPMP/BWP/3752/03/adopted
CPMP Position Statement on Non-Remunerated And Remunerated Donors: Safety And Supply of Plasma-Derived Medicinal Products	EMEA/CPMP/BWP/1818/02/final
Position paper on Plasma-Derived Medicinal Products: Alt Testing (Corrigendum, Sept. 1999)	CPMP/BWP/385/99
Reflection paper on viral safety of plasma-derived medicinal products with respect to Hepatitis E virus	EMA/CHMP/BWP/723009/2014
Guideline on the replacement of rabbit pyrogen testing by an alternative test for plasma derived medicinal products	EMEA/CHMP/BWP/452081/2007
Guideline on the Warning on transmissible agents in summary of product characteristics (SmPCs) and package leaflets for plasma derived medicinal products	EMA/CHMP/ BWP/360642/2010
Points to consider for assessors. New factor VIII and factor IX products: potency determination for labelling and assays for testing post-infusion samples	EMA/CHMP/BPWP/231587/2015

Title of the European Medicines Agency guideline (see for more http://www.ema.europa.eu)	**Guideline no.**
Note for guidance on Virus Validation Studies: The Design, Contribution and Interpretation of Studies validating the Inactivation and Removal of Viruses	CPMP/BWP/268/95
Workshop report: Characterisation of new clotting factor concentrates (FVIII, FIX) with respect to potency assays used for labelling and testing of post infusion samples	EMA/135928/2014
EMEA Workshop on the Plasma Master File	EMEA/CPMP/BWP/1737/02
Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials	EMA/CAT/22473/2025
Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products	EMA/CAT/80183/2014
Guideline on the core SPC for human plasma derived Hepatitis-B immunoglobulin for Intramuscular Use	CPMP/BPWG/4222/02
Guideline on the Core SPC for human plasma derived Hepatitis-B immunoglobulin for Intravenous Use	CPMP/BPWG/4027/02
Guideline on the core SmPC for Human Anti-D Immunoglobulin for Intravenous Use	EMA/CHMP/BPWP/319619/2005 Rev. 2
Guideline on the core SmPC for Human Anti-D Immunoglobulin for Intramuscular Use	EMA/CHMP/BPWP/29205/2005 rev. 2
Guideline on the core SPC for Human Plasma Derived von Willebrand Factor	CPMP/BPWG/278/02
Core SPC for Human Varicella Immunoglobulin for Intramuscular Use	CPMP/BPWG/3726/02
Core SPC for Human Rabies Immunoglobulin for Intramuscular Use	CPMP/BPWG/3728/02
Core SPC for Human Tetanus Immunoglobulin for Intramuscular Use	CPMP/BPWG/3730/02
Core SPC for Human Tick-Borne Encephalitis Immunoglobulin for Intramuscular Use	CPMP/BPWG/3732/02
Guideline on core summary for product characteristics for Human Albumin Solution – Revision 3	EMA/CHMP/BPWP/494462/2011
Core SPC for Human Prothrombin Complex Products	CPMP/BPWG/3735/02
Guideline on core SmPC for Plasma-derived Fibrin Sealant / Haemostatic Products	EMA/CHMP/BPWP/598816/2010 Rev. 1
Guideline on core SmPC for Human Normal Immunoglobulin for Intravenous administration (IVIg) – Rev. 6	EMA/CHMP/BPWP/94038/2007 Rev. 6 Corr.
Guideline on the Core SPC for Human Plasma derived Antithrombin	CPMP/BPWG/3226/99
Guideline on core SmPC for Human Normal Immunoglobulin for Subcutaneous and Intramuscular administration	EMA/CHMP/BPWP/143744/2011 rev. 1
Guideline on core SmPC for Human Plasma Derived and Recombinant Coagulation Factor VIII Products – Revision 3	EMA/CHMP//BPWP/1619/1999
Guideline on core SmPC for Human Plasma Derived and Recombinant Coagulation Factor IX Products – revision 3	EMA/CHMP/BPWP/277622/2024 rev. 3
Guideline on core summary of product characteristics (SmPC)for human fibrinogen products	EMA/CHMP/BPWP/691754/2013 Rev 1

Other binding documents:
European Pharmacopoeia, current edition of European Pharmacopoeia Online, https://pheur-online.edqm.eu/home/

European Commission directives	2003/63/EC 2001/83/EC 2002/98/EC 2004/33/EC 2005/61/EC 2005/62/EC 2002/364/EC
Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Certain Related Acts (Pharmaceuticals Act), as amended	
Decree No. 228/2008 Coll., on the Marketing Authorisation of Medicinal Products, as amended	
Decree No. 143/2008 Coll., on the Establishment of Detailed Requirements for Ensuring the Quality and Safety of Human Blood and Its Components (Decree on Human Blood), as amended	
SÚKL Guidelines generally applicable to the marketing authorisation of medicinal products (for more information, see http://sukl.gov.cz/o-nas/pokyny-a-formulare/)	