IPFA Donor Information Standard:
Plasma Derived Medicinal Products

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Approved: by the IPFA Executive Board, October 2018

Background

The objective of the IPFA Standard for Donor Information is to define the ethical and guiding principles to maintain and enhance the quality of donor information of its member organisations involved in the collection of human blood and plasma and the manufacture and supply of medicinal products derived from human plasma.

This voluntary standard was developed by the IPFA Working Group on Regulatory and Clinical Affairs (WGRCA) and was approved by the IPFA Board of Directors on October 16th, 2018, in Boston/Braintree, MA, USA.

For questions about this IPFA Standard contact International Plasma and Fractionation Association

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1. Introduction

Around the world people depend on vital protein therapeutics derived from human plasma. Plasma-derived medicines are essential for the treatment of coagulation factor deficiencies such as haemophilia, immune deficiencies as well as immune system related diseases such as inflammatory and auto-immune diseases, and circulatory dysfunctions such as shock. These medicines are recognised by the World Health Organisation (WHO) as essential for any health care programme.

A donation of the source material from which these medicinal products are manufactured, is considered voluntary and non-remunerated if the person gives blood, plasma of his/her own free will and receives no payment for it, either in the form of cash, or in kind which could be considered a financial gain for the donor.

These individuals who donate their blood or plasma provide a unique and precious gift in an act of human solidarity. Blood and plasma collection services have a reciprocal duty of care towards these donors. Donors should be provided with high standards of ethical care and safety. Informed consent is a process based on the ethical principles of autonomy and respect for the individual. These facilities must therefore initiate donor information or education services to enable these individuals to be fully informed and understand the process, destination(s) and ultimate use(s) of their donation.

2. Scope

This standard applies to facilities that collect blood from which the plasma is recovered or directly collected through plasmapheresis from donors for further processing via fractionation into plasma derived therapeutics (Appendix 1).These information standards are intended to be provided in addition in Europe to the Directive 2004/33/EC of 22 March 2004 Annex II Information Requirements, Part A and in the US to the required informed consent procedure under 21 Code of Federal Regulations (CFR) 640.61–Informed consent and the FDA Guidance for Industry[1].

[1] Guidance for Industry: Informed Consent Recommendations for Source Plasma Donors Participating in Plasmapheresis and Immunization Programs (http://www.fda.gov/cber/guidelines.htm)

3. Purpose

This Standard focuses on educating and informing donors on the destination of their voluntary recovered plasma and source plasmapheresis donations and use for further processing via fractionation into plasma derived therapeutics.

The purpose of this standard is to establish minimum requirements for education and information provided to donors to:

a) Improve donor knowledge and insight into the full extent of the use of their donation.
b) Promote transparency to ensure sufficient information is provided to the donor to make an informed decision so that informed consent is provided with full knowledge.

Each organisation may provide the information in any format of their choice, including very limited length of text, as well as virtual material, as long as it contains the main messages and criteria and fulfils the objectives.

4. Abbreviations and acronyms

PDMP	Plasma Derived Medicinal Product
SOP	Standard Operating Procedure
US FDA	United States Food and Drug Administration
EC	European Community

5. Terms and Definitions

5.1 Recovered plasma

Plasma recovered from whole blood donation after blood components have been separated thereof.

5.2 Source plasma

Plasma collected by apheresis, intended for fractionation and the manufacturing of medicinal products.

5.3 Plasma derived medicinal product (PDMP)

Medicinal products (such as human serum albumin, various immune globulins and various coagulation factor concentrates and other proteins) manufactured from human plasma.

6. Requirements

6.1 Pre-donation information on the utilization and destination of their donation is required to be provided at the time an individual registers for blood/plasma donation to:

a) Ensure donor awareness of the importance of voluntary non-remunerated donation, particularly regular donation, to maintain an adequate supply of safe plasma as source material for patients who require plasma derived medicinal products.
b) Foster and increase donor's trust and confidence in the service and secure the donor's cooperation.

6.2 Each blood or plasma centre shall have an electronic, paper or video-based donor information and education system (or materials) based on these standards to provide relevant and appropriate information to donors.

6.3 The information provided must be factual, culturally appropriate and in a language and form that is clear and easy to understand by all donors. This means that the information is presented in simple language and in a way that allows the recipient to understand and act on it after a single reading/visual.

6.4 The content must be adapted (language, tone, style, words, images, graphics, format, layout, design and amount of information) to ensure it is easy, accessible and meaningful for the target audience.

6. 5 In the educational materials, the following content should be addressed:

a) Nature and use of blood and its components to provide plasma for fractionation via whole blood and plasmapheresis. Nature and proteins of interest in human plasma to illustrate the donation supports a variety of injectable biological therapeutics.
b) Overview of pooling plasma and general elements of the fractionation process to isolate specific proteins of interest to create various therapeutic PDMPs (refer to Appendix 3 for optional detail). This is optional, only if donor IS interested it can be presented.
c) A few simple examples of the patient populations and acute and chronic clinical conditions the PDMPs treat (refer to list from Appendix 2 for detail).
d) The one donation- many recipients concept to convey that the donation is essential to support a variety of patients and conditions.
e) The importance of donor compliance in the donor selection process; and the donor's duties and responsibilities to ensure a safe donation.
f) Geographical extent of supply of plasma to companies and markets of PDMP in response to patient needs.

6.6 User testing or other form of donor consultation ensures that donor's views on the content, design and layout of the information are taken into account so that the final material key messages are understood. The donor's comprehension of the information shall be assessed initially in order to assure their understanding of the content. The comprehension assessment methods may be determined by the individual service/centre.

6.7 The educational material should address how donors with doubts or concerns and/or any anxiety are reassured. Furthermore, an explanation must be given on the confidentiality and privacy rules.

6.8 Training in blood or plasma donor education should be provided for all staff who interact with prospective and current donors. These include nurses, phlebotomists, doctors, donor recruitment staff and volunteers. The purpose of training in blood or plasma donor counselling is to provide staff with the necessary knowledge and skills to conduct education effectively.

7. Audit and Compliance Verification

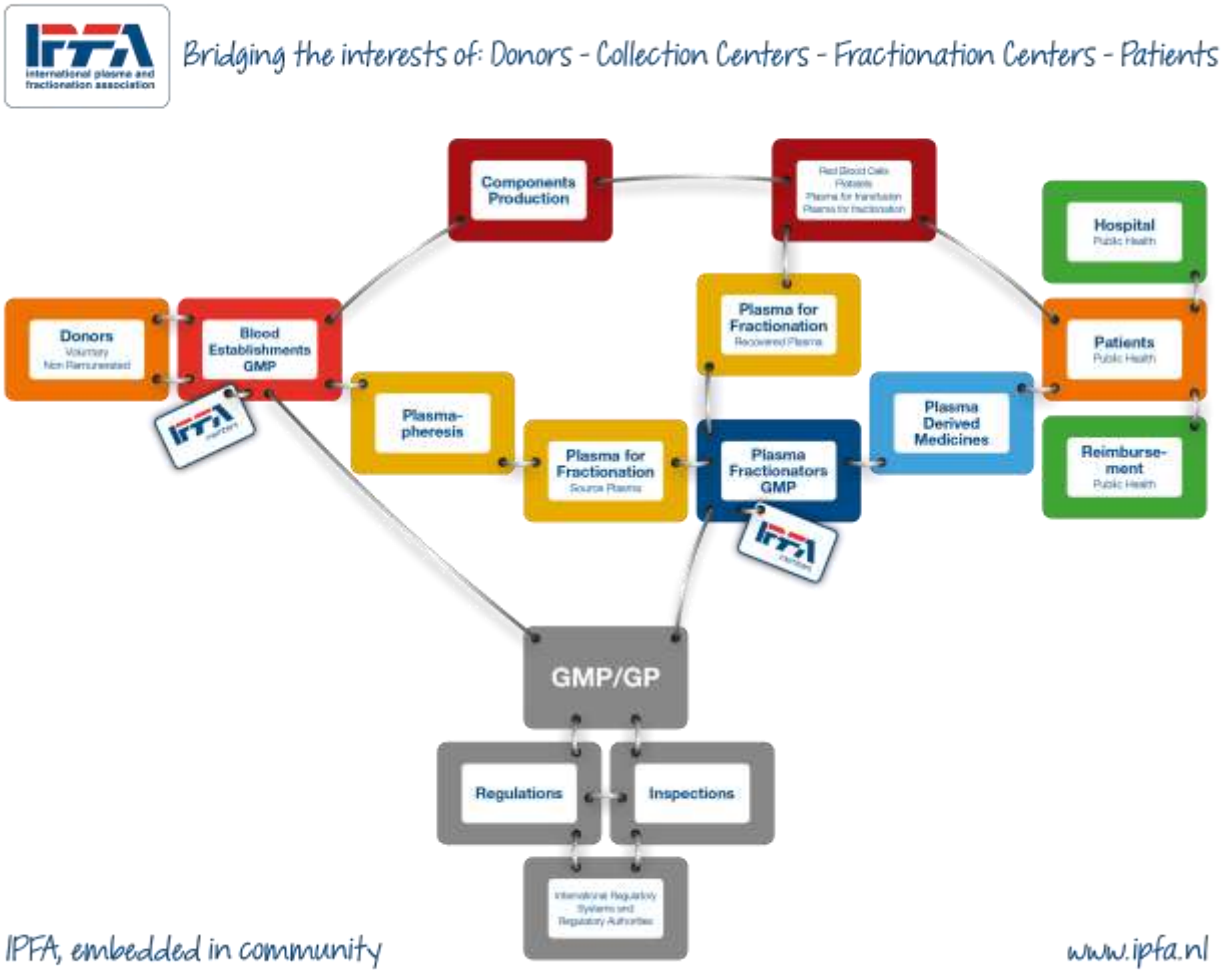
7.1 During the internal audit, auditors shall request the facility SOPs that relate to the Donor Information PDMP Standard. They shall then review the procedures for compliance to the Standard.

7.2 During a regulatory authority facility audit, auditors may review material that relate to the Donor Information PDMP Standard to ensure the blood or plasma centre is following the SOPs.

8. List of Appendices

Appendix 1: IPFA Plasma Chain
Appendix 2: Plasma Products and Clinical Applications
Appendix 3: Plasma Fractionation Process

Appendix 1: IPFA Plasma Chain



Appendix 2: Plasma Products and Clinical Applications

The detail provided here is optional and may be used as a reference to extract information to provide simpler material.

Burnouf T., Padilla A., Schaerer C. et al, Contributions from Urbaniak S., Strengers P. ANNEX 4 WHO recommendations for the production, control and regulation of human plasma for fractionation, Annex 1; Adopted by the 56th meeting of the WHO Expert Committee on Biological Standardization, 24-28 October 2005.

Products	Main Indications
Albumin	
Human Serum Albumin	Volume replacement
Blood Coagulation factors	
Factor VIII[33]	Haemophilia A
Prothrombin complex (PCC/PPSB)[34]	Complex liver diseases; warfarin or coumarin derivatives reversal[35]
Factor IX	Haemophilia B
Factor VII	Factor VII deficiency
Von Willebrand Factor	von Willebrand factor deficiency (Type 3 and severe forms of Type 2)
Factor XI	Haemophilia C (FXI deficiency)
Fibrinogen	Fibrinogen deficiency
Factor XIII	Factor XIII deficiency
Activated PCC	Haemophilia with anti-FVIII (or FIX) inhibitors
Protease inhibitors	
Antithrombin	Antithrombin III deficiency
Alpha 1 antitrypsin	Congenital deficiency of alpha 1 antitrypsin with clinically demonstrable panacinar emphysema
C1-inhibitor	Hereditary angioedema
Anticoagulants	
Protein C	Protein C deficiency / (thrombosis)
Fibrin sealant (fibrin glue)[36]	Topical haemostatic / healing /sealing agent (surgical adjunct)
Intramuscular Immunoglobulins (IMIG)	
Normal (polyvalent)	Prevention of hepatitis A (also rubella, and other specific infections)
hepatitis B	Prevention of hepatitis B
.tetanus	treatment or prevention of tetanus infection
anti-Rho(D)	Prevention of the haemolytic disease of the new-born
Rabies	Prevention of rabies infection
Varicella/zoster	Prevention of chicken-pox infection
Intravenous Immunoglobulins (IVIG)	
normal (polyvalent)	Replacement therapy in immune deficiency states immune modulation in immune disorders
Cytomegalovirus (CMV)	Prevention of CMV infection (e.g.after Bone Marrow Transplantation)
Hepatitis B	Prevention of HBV infection (e.g.liver transplant)
Rho (D)	Prevention of the haemolytic disease of the new-born.
Intravenous Immunoglobulins M	septic shock; binding of endotoxins

[33] Some factor VIII concentrates containing von Willebrand factor are effective for the treatment of von Willebrand disease

[34] Prothrombin complex contains factor II, factor VII, factor IX, and factor X. The content in factor VII may vary depending upon products.

[35] May be used, in the absence of purified plasma products, for substitutive therapy in Factor VII, Factor X, or Protein C deficiency. Whenever available, purified Factor IX should be used to treat hemophilia B.

[36] Product obtained by mixing a concentrate rich in fibrinogen and a concentrate rich in thrombin

APPENDIX 3: Plasma Fractionation Process

The detail provided here is optional and may be used as a reference to extract information to provide simpler material.

Burnouf T. Current status and new developments in the production of plasma derivatives. 2016 International Society of Blood Transfusion, ISBT Science Series (2016) 11 (Suppl. 2), 18–25. Fig.1

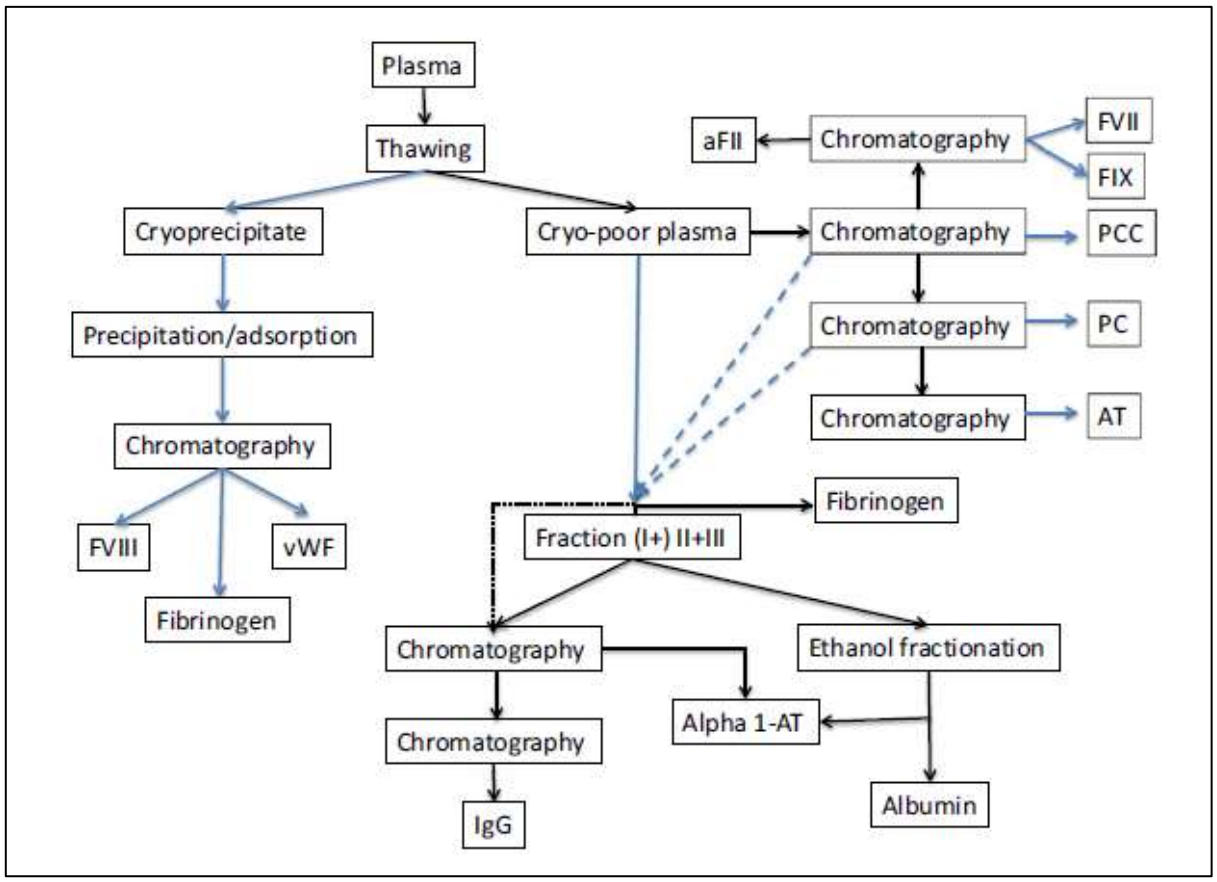


Fig. 1 Current evolution of the traditional plasma fractionation process illustrating the increasing use of chromatography (a) to isolate labile proteins sequentially from cryoprecipitate-poor plasma and (b) to purify immunoglobulins from fractions generated by ethanol fractionation. Abbreviations: alpha 1-AT, alpha 1-antitrypsin; aFII, activated factor II (thrombin); AT, antithrombin; FVII, factor VII; FVIII, factor VIII; FIX, factor IX; IgG, immunoglobulin G; PC, protein C; PCC, prothrombin complex concentrate; vWF, von Willebrand factor.