

# Technical Guide

for the elaboration and use of  
monographs on  
**human plasma-derived  
products**

European Pharmacopoeia

**European Directorate for the Quality of Medicines & HealthCare**



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# TECHNICAL GUIDE FOR THE ELABORATION AND USE OF MONOGRAPHS ON HUMAN PLASMA-DERIVED PRODUCTS

## 1. PURPOSE OF THE GUIDE

This document is intended to provide guidance to authors (and contributors) and users of European Pharmacopoeia (Ph. Eur.) monographs on human plasma-derived products. This applies in particular to:

- Group of Experts No. 6B (Human blood-derived products);
- authorities responsible for granting marketing authorisations for human plasma-derived products;
- Official Medicines Control Laboratories (OMCLs);
- manufacturers of human plasma-derived products;
- public and private analytical laboratories working for one of the above;
- the Secretariat of the European Pharmacopoeia and any other departments of the European Directorate for the Quality of Medicines & HealthCare (EDQM).

## 2. STATUS AND SCOPE OF THE GUIDE

The monographs and general chapters of the European Pharmacopoeia set out the official standards for medicinal products. This guide provides information on the elaboration and use of these standards but has no official status. In the event of doubt or dispute, the text of the European Pharmacopoeia alone is authoritative.

## 3. GENERAL INFORMATION

### 3.1. PHARMACOPOEIAL REQUIREMENTS

Monographs and general chapters of the European Pharmacopoeia must be interpreted with reference to the *General Notices*. All users of the European Pharmacopoeia must be familiar with this text.

The main items relevant for human plasma-derived products are given below:

Statements in monographs are mandatory requirements unless otherwise stated: “*Unless otherwise indicated in the General Notices or in the monographs, statements in monographs constitute mandatory requirements. General chapters become mandatory when referred to in a monograph, unless such reference is made in a way that indicates that it is not the intention to make the text referred to mandatory but rather to cite it for information*” (Ph. Eur. 7<sup>th</sup> Edition).

As regards compliance with monographs, the *General Notices* state that: “*An article [that is the subject of a monograph] is not of Pharmacopoeia quality unless it complies with all the*

1 requirements stated in the monograph. This does not imply that performance of all the tests in  
2 a monograph is necessarily a prerequisite for a manufacturer in assessing compliance with  
3 the Pharmacopoeia before release of a product. The manufacturer may obtain assurance that  
4 a product is of Pharmacopoeia quality from data derived, for example, from validation  
5 studies of the manufacturing process and from in-process controls. Parametric release in  
6 circumstances deemed appropriate by the competent authority is thus not precluded by the  
7 need to comply with the Pharmacopoeia” (Ph. Eur. 7<sup>th</sup> Edition).

8 As regards alternative methods, the *General Notices* state that: “The tests and assays  
9 described are the official methods upon which the standards of the Pharmacopoeia are based.  
10 With the agreement of the competent authority, alternative methods of analysis may be used  
11 for control purposes, provided that the methods used enable an unequivocal decision to be  
12 made as to whether compliance with the standards of the monographs would be achieved if  
13 the official methods were used. In the event of doubt or dispute, the methods of analysis of the  
14 Pharmacopoeia are alone authoritative” (Ph. Eur. 7<sup>th</sup> Edition).

### 15 **3.2. ALTERNATIVE METHODS**

16 The test methods prescribed in monographs are the reference methods on which the quality  
17 standards are based. As indicated above under Pharmacopoeial requirements, other methods  
18 of analysis may be used for a variety of reasons. Firstly, pharmacopoeial methods have been  
19 chosen for application to all the relevant products that were available at the time of their  
20 elaboration. Other available methods can be used if it is demonstrated by validation that the  
21 alternative method is equivalent to the official method or more suitable, in accordance with  
22 the *General Notices*. Secondly, the methods have been developed for application in a variety  
23 of laboratories with standard equipment but this does not rule out the use of alternative,  
24 validated methods. Monographs are revised periodically to keep pace with progress in  
25 techniques but pending these revisions, new methods can be used as alternatives if validated  
26 and authorised by the competent authorities.

#### 27 **Use of Animals**

28 In accordance with the provisions of the *European Convention for the Protection of*  
29 *Vertebrate Animals Used for Experimental and Other Scientific Purposes* (1986)<sup>1</sup> and the  
30 European Directive<sup>2</sup> on the same principles, Ph. Eur. tests must be carried out in such a way  
31 as to use the minimum number of animals for a significant result and to cause the least pain,  
32 suffering, distress or lasting harm. Humane endpoints must be used wherever possible for all  
33 tests even if not referred to in a specific monograph, since references to humane endpoints are  
34 included as examples only where practical advice can be given.

### 35 **3.3. GENERAL CHAPTERS AND MONOGRAPHS**

36 The following general chapters published under headings 2.6. *Biological tests* and 2.7.  
37 *Biological assays* apply whenever they are given as a reference in a monograph on a blood  
38 product:

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<sup>1</sup> European convention for the protection of vertebrate animals used for experimental and other scientific purposes. European Treaty series No. 123. Council of Europe (1986).

<sup>2</sup> Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes. Official Journal L 358, pp.1-28. European Union (1986).

1 **Biological tests specific to plasma-derived products:**

- 2 – Prekallikrein activator (2.6.15);
- 3 – Test for anticomplementary activity of immunoglobulin (2.6.17);
- 4 – Anti-A and anti-B haemagglutinins (2.6.20);
- 5 – Activated coagulation factors (2.6.22);
- 6 – Test for anti-D antibodies in human immunoglobulin (2.6.26).

7 **Biological assays specific to plasma-derived products:**

- 8 – Assay of human coagulation factor VIII (2.7.4);
- 9 – Test for Fc function of immunoglobulin (2.7.9);
- 10 – Assay of human coagulation factor VII (2.7.10);
- 11 – Assay of human coagulation factor IX (2.7.11);
- 12 – Assay of heparin in coagulation factors (2.7.12);
- 13 – Assay of human anti-D immunoglobulin (2.7.13);
- 14 – Assay of human antithrombin III (2.7.17);
- 15 – Assay of human coagulation factor II (2.7.18);
- 16 – Assay of human coagulation factor X (2.7.19);
- 17 – Assay of human von Willebrand factor (2.7.21);
- 18 – Assay of human coagulation factor XI (2.7.22);
- 19 – Assay of human plasmin inhibitor (2.7.25);
- 20 – Assay of human protein C (2.7.30);
- 21 – Assay of human protein S (2.7.31);
- 22 – Assay of human  $\alpha$ -1-proteinase inhibitor (2.7.32).

23 **Additional tests not restricted to blood products:**

- 24 – Sterility (2.6.1);
- 25 – Pyrogens (2.6.8);
- 26 – Bacterial endotoxins (2.6.14);
- 27 – Nucleic acid amplification techniques (2.6.21): *Validation of nucleic acid*
- 28 *amplification techniques (NAT) for the detection of hepatitis C virus (HCV) RNA in*

1            *plasma pools : guidelines, and Validation of nucleic acid amplification techniques*  
2            *(NAT) for the quantification of B19 Virus (B19V) DNA in plasma pools: guidelines;*

3            – Monocyte-activation test (2.6.30).

4 Monographs on plasma-derived products are published in the European Pharmacopoeia in  
5 alphabetical order of the title.

### 6    **3.4. HOW MONOGRAPHS AND CHAPTERS ARE ELABORATED AND UPDATED**

#### 7    3.4.1. **Inclusion of a new general chapter or a new monograph in the European** 8            **Pharmacopoeia**

9    Proposals to add a new text on the work programme can be made by:

10            – the Chair of the European Pharmacopoeia Commission;

11            – a delegation;

12            – the chair of Group 6B;

13            – the Secretariat of the Ph. Eur., for example on the basis of information and data  
14            provided via the EDQM *Helpdesk*<sup>3</sup> by a manufacturer or by a user of the European  
15            Pharmacopoeia.

16    It is the European Pharmacopoeia Commission which accepts the proposal or not, and if  
17    accepted, it adds the item to the work programme of the Group of Experts (see the *Rules of*  
18    *procedure of the European Pharmacopoeia Commission*<sup>4</sup>).

19    For many classes of medicinal substances or products, monographs are usually (but not  
20    always) included in the European Pharmacopoeia only when the product is produced by more  
21    than one manufacturer. This limitation is not always applied since it has been found that there  
22    can be a need for an official standard even when there is only one producer.

23    In general, the standards that are attained by the products that already on the market are taken  
24    into consideration during the elaboration of a new monograph. Consequently, where there is  
25    sufficient information demonstrating that the product is of Pharmacopoeia quality, it will not  
26    be necessary to retest these products to show compliance with the pharmacopoeial  
27    requirements when the monograph is finalised and published.

28    Once the new monograph is drafted, the monograph is published in *Pharmeuropa* for public  
29    enquiry. All the interested parties have 3 months to send their comments to their National  
30    Pharmacopoeial Authority (NPA), which centralises all the comments from their country.  
31    NPAs then have 2 months to send the compiled comments to the Secretariat of the Ph. Eur.  
32    via the EDQM *Document Review Tool (DRT)*<sup>5</sup>. Manufacturers outside Europe and pan-  
33    European organisations have 3 months to send their comments to the Secretariat via the  
34    *Helpdesk*<sup>3</sup>.

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<sup>3</sup> [www.edqm.eu/hd](http://www.edqm.eu/hd)

<sup>4</sup> Rules of procedure of the European Pharmacopoeia Commission. PA/PH/SG (07) 4 COM 1R. Council of Europe, European Directorate for the Quality of Medicines & HealthCare (2007).

<sup>5</sup> <http://drt.edqm.eu>

1 The Secretariat makes a consolidated document from all these comments.

2 The consolidated comments are then examined by Group 6B at the meeting following the end  
3 of the consultation period.

4 After the study of these comments, if there is no major change in the text and if no restrictions  
5 are added to the text published for comment, the text is proposed for adoption at the next  
6 Commission session. If there is a major change in the text or if restrictions are added, the text  
7 is published again for public enquiry in *Pharmeuropa*.

8 If the text is adopted, it is published in the European Pharmacopoeia 6 months after the  
9 Commission session, and implemented 6 months later. Should the text not be adopted, either  
10 it will go back to the group or no specific monograph on this particular product will be  
11 published in the European Pharmacopoeia.

#### 12 3.4.2. **Revision of general chapters and monographs for human plasma-derived products**

13 Proposals to revise a text can be made by:

14 – the Chair of the European Pharmacopoeia Commission;

15 – a delegation;

16 – the chair of Group 6B;

17 – the Secretariat of the Ph. Eur., for example on the basis of information and data  
18 provided via the *Helpdesk*<sup>3</sup> by a manufacturer or by a user of the European  
19 Pharmacopoeia.

20 It is the European Pharmacopoeia Commission that refers requests for revision to the relevant  
21 Group of Experts (see the *Rules of Procedure of the European Pharmacopoeia Commission*<sup>4</sup>).

22 A request for revision must be submitted along with a justification for this revision, supported  
23 by data and documents.

24 During the revision of a monograph, the standards attained by blood products that are already  
25 on the market will be taken into consideration.

26 Once the monograph is revised, it is published in *Pharmeuropa* for public enquiry. The  
27 interested parties have 3 months to send their comments to their NPA, which centralises all  
28 the comments of their country. NPAs then have 2 months to send the compiled comments to  
29 the Secretariat of the Ph. Eur. via the DRT<sup>5</sup>. Manufacturers outside Europe and pan-European  
30 organisations have 3 months to send their comments to the Secretariat of the Ph. Eur. via the  
31 *Helpdesk*<sup>3</sup>. The Secretariat makes consolidated comments from all these comments.

32 The consolidated comments are studied by Group 6B at the meeting following the end of the  
33 consultation period.

34 After the study of these comments, if there is no major change in the text and if no restrictions  
35 are added to the text published for comments, the text is proposed for adoption at the next  
36 Commission session. If there is a major change in the text or if restrictions are added, the text  
37 is published again for public enquiry in *Pharmeuropa*.

1 If the revised text is adopted, it is published in the European Pharmacopoeia 6 months after  
2 the Commission session, and implemented 6 months later. Should the text not be adopted, it  
3 will either go back to the group for further study/revision or stay as it is and not be revised.

## 4 **4. CONTENT OF THE MONOGRAPHS**

### 5 **4.1. STRUCTURE AND CONTENT OF THE MONOGRAPHS ON HUMAN PLASMA-DERIVED** 6 **PRODUCTS**

#### 7 **4.1.1. General points**

8 The pharmacopoeial requirements for plasma-derived products and the tests to be carried out  
9 are those described in the relevant specific monographs, where one exists.

10 The provisions of the “base” monographs, i.e. *Human plasma for fractionation (0853)*,  
11 *Human normal immunoglobulin (0338)* and *Human normal immunoglobulin for intravenous*  
12 *administration (0918)* apply to all fractionated products, human normal specific  
13 immunoglobulin and human normal specific immunoglobulin for intravenous administration,  
14 respectively, including those for which there is no specific monograph. The base monographs  
15 prescribe essential requirements which supplement and expand on requirements contained in  
16 the monographs on specific products. The authors and users of specific monographs must be  
17 familiar with the contents of the relevant monographs in order to be able to draft or use the  
18 specific monographs correctly.

19 The requirements given in the base monographs are usually not repeated in the specific  
20 monographs. The specific monographs include a reference to the base monograph.

21 The specific monographs must be used and applied, taking account of the explanations,  
22 guidance and requirements given in all documents mentioned above, including the base  
23 monographs.

24 It is expected that the test and assay methods used routinely are appropriately transferred and  
25 checked for suitability by the users, in accordance with accepted procedures, e.g. those in the  
26 Technical Guide for the Elaboration of Monographs of the Ph. Eur.

27 The monographs are regularly updated to be in line with the guidelines established by the  
28 European Medicines Agency (EMA) on plasma-derived products<sup>6</sup> such as the core Summary  
29 of Product Characteristics.

#### 30 **4.1.2. Sections of the monographs**

31 The various sections are mandatory, with the exception of the Storage section and for some  
32 items, the Labelling section.

33 Informational statements are identified by their content and drafting style. See also the  
34 *General Notices* (current edition of the Ph. Eur.).

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<sup>6</sup> [www.ema.europa.eu/htms/human/humanguidelines/biologicals.htm](http://www.ema.europa.eu/htms/human/humanguidelines/biologicals.htm) and  
[www.ema.europa.eu/htms/human/humanguidelines/efficacy.htm](http://www.ema.europa.eu/htms/human/humanguidelines/efficacy.htm)

## 1 DEFINITION

2 This section defines the scope of the monograph and its applicability to products on the  
3 market. The composition of the product is briefly stated.

4 It states:

- 5 – the physical status of the preparation (liquid or freeze-dried);
- 6 – the route of administration (for immunoglobulins);
- 7 – the source of the active substance (normally: human plasma for fractionation);
- 8 – the main (active) protein component(s);
- 9 – a description of the active substance (if applicable);
- 10 – other possible active substances usually associated with the intended active substance;
- 11 – possible contaminating active substances (e.g. IgA in immunoglobulins or activated  
12 coagulation factors in factor preparations);
- 13 – other ingredients (e.g. heparins);
- 14 – whether excipients, stabilisers and other auxiliary substances are allowed, and  
15 examples of these substances might be provided;
- 16 – the potency or specific biological activity, whichever applicable;
- 17 – for specific immunoglobulins: exceptions and/or additions to the requirements for  
18 normal immunoglobulin preparations.

19 Substances allowed are included in the Definition section. By default, should a substance or  
20 class of auxiliary substances (excipients, stabilisers, other ingredients, etc) not be mentioned  
21 in the Definition section, it should be considered as prohibited. Prohibited substances are  
22 included in the Production section

23 The monograph sets the official standard for all products covered by this definition.

24 If a new plasma-derived product is developed with an active substance covered by a specific  
25 monograph but of a new type that falls outside the existing monograph, this may lead to  
26 revision of the monograph or elaboration of a new one. If a product is not covered by the  
27 scope of a specific monograph, the monograph is not applicable to this product. Only the  
28 “base” monographs apply in this case.

## 29 PRODUCTION

30 It describes the essential features of the manufacturing process, up to and including batch  
31 release, with development/validation tests that may be carried out in-process or on the final  
32 lot to provide assurance that the product is of Pharmacopoeia quality (where not applied as  
33 routine batch test).

34 This section is primarily addressed to manufacturers to provide advice. Apart from the  
35 monograph on *Human plasma for fractionation (0853)*, monographs on blood-derived

1 products in the Ph. Eur. cover products prepared industrially in batches. Preparations  
2 produced in blood banks/transfusion centres (e.g. red cell concentrates, fresh frozen plasma)  
3 are not covered by the Ph. Eur. Nevertheless, the principles described in the *Guide to the*  
4 *preparation, use and quality assurance of blood components* (current edition) for donor  
5 selection and blood collection shall be considered.

6 The Production section contains appropriate details on the production method, including  
7 aseptic filling and freeze-drying, where applicable. In addition, standard sentences are added  
8 to ensure that production steps include (list not exhaustive, only general cases are detailed  
9 below):

- 10 – procedures to maintain functional integrity of the substance;
- 11 – procedures designed to minimise activation of coagulation factors, where  
12 applicable;
- 13 – procedures designed to remove, inactivate and control agents of infection;
- 14 – procedures for validation of removal of auxiliary substances;
- 15 – procedures for validation of lot-to-lot consistency that are not verified on the  
16 final lot;
- 17 – prohibition of the use of antimicrobial preservatives, antibiotics or other  
18 substances (whenever applicable).

## 19 CHARACTERS

20 The statements under the heading *Characters* are not to be interpreted in a strict sense and are  
21 not requirements.

22 This section states:

- 23 – the physical status (liquid, dry powder, frozen solid);
- 24 – the appearance of the product (e.g. colour, opalescence, viscosity).

## 25 IDENTIFICATION

26 This section describes how to identify the product. In plasma-derived product monographs,  
27 the Identification section generally comprises an immunoelectrophoresis or should comply  
28 with the limit of the assay.

## 29 TESTS

30 General tests, e.g. water, pH, solubility, pyrogens or bacterial endotoxins and other specific  
31 tests if applicable, are described and limits are given unless otherwise justified. The product  
32 should comply with these requirements throughout its shelf-life. The tests apply to the final  
33 lot and should be applicable for check analysis, for example by an official control laboratory.  
34 Tests, including limits, should be validated and should be applicable to all products available  
35 in Europe.

1 **Purity tests (the lists of tests are provided as examples and are not exhaustive)**

2 Typically, monographs on plasma-derived products may contain the following tests:

- 3 – pH (2.2.3);
- 4 – Osmolality (lower limit only) (2.2.35);
- 5 – Solubility;
- 6 – Water (2.5.12 or 2.5.32);
- 7 – Total protein (2.5.33);
- 8 – Protein composition;
- 9 – Molecular size distribution (2.2.30) (for polymer and aggregates).

10 Typically, monographs for coagulation factor preparations may contain:

- 11 – a test for activated coagulation factors, and
- 12 – a test on the heparin and/or thrombin content.

13 The monographs for normal immunoglobulin preparations contain additional class-specific  
14 tests:

- 15 – IgA content;
- 16 – Anti-A and anti-B haemagglutinins (2.6.20);
- 17 – Anti-D antibodies (2.6.26);
- 18 – Antibodies to hepatitis B surface antigen;
- 19 – Antibodies to hepatitis A virus.

20 Since other impurities/components/contamination may be clinically relevant in certain blood  
21 products, additional tests may be included:

- 22 – Prekallikrein activator;
- 23 – B19 virus DNA.

24 **Safety tests**

25 The monographs contain typically tests for:

- 26 – Sterility (2.6.1);
- 27 – Pyrogens (2.6.8) and/or Bacterial endotoxins (2.6.14).

28 ***Alternative test methods***

29 The European Pharmacopoeia Commission has a policy of regular review of animal tests  
30 prescribed in monographs with a view to their replacement by *in vitro* methods wherever

1 possible, in accordance with the *European Convention for the Protection of Vertebrate*  
2 *Animals Used for Experimental and Other Scientific Purposes*<sup>1</sup> and with the EU Directive  
3 86/609/EEC<sup>2</sup>.

4 The current policy of Group 6B is to introduce, wherever possible, a provision for the use of  
5 an *in vitro* method as a preferred alternative to the pyrogens test in rabbits. Particular interests  
6 are given to the following 2 *in vitro* methods:

- 7 – the bacterial endotoxins test (BET) (2.6.14), and
- 8 – the monocyte-activation test (2.6.30).

9 A guideline<sup>7</sup> on the replacement of rabbit pyrogen testing by an alternative test for plasma-  
10 derived medicinal products was elaborated by the Biologics Working Party (BWP) of the  
11 Committee for Medicinal Products for Human Use (CHMP) of the EMA. The purpose of this  
12 guidance is to highlight points to be addressed in any justification for the use of a test for  
13 bacterial endotoxins as an alternative to a test for pyrogens for medicinal products derived  
14 from human blood and human plasma.

15 The replacement of the pyrogen test (2.6.8) by an *in vitro* method must be based on historical  
16 data and a validation should be performed.

## 17 ASSAY/POTENCY

18 A potency test is included in each specific monograph but it is sometimes described in a  
19 separate chapter which is referred to in the specific monograph.

20 The activity of a plasma-derived product is to be expressed either in units of mass per volume  
21 (e.g. g/mL, or g per container) or in International Units per container or per volume.

22 The assay procedures may be either immunoassays for immunoglobulin preparations  
23 (described in 2.7.1 and 2.7.13) or chromogenic assays developed for coagulations factor  
24 determinations (e.g. 2.7.4). Other assays may be developed and described on a case-by-case  
25 basis.

26 The limit applied in the potency assay is typically 80-120 per cent. In some assays, where  
27 higher precision normally can be achieved, the potency should be 90-110 per cent of the  
28 nominal value.

29 The fiducial limits of the assay are essential as an expression of the precision achieved in the  
30 specific assay. They shall normally be 80-125 per cent of the estimated potency when  
31 logarithmic values are used, or 80-120 per cent when a linear scale is used.

32 The terms “estimated potency” and “stated potency” have to be understood in accordance  
33 with the definitions mentioned in Ph. Eur. general chapter 5.3. *Statistical analysis of results of*  
34 *biological assays and tests*.

### 35 ***Alternative assay methods***

36 The general statements given above on the use of alternative methods are also valid for assays  
37 that involve use of animals.

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<sup>7</sup> EMEA/CHMP/BWP/452081/2007

1 STORAGE

2 This section is given for information. It gives information on storage conditions (e.g.  
3 protection from light, type of glass container, vacuum or inert gas). The storage conditions are  
4 indicated by the manufacturer. They have been validated by stability testing that showed that  
5 the product will comply throughout the period of validity. Unless otherwise indicated in a  
6 specific monograph, the storage of products is expected to conform to that described in the  
7 base monograph.

8 LABELLING

9 The appropriate requirements of the labelling statements described in the base monograph  
10 apply to all products. In some cases additional information may be necessary for a particular  
11 product. This information is then included in the Labelling section of the specific monograph  
12 and this is supplementary to the requirements of the base monographs.

13 The status of the labelling is defined in the *General Notices*: “*In general, labelling of*  
14 *medicines is subject to supranational and national regulation and to international*  
15 *agreements. The statements under the heading Labelling are not therefore comprehensive*  
16 *and, moreover, for the purposes of the Pharmacopoeia only those statements that are*  
17 *necessary to demonstrate compliance or non-compliance with the monograph are mandatory.*  
18 *Any other labelling statements are included as recommendations. When the term ‘label’ is*  
19 *used in the Pharmacopoeia, the labelling statements may appear on the container, the*  
20 *package, a leaflet accompanying the package, or a certificate of analysis accompanying the*  
21 *article, as decided by the competent authority”.*

22 The instructions on the label are determined on a case-by-case basis. When applicable,  
23 information shall be given of how to reconstitute the product prior to use, or contain  
24 information necessary for the application of monograph.

1 **4.2. MONOGRAPHS NOT COVERED BY THIS TECHNICAL GUIDE**

2 This technical guide only covers those monographs elaborated for human plasma-derived  
3 products.

4 Monographs covering products not derived from plasma and that might be elaborated by  
5 Group 6B, are not covered by the present Technical Guide.

6 **5. RELATIONSHIP BETWEEN BASE MONOGRAPHS AND SPECIFIC**  
7 **MONOGRAPHS**

8 The following figure illustrates the editorial relationship that exists between the drafting of  
9 monographs on plasma-derived products. This representation does not consider the functional  
10 relationship between the products.

## HUMAN PLASMA-DERIVED PRODUCT MONOGRAPHS

**Anticoagulants and preservative solutions for human blood (0209)**

### Human plasma for fractionation (0853)

**Human plasma (pooled and treated for virus inactivation) (1646)**

**Human normal immunoglobulin (0338)**

Human anti-D immunoglobulin (0557)  
Human hepatitis B immunoglobulin (0722)  
Human hepatitis A immunoglobulin (0769)  
Human varicella immunoglobulin (0724)  
Human rabies immunoglobulin (0723)  
Human rubella immunoglobulin (0617)  
Human tetanus immunoglobulin (0398)  
Human measles immunoglobulin (0397)

**Human normal immunoglobulin for intravenous administration (0918)**

Human anti-D immunoglobulin for intravenous administration (1527)  
Human varicella immunoglobulin for intravenous administration (1528)  
Human hepatitis B immunoglobulin for intravenous administration (1016)

**Human Coagulation factors**

Human coagulation factor VII (1224)  
Human coagulation factor VIII (0275)  
Human coagulation factor IX (1223)  
Human coagulation factor XI (1644)

**Other fractionated products**

Human albumin solution (0255)  
Human fibrinogen (0024)  
Fibrin sealant kit (0903)  
Human antithrombin III concentrate (0878)  
Human prothrombin complex (0554)  
Human von Willebrand factor (2298)  
Human  $\alpha$ -1-proteinase inhibitor (2387)