

REGISTRY OF CLOTTING FACTOR CONCENTRATES

Fifth Edition, 2004

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Registry of Clotting Factor Concentrates

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Background

Concentrates are distributed widely around the world through sales and through formal and informal donations. Persons with hemophilia travel around the world. Purchasers and recipients ask international agencies to characterize all manner of concentrates. To aid in identification of various brands, a registry of concentrates intended for treatment of congenital plasma clotting factor deficiencies was begun by the Factor VIII and IX Subcommittee of the Scientific and Standardization Committee of the International Society on Thrombosis and Hemostasis (ISTH) in 1997. It is updated annually and distributed as a paper document. It is made available on the Internet by the World Federation of Hemophilia (WFH, www.wfh.org.)

Methods

Known fractionators are asked to submit data annually. Submitted data are published without any attempt at validation, unless the authors recognize a possible error. Listing herein does not constitute endorsement by WFH or by ISTH.

Fractionators are asked to indicate purification level as "specific activity", the amount of the desired clotting factor per mg of total protein, subtracting any added albumin, "SA s alb". Specific activity may have been actually measured or may have been calculated as an approximation. Methods of estimating or measuring specific activity vary, e.g. added albumin preparations are not equally purified, so the reader is cautioned to take these figures as rough guides only.

Direct tests for the presence of virus, using, for example, polymerase chain reaction, is described as "NAT", nucleic acid testing. Retention of plasma after donation and before

processing, formerly called "quarantine" in these Tables, is now called "inventory hold". The purpose of inventory hold is to allow time for further information about a donor to be discovered or to allow repeat testing of a donor.

We tried to retain the wording of respondents in these tables whenever possible. We sometimes imposed uniformity of expression for the sake of clarity or brevity. Within each table, concentrates are grouped, first, according to method of fractionation, then, according to method of viral inactivation or degree of purification from lowest to highest, and, when these groupings were inadequate, alphabetically by concentrate name or company name. Concentrates within a table from a specific company were grouped together unless other characteristics made separation sensible. When a given concentrate has more than one name, both names are listed in one row (e.g. NovoSeven and Niasstase); if they have more than one distributor (e.g., Kogenate FS and Helixate FS), they are listed in adjacent rows.

Agencies contemplating purchase of concentrates are advised to consult the WFH's 2003 publication entitled: "Guide for the Assessment of Clotting Factor Concentrates for the Treatment of Hemophilia" by Albert Farrugia.

Comments on plasma

When plasma is obtained from donations of whole blood, it is called "recovered plasma". Plasma obtained by apheresis is called "source plasma". Whole blood donors are not paid substantially in any of the countries responding to this Registry. (Small sums may be paid for out-of-pocket expenses.) Donors of apheresis plasma typically are paid; in a few countries, they may be unpaid.

Several national fractionation centers produce concentrate from their own domestic recovered plasma for use in their own countries. A few

large fractionators (CSL in Australia, Grifols in Spain, Octapharma in Austria) can take the plasma of a given small country and fractionate it in a separate batch into concentrate to be returned to the donor country, a process called "contract" or "toll" fractionation. Several European fractionators use plasma obtained by apheresis (source plasma) from countries permitting paid apheresis. The USA is the major producer of source plasma. Such plasma may be blended with smaller amounts of unpaid recovered plasma, as indicated in the Tables.

This year's data

Only one change in management of a fractionation plant is reported for 2003: Grifols Biologicals now is in charge of the plant in Los Angeles formerly run by Alpha Therapeutic Corporation. CSL recently announced its acquisition of Aventis Behring, but no changes in nomenclature have yet been made.

TABLE 1-A: SEROLOGIC TESTS ON INDIVIDUAL DONOR PLASMA

PLASMA SOURCE	Syphilis	HIV 1-2	p-24 antigen	HTLV-1	HTLV-2	HBcAg	HBcAb	HBsAg	HBsAb	HCV Ab	ALT	B-19 parvovirus
USA paid apheresis (Grifols)	Yes ¹	Yes	NO ²	No	No	No	No	Yes	No	Yes	Yes	No
Other USA paid apheresis ³	Yes ¹	Yes	Yes ²	No	No	No	No	Yes	No	Yes	Yes	No
USA Red Cross unpaid	Yes ¹	Yes	Yes ²	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
Baxter BioScience: USA, Austria, Germany	1 st donation & at intervals	Yes	Yes, selected centers	No	No	No	No	Yes	No	Yes	Yes	No
Aventis Behring: Austria, Germany	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No
Biotest: Austria, Belgium, Germany	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No
Intersero: Austria, Belgium, Germany	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No
German Red Cross BSD NSTOB	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No
Octapharma: Austria, Germany	Yes	Yes	No ⁴	No	No	No	No	Yes	No	Yes	Yes	No
Octapharma: Sweden	Yes	Yes	No	1 st donation	1 st donation	No	1 st donation	Yes	No	Yes	Yes	No
Finnish Red Cross BTS: Finland, unpaid	Yes	Yes	No	1 st donation & q 3 yrs	1 st donation & q 3 yrs	No	No	Yes	No	Yes	Yes	No
Sanquin: The Netherlands	Yes	Yes	No	Yes	Yes	No	No	Yes	No	Yes	No	No
LFB: France & Western Europe ^{5,6}	Yes	Yes ⁶	No	Yes	Yes	No	Yes	Yes	No	Yes ⁶	Yes	No
Grifols: Spain, Czech Rep., Slovakia	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No
Kedrion: Italy	Yes	Yes	No ⁴	No	No	No	No	Yes	No	Yes	Yes	No
Natal Bioproducts: South Africa	Yes	Yes	Yes	No	No	No	No	Yes	No	Yes	No	No
Australian Red Cross Blood Service ⁷	Yes	Yes	No	Yes	Yes	No	No	Yes	No	Yes	No	No
New Zealand Blood Service ⁷	Yes	Yes	No	1 st donation	1 st donation	No	No	Yes	No	Yes	No	No
Hong Kong Red Cross BTS ⁷	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No
Japan	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Korean Red Cross: South Korea ⁸	Yes	Yes	Yes	No	No	No	No	Yes ⁵	No	Yes	Yes	No
Shanghai RAAS: China	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No

1. Performed every 4 months in accordance with the US Code of Federal Regulations.

2. Not required if a US FDA licensed HIV-1 NAT test has been approved as an alternative to HIV-1 p24 Ag testing is used, as instituted by Grifols.

3. US paid apheresis “source” plasma is used by several European fractionators, as identified in attached tables; US unpaid plasma (“recovered” from whole blood donations) is used by some fractionators in other countries. Some US recovered plasma may come from the American Red Cross and some from other licensed US blood banks.

4. Octapharma (Austria) and Kedrion (Italy) point out that the p24 Ag test is performed on the US plasma they utilize but not on their European plasma.

5. LFB uses plasma from unpaid donors from certain western European countries which comply with French specifications.

6. Since 2001, NAT tests for HCV and HIV have been performed on individual donations at blood centers utilized by LFB.

7. CSL Bioplasma in Australia fractionates plasma on a contract (toll) basis for the Australian RCBS, New Zealand BS, Hong Kong RC BTS, Malaysia BTS and the Health Sciences Authority of Singapore.

8. NAT tests for HCV are performed on individual donations in Korea.

TABLE 1-B. PLASMA INVENTORY HOLD AND NAT TESTING OF MINI-POOLS

COMPANY OR FRACTIONATOR	INVENTORY HOLD	MINI-POOL SIZE	MINI-POOL NAT TESTS	MANUFACTURING POOL NAT TESTS	NAT ON FINAL PRODUCT
American Red Cross	60 days	16	HCV, HIV	HAV, HBV, HCV, HIV	
Aventis Behring: USA, Germany	60+ days		HAV, HBV, HCV, HIV, B-19 parvovirus	HAV, HBV, HCV, HIV, B-19 parvovirus	
Baxter BioScience: USA, Vienna	60+ days	512	HAV, HBV, HCV, HIV, B-19 parvovirus	HAV, HBV, HCV, HIV 1-2, B-19 parvovirus	
Bayer: USA	60+ days	96 or 480	HBV, HCV, HIV 1, B-19 parvovirus	HBV, HCV, HIV-1, B-19 parvovirus	
Grifols: USA	60+ days	512 or fewer	HAV, HBV, HCV, HIV, B-19 parvovirus	European requirement	HAV, HBV, HCV, HIV
BPL, UK: US plasma used	60	512	HAV, HBV, HCV, HIV 1-2, B-19 parvovirus	European requirement	
SNBTS, UK: US & German plasma used	21+ days	24 and 96	HAV, HBV, HCV, HIV-1, B-19 parvovirus	European requirement	
Biotest: Germany	60 days	960	HAV, HBC, HCV, HIV 1, B-19 parvovirus	HBV, HCV, HIV	
Intersero: Germany	60+ days	96	HAV, HBV, HCV, HIV-1, B-19 parvovirus	European requirement	HCV, HIV 1-2, p-24 Ag
German RC BSO NSTOB	2 months	48	HAV, HBV, HCV, HIV-1, B-19 parvovirus	European requirement	
Octapharma: Austria	2 months	10-140	HCV, B-19 parvovirus	European requirement	
Octapharma: Sweden	2 months	480	HAV, HCV, B-19 parvovirus	European requirement	
Finnish Red Cross: Finland		96 – 480	HCV, B-19 parvovirus	HCV, HIV, B-19 parvovirus	
Sanquin: The Netherlands		48	HCV, HIV	European requirement	
LFB: France	3+ months	(1) 100; (2) 1000	(1) B-19 parvovirus; (2) HAV, HCV	HAV, HBV, HCV, HIV, B-19 parvovirus	
Grifols: Spain	3+ months	512 or fewer	HAV, HBV, HCV, HIV, B-19 parvovirus	HBV, HCV, HIV	
Kedrion: Italy	60+ days	480 or fewer	HBV, HCV, HIV, B-19 parvovirus (HAV if required)	European requirement	
Natal Bioproducts, South Africa	21+ days	1500	HCV, HIV	HCV, HIV	
CSL Ltd, Australia		480	HCV, HIV		
Australian Red Cross Blood Service Fractionated at CSL		24 (ARCBS), 480 (CSL)	HCV, HIV (both sites)		
New Zealand Blood Service Fractionated at CSL		16 (NZBS), 480 (CSL)	HCV, HIV (NZBS), HCV, HIV (CSL)		
Hong Kong Red Cross BTS Fractionated at CSL		24 (HK), 480 (CSL)	HCV, HIV (HK*); HCV, HIV (CSL)		
GreenCross: South Korea		< 450	HAV, HCV	HAV, HBV, HCV, HIV	HAV, HBV, HCV, HIV
Japanese Red Cross: Japan	6 months	50	HBV, HCV, HIV	HBV, HCV, HIV	HAV, HBV, HCV, HIV
Kaketsuken: Japan	6 months	50	HBV, HCV, HIV-1	HBV, HCV, HIV-1	HAV, HBV, HCV, HIV-1
Benesis, Japan	6 months	50	HBV, HCV, HIV-1	HBV, HCV, HIV-1	HAV, HBV, HCV, HIV-1, B-19 parvovirus
Shanghai RAAS: China	60+ days	48	HBV, HCV, HIV-1	HBV, HCV, HIV-1	HBV, HCV, HIV-1

* These tests are performed for Hong Kong by the Australian Red Cross

TABLE 2. FACTOR VIII CONCENTRATES MADE BY PRECIPITATION (PPT), GEL PERMEATION OR ION EXCHANGE CHROMATOGRAPHY

BRAND	COMPANY	MADE AT OR BY	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb* FVIII IU/mg	COMMENT
Factor 8 Y	BioProducts Lab.	Elstree, England	USA: paid apheresis	Both	Heparin/glycine ppt	Dry heat, 80° C, 72 hr	2.5 - 4	Contains VWF
AHF (High Purity)	CSL Ltd	Melbourne, Australia	New Zealand, Hong Kong, Malaysia, unpaid	Export	Heparin/ glycine precipitation, gel filtration chromatography	Dry heat, 80° C, 72 hr	2 – 5	Contains VWF
Haemosolvate Factor VIII	Natal Bioproducts	Durban, South Africa	South Africa & USA, unpaid	Both	Heparin/ glycine ppt	TNBP/ polysorbate 80	8 – 12	No albumin added
HEMORAAS, SD plus H	Shanghai RAAS	Shanghai, China	China: paid and unpaid apheresis	Both	PEG/ glycine ppt	S/D, dry heat 100° C, 30 min	< 30	No albumin added, contains VWF
Haemate P (= Haemate HS)	Aventis Behring	Marburg, Germany	USA, Germany, Austria: paid & unpaid	Both	Multiple precipitation	Pasteurization, 60° C, 10 hr	38	Albumin added, contains VWF, ratio vWF/FVIII > 2.2
Humate P	Aventis Behring	Marburg, Germany	USA: paid apheresis	To USA	Multiple precipitation	Pasteurization, 60° C, 10 hr	38	Same as above
Conco-eight-HT	Benesis	Osaka, Japan	Japan: unpaid	Domestic	Glycine precipitation, gel filtration	TNBP/ polysorbate 80 & dry heat, 60° C, 72 hr	50	Albumin added
Koate DVI	Bayer	Clayton, NC, USA	USA: paid apheresis	Both	Multiple precipitation and size exclusion chromatography	TNBP/ polysorbate 80 & dry heat, 80° C, 72 hr	>20	Albumin added, contains VWF
BIOSTATE	CSL Ltd	Melbourne, Australia	Australia, Singapore: unpaid; USA: paid	Both	Heparin/ glycine ppt, gel filtration chromatography	TNBP/ polysorbate 80 & dry heat, 80° C, 72 hr	50	Albumin added, contains VWF; SA without albumin & VWF = 180
HEMORAAS-IP, SD plus H	Shanghai RAAS	Shanghai, China	China: paid and unpaid apheresis	Both	PEG ppt & ion exchange chromatography	S/D; dry heat, 100° C, 30 min	< 100	No albumin added
HEMORAAS-HP, SD plus H	Shanghai RAAS	Shanghai, China	China: paid and unpaid apheresis	Both	PEG ppt & ion exchange chromatography	S/D; dry heat, 100° C, 30 min	> 100	No albumin added
GreenEight	Greencross PD	Seoul, Korea	Korea: unpaid	Domestic	Ion exchange chromatography	TNBP/polysorbate	100+	No albumin added, contains VWF
Confact F	Kaketsuken	Kumamoto, Japan	Japan: unpaid	Domestic	Ion exchange chromatography	Dry heat, 65° C, 96 hr; 35 nm nanofiltration	50	Albumin added
Immunate	Baxter BioScience	Vienna, Austria	USA, Austria, Czech Republic, Germany, Sweden: mostly paid apheresis	Both	Ion exchange chromatography	Polysorbate 80; vapor-heat, 60° C, 10 hr at 190 mbar	Mean 70, SD 30	Albumin added, contains VWF
Liberate HT	SNBTS	Edinburgh, Scotland	USA & Germany: unpaid	Both	Ion exchange chromatography	TNBP/ polysorbate 80 & dry heat, 80° C, 72 hr	100	No albumin added, contains VWF
Emoclot D.I.	Kedrion	Italy	Europe and USA: paid & unpaid	Both	Ion exchange chromatography	TNBP/polysorbate 80 & dry heat, 100° C, 30 min	> 80	No albumin added, contains VWF
Haemoctin SDH	Biotest	Dreieich, Germany	USA, Austria, Belgium, Germany: paid & unpaid	Both	Anion exchange chromatography	TNBP/polysorbate 80 & dry heat, 100° C, 30 min	100	No albumin added, contains VWF
Faktor VIII SDH Intersero	Intersero	Dreieich, Germany	USA, Austria, Belgium, Germany: paid & unpaid	Domestic	Anion exchange chromatography	TNBP/polysorbate 80 & dry heat, 100° C, 30 min	100	No albumin added, contains VWF
Octanate	Octapharma	Vienna, Austria & Lingolsheim, France	USA, Austria, Germany	Both	Ion exchange chromatography	TNBP/polysorbate 80 & dry heat, 100° C, 30 min	> 100	No albumin added, contains VWF
FACTANE	LFB	France	Western European unpaid	Both	Chromatography	TNBP/ polysorbate 80 & 35-15 nm nanofiltration	100 or more	
Beriate P = Beriate HS	Aventis Behring	Marburg, Germany	USA, Austria, Germany: paid & unpaid	Both	Ion exchange chromatography	Pasteurization, 60° C, 10 hr	170	No albumin, stabilized in amino acids & sucrose

*Specific activity (excluding albumin) FVIII IU/mg protein

Porcine factor VIII:

HYATE-C	IPSEN	Wrexham, Wales, UK	Porcine plasma	Both	Cryoprecipitation & polyelectrolyte ion exchange chromatography	None: end product cell culture viral screen		For patients with inhibitors to human factor VIII
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TABLE 3. FACTOR VIII CONCENTRATES: HEPARIN LIGAND, IMMUNOAFFINITY CHROMATOGRAPHY, OR RECOMBINANT

BRAND	COMPANY	MADE AT OR BY	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA S ALB FVIII IU/ MG	COMMENTS
Alphanate	Grifols	Los Angeles, CA, USA	USA: paid apheresis	Both	Heparin ligand chromatography	TNBP/polysorbate 80 & dry heat, 80° C, 72 hr	140	Albumin added, contains VWF; SA s alb & VWF = 1000-3000
Fanhdi	Grifols	Barcelona, Spain	USA: paid apheresis	Both	Same as above	Same as above	100 or more	As above
Fanhdi	Grifols	Barcelona, Spain	Spain: unpaid recovered & apheresis	Domestic only	Same as above	Same as above	100 or more	As above
Fanhdi	Grifols	Barcelona, Spain	Czech Rep. recovered & apheresis	To Czech Rep.	Same as above	Same as above	100 or more	As above
Monoclate P	Aventis Behring	Kankakee, IL, USA	USA; paid apheresis	Both	Monoclonal Ab affinity chromatography	Pasteurization at 60° C, 10 hr	> 3000	Albumin added, no VWF
Hemofil M AHF	Baxter BioScience	Los Angeles, CA, USA	USA: paid apheresis	Both	Monoclonal Ab affinity & ion exchange chromatography	TNBP/ Octoxynol 9	Approx. 2000	Albumin added, no functional VWF
Monarc-M	American Red Cross	Baxter, Los Angeles	USA: unpaid recovered	Both	Same as above	Same as above	Approx. 2000	As above
Replenate	Bio Products Laboratory	Elstree, England, UK	USA: paid apheresis	Domestic	Monoclonal Ab affinity & ion exchange chromatography	TNBP/ Triton X 100	> 2000	As above
Amofil	Finnish Red Cross BTS	Octapharma, Stockholm	Finland: unpaid recovered	Domestic	Same as above	Same as above	> 2000	As above
Octanativ-M	Octapharma	Stockholm, Sweden	Swedish unpaid recovered & apheresis	Both	Same as above	Same as above	>2000	As above
Aafact	Sanquin, CLB	Amsterdam, Netherlands	Netherlands: unpaid	Domestic	Same as above	Same as above	> 2000	As above
GreenMono	Greencross PD	Seoul, Korea	Korea: unpaid	Domestic	Same as above	Same as above	> 2000	As above
Cross Eight M	Japanese Red Cross	Chitose City, Japan	Japan: unpaid	Domestic	Same as above	TNBP/ Triton X 100 & nanofiltration	> 2000	As above

Recombinant factor VIII concentrates

Kogenate FS = KOGENATE Bayer (in EU)	Bayer	Berkeley, CA, USA	None, recombinant	Both	Recombinant: ion exchange & immunoaffinity chromatography	TNBP/ polysorbate 80	4000	Full-length rFVIII; no VWF. Formulated with sucrose. Albumin not added during purification or formulation.
Helixate NexGen = Helixate FS	Aventis Behring	Bayer, Berkeley, CA	None, recombinant	Both	As above	TNBP/ polysorbate 80	4000	As above
Recombinate rAHF	Baxter BioScience	Thousand Oaks, CA, USA	None, recombinant	Both	As above		> 4000	Full length rFVIII, no functional VWF.: Human serum albumin added as stabilizer
Advate rAHF PFM	Baxter Bioscience	Neuchatel, Switzerland	None, recombinant	Both	Recombinant	TNBP/ polysorbate 80, Triton X 100	4000 – 10,000	Full-length rFVIII, no functional VWF: no addition of human- or animal-derived plasma proteins or albumin in the cell culture, purification or final formulation.
ReFacto	Wyeth	St. Louis, MO, USA & Stockholm, Sweden	None, recombinant	Both	Recombinant	TNBP/ Triton X 100	13,000	B-domain-deleted FVIII, no VWF. No albumin added in formulation.

TABLE 4: PROTHROMBIN COMPLEX CONCENTRATES (PCC)

BRAND	COMPANY	MADE AT OR BY	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA: F. IX, IU/ mg	COMMENTS
Proplex – T	Baxter BioScience	Los Angeles, CA, USA	USA: paid apheresis	Both	Tricalcium phosphate absorption, PEG fractionation	Exposure to 20% ethanol; dry heat, 60° C, 144 hr	> 8	Heparin added; maximum 3.5 U factor VII per IU factor IX
Beriplex P/N	Aventis Behring	Marburg, Germany	USA, Austria, Germany paid/unpaid	Both	DEAE-sephadex	Pasteurization at 60° C, 10 hr, & nanofiltration	3.5 – 5	Anti-thrombin III, heparin & albumin added
Faktor IX HS	Aventis Behring	Marburg, Germany	USA, Austria, Germany; paid/unpaid	Both	DEAE-sephadex	Pasteurization at 60° C, 10 hr, & nanofiltration	15	Contains high amount of factor X
Haemosolvex Factor IX	Natal Bioproducts	Durban, South Africa	South Africa: unpaid	Both	DEAE-sephadex	TNBP/polysorbate 80	1.5	No albumin added
Profilnine SD	Grifols	Los Angeles, CA, USA	USA: paid pheresis	Both	DEAE cellulose adsorption	TNBP/polysorbate 80	4	Anti-thrombin III & heparin added; no albumin added
Prothrombinex- HT	CSL Ltd.	Melbourne, Australia	Australia, New Zealand, Hong Kong, Malaysia, unpaid	Both	DEAE cellulose absorption	Dry heat, 80° C, 72 hr	1 – 5	Anti-thrombin III & heparin added; no albumin added
Prothromplex-T	Baxter BioScience	Vienna, Austria	USA, Austria, Czech Rep., Germany, Sweden: mostly paid apheresis	Both	Ion exchange adsorption	Vapor heat, 60° C for 10 hr at 190 mbar, then 80° C for 1 hr at 375 mbar		Anti-thrombin III & heparin added
Bebulin VH	Baxter BioScience	Vienna, Austria	USA: paid apheresis	Export to USA	Same as above	Same as above		Heparin added
HT DEFIX	SNBTS	Edinburgh, Scotland	USA & Germany: unpaid	Both	Ion exchange chromatography	Dry heat, 80° C, 72 hr	2	Anti-thrombin III added
Octaplex	Octapharma	Vienna, Austria	USA, Austria, Germany	Both	Ion exchange chromatography	TNBP/ polysorbate 80, nanofiltration		Heparin added, no anti-thrombin or albumin added, low factor VIIa content
Facnyne	Greencross PD	Seoul, Korea	Korea: unpaid	Domestic	Ion exchange chromatography	TNBP/ polysorbate 80	@ 6 – 7	No albumin added
Cofact	Sanquin	Amsterdam, Netherlands	Netherlands: unpaid	Both	DEAE ion exchange chromatography	TNBP/polysorbate 80 & Nanofiltration		Anti-thrombin III added
PPSB-human SD/Nano 300/600	German Red Cross NSTOB	Springe, Germany	Germany: unpaid	Domestic	DEAE-sephadex, ion exchange chromatography	TNBP/ polysorbate 80 & Two nanofiltration steps, 50 nm & 15 nm	1	Anti-thrombin III & heparin added; no albumin added
UMAN Complex D.I.	Kedrion	Italy	Europe & USA, unpaid & paid	Both	Anion exchange: DEAE-sephadex/ sepharose chromatography	TNBP/ polysorbate 80 & Dry heat, 100° C, 30 min	< 1.6	Anti-thrombin III & heparin added; no albumin added; factor II & factor X titration
KASKADIL	LFB	France	Western Europe, unpaid	Both	DEAE-sephadex absorption, anion exchange chromatography	TNBP/ polysorbate 80	0.6	

Activated Prothrombin Complex Concentrates (APCC), for patients with inhibitors

Autoplex-T	NABI	Baxter Bio Science, Los Angeles, CA, USA	USA: paid apheresis	Both	Tricalcium phosphate absorption, PEG fractionation; surface-activated PCC	Exposed to 20% ethanol; dry heat, 60° C, 144 hr		Heparin added
FEIBA VH	Baxter BioScience	Vienna, Austria	USA, Austria, Czech Rep., Germany, Sweden, mostly paid apheresis	Both	Surface-activated PCC, batch- controlled	Vapor heat, 60° C, 10 hr, 190mbar then 80° C, 1 hr, 375 mbar		No heparin added

TABLE 5: HIGHLY PURIFIED FACTOR IX CONCENTRATES

BRAND	COMPANY	MADE AT OR BY	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	S.A. s ALB, F IX IU/MG	COMMENTS
Berinin-P = Berinin HS	Aventis Behring	Marburg, Germany	USA, Austria, Germany: paid & unpaid	Both	DEAE-sephadex, heparin affinity chromatography	Pasteurization at 60°, 10 hr	146	Anti-thrombin III & heparin added; no albumin added
Immunine	Baxter BioScience	Vienna, Austria	USA, Austria, Czech Rep., Germany, Sweden: mostly paid apheresis	Both	Ion exchange & hydrophobic interaction chromatography	Polysorbate 80 & vapor heat, 60° C, 10 hrs, 190 mbar then 80° C, 1 hr, 375 mbar	Approx. 100	
Hemo-B-RAAS	Shanghai RAAS	Shanghai, China	China: unpaid & paid apheresis	Both	Ion exchange & affinity chromatography	Solvent/ detergent, dry heat & nanofiltration	> 50	No albumin added
Bemofil	Finnish Red Cross BTS	Finnish Red Cross, Helsinki, Finland	Finland: unpaid recovered	Both	Ion exchange & affinity chromatography	Solvent/ detergent, 15 nm nanofiltration	> 110	
Octanyne	Octapharma	Vienna, Austria	USA, Austria, Germany	Export	Ion exchange & affinity chromatography	TNBP/ polysorbate 80	50 – 100	No albumin added
Octanyne F	Octapharma	Vienna, Austria & Lingolsheim, France	USA, Austria, Germany, Sweden	Both	Ion exchange & affinity chromatography	TNBP/ polysorbate 80 & nanofiltration	> 100	No albumin added
Nanotiv	Octapharma	Stockholm, Sweden	Sweden: recovered & apheresis	Both	Ion exchange & heparin ligand chromatography	TNBP/ Triton X 100 & nanofiltration	190	No albumin added
HIP FIX	SNBTS	Edinburgh, Scotland	USA & Germany: unpaid	Both	Ion exchange & heparin ligand chromatography	TNBP/ polysorbate 80; dry heat, 80° C, 72 hrs	180	Anti-thrombin III added, no albumin added
Mono FIX-VF	CSL Ltd.	Melbourne, Australia	Australia, New Zealand, Singapore, Hong Kong: unpaid	Both	Ion exchange & heparin affinity chromatography	TNBP/ polysorbate 80 & nanofiltration	70	Anti-thrombin III & heparin added, no albumin added
Christmassin-M	Benesis	Osaka, Japan	Japan: unpaid	Domestic	Ion exchange & immunoaffinity chromatography	TNBP/ polysorbate 80; dry heat, 60° C, 72 hr; 15 nm nanofiltration	Approx 170	Albumin added
Aimafix D.I.	Kedrion	Italy	Europe & USA: paid & unpaid	Both	Anion exchange, DEAE sephadex/sepharose & heparin affinity chromatography	TNBP polysorbate 80, dry heat, 100° C, 30 min; nanofiltration 35 + 15 nm	> 100	Anti-thrombin III & heparin added, no albumin added
BETAFACT	LFB	France	Western Europe, unpaid	Both	DEAE-sephadex, anion exchange, affinity chromatography	TNBP/ polysorbate 80, 15 nm nanofiltration	> 110	No albumin added
Faktor IX SDN	Biotest	LFB, France	Western Europe, unpaid	Austria & Germany	As above	As above	> 110	No albumin added
NOVIX	Grifols	Barcelona, Spain	1. USA paid 2. Spain unpaid 3. Czech Rep. unpaid	1. Both 2. Domestic 3. Czech Rep.	Precipitation & multiple chromatography	Solvent detergent, 15 nm nanofiltration	> 150	No albumin added
Alphanine	Grifols	Los Angeles, CA, USA	USA: paid apheresis	Both	Ion exchange, carbohydrate ligand chromatography	TNBP/ polysorbate 80, nanofiltration	210	No albumin added
Mononine	Aventis Behring	Kankakee, IL, USA	USA: apheresis paid	Both	Immunoaffinity chromatography	Sodium thiocyanate & ultrafiltration	> 190	
Nonafact	Sanquin	Amsterdam, The Netherlands	The Netherlands: unpaid	Both	Immunoaffinity chromatography	TNBP/ polysorbate 80; nanofiltration	200 or more	No albumin added
Novact M	Kaketsuken	Kumamoto, Japan	Japan: unpaid	Domestic	Immunoaffinity chromatography	Dry heat, 65° C, 96 hr; 15 nm nanofiltration	Approx 200	Albumin added
Replenine – VF	BioProducts Lab.	Elstree, England, UK	USA: paid apheresis	Both	Metal chelate chromatography	Solvent-detergent; 15 nm nanofiltration	200	No albumin added

Recombinant factor IX concentrate

BeneFIX	Wyeth	Cambridge, MA; McPherson, KS, USA	None, recombinant	Both	Recombinant	Nanofiltration	200 +	No albumin added
BeneFIX	Baxter SA (Switzerland)	Wyeth, USA	None, recombinant	Europe	Recombinant	Nanofiltration	200+	No albumin added

TABLE 6: OTHER CLOTTING FACTOR CONCENTRATES

BRAND	COMPANY	MADE AT	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	COMMENTS
Clottagen (fibrinogen)	LFB	France	Western Europe, unpaid	Both	Cryoprecipitate, adsorption on aluminum hydroxide gel, anion exchange chromatography	TNBP/ polysorbate 80	
Fibrinogen HT	Benesis	Osaka, Japan	Japan: unpaid	Domestic	Ethanol fractionation, glycine precipitaion	TNBP / polysorbate 80; dry heat, 60° C, 72 hr	No albumin added
Fibrinogen	SNBTS	Edinburgh, Scotland	USA & Germany, unpaid	Both	Multiple precipitation, ion exchange chromatography	TNBP/ polysorbate 80; dry heat, 80° C, 72 hr	No albumin added
FIBRORAAS (fibrinogen)	Shanghai RAAS	Shanghai, China	China: paid & unpaid apheresis	Both	Multiple fractionation	TNBP/ polysorbate 80	
Haemocomplettan P = Haemocomplettan HS (fibrinogen)	Aventis Behring	Marburg, Germany	USA, Austria, Germany; paid & unpaid	Both	Multiple precipitation	Pasteurization at 60° C, 20 hr	Albumin added
Factor VII	Baxter BioScience	Vienna, Austria	USA, Austria, Czech Republic, Germany, Sweden: mostly paid apheresis	Both	Aluminum hydroxide absorption	Vapor heat, 60° C, 10 hr at 190 mbar then 80° C, 1 hr at 375 mbar	
Factor VII	Bio Products Lab.	Elstree, England, UK	USA: paid apheresis	Both	Ion exchange chromatography	Dry heat, 80° C, 72 hr	S.A. 1.5 – 2 U/ mg protein
FACTEUR VII	LFB	France	France: unpaid recovered & apheresis	Both	DEAE adsorption, anion exchange chromatography	TNBP/ polysorbate 80	SA 1-2 U/ mg protein; no albumin added
Factor XI	Bio Products Lab.	Elstree, England, UK	USA: paid apheresis	Both	Affinity heparin sepharose chromatography	Dry heat, 80° C, 72 hr	Heparin, Anti-thrombin III added, S.A. 3- >5 U/ mg protein
HEMOLEVEN (Factor XI)	LFB	France	Western Europe, unpaid	Both	Dialysis, cation exchange chromatography	Solvent/ detergent, 15 nm nanofiltration	Heparin, Anti-thrombin III added, C-1 esterase inhibitor added
WILFACTIN	LFB	France	Western Europe, unpaid	Both	Aluminum hydroxide absorption, anion exchange & affinity chromatography	TNBP / polysorbate 80	> 60 units ristocetin cofactor (VWF:RCo) per mg; low FVIII content; high molecular weight multimers of VWF present
Fibrogammin P = Fibrogammin HS (Factor XIII)	Aventis Behring	Marburg, Germany	USA, Austria, Germany: paid & unpaid	Both	Multiple precipitation	Pasteurization at 60° C, 10 hr	Albumin added

Recombinant product

NovoSeven (Factor VIIa) = Niasase (in Canada)	NovoNordisk	Copenhagen, Denmark	None	Both	Recombinant	None	Primarily intended for hemostasis in presence of inhibitors
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Please note that four products, intended primarily or solely for management of patients with inhibitors, are listed in three different tables: porcine factor VIII in Table 2, two activated prothrombin complex concentrates in Table 4, and recombinant activated factor VII in Table 6.