FACTS AND FIGURES

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REGISTRY OF CLOTTING FACTOR CONCENTRATES

Eighth Edition, 2008

Mark Brooker
World Federation of Hemophilia

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FEDERACIÓN MUNDIAL DE HEMOFILIA
Treatment for All

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World Federation of Hemophilia
1425 René Lévesque Boulevard West, Suite 1010
Montréal, Québec H3G 1T7
CANADA
Tel. : (514) 875-7944
Fax : (514) 875-8916
E-mail: wfh@wfh.org
Internet: www.wfh.org

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Registry of Clotting Factor Concentrates
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Introduction

The Registry was created in 1997 by Dr. Meirione Costa e Silva and Dr. Carol Kasper for the International Society on Thrombosis and Haemostasis. Its purpose is to help medical personnel identify available concentrates and stay abreast of pharmaceutical company changes.

The registry provides an overview of available products and clarifies differences among them. It also helps doctors and pharmacists identify products that patients are offered during their foreign travels or those they may bring home with them, or have sent to them. Similarly, foreign patients traveling abroad may bring along their own concentrates, which may not be familiar to local healthcare personnel.

Agencies contemplating bulk purchase of concentrates are advised to consult the WFH's publications *Guide for the Assessment of Clotting Factor Concentrates for the Treatment of Hemophilia* by Albert Farrugia and *Guide to National Tenders for the Purchase of Clotting Factor Concentrates* by Brian O'Mahony.

Plasma obtained from donations of whole blood is called recovered plasma. Plasma obtained by apheresis is called source plasma. Donors of whole blood are not paid any substantial amount in any of the countries listed in this registry. Donors of apheresis plasma are paid in most countries.

Several national fractionation centres produce concentrate from domestic recovered plasma for domestic use. A few fractionators (for example, CSL in Australia, Grifols in Spain, Sanquin in The Netherlands) accept plasma from small countries, fractionate it separately, and return it as concentrate to the donor country, a process called contract or toll fractionation. Several fractionators use source plasma from countries permitting paid apheresis. Such plasma may be blended with smaller amounts of unpaid recovered plasma. The Scottish National Blood Transfusion Service (SNBTS) no longer manufactures fractionated plasma products.

Within the tables, concentrates are grouped first according to method of fractionation, then according to method of viral inactivation or degree of purification from lowest to highest. Fractionators cite the purification level of clotting factors as specific activity, or the amount of the desired clotting factor per milligram of total protein, minus any added albumin (SA s Alb). Specific activity may actually be measured or may be an approximation. Retention of plasma after donation and before processing to ascertain further information about a donor is called inventory hold or quarantine.

Tables 1A and 1B describe measures that help ensure the safe use of plasma. The array of serologic tests varies slightly from country to country. More sensitive nucleic acid tests that directly detect viruses are becoming commonplace.

Table 2 lists FVIII concentrates made by techniques generally associated with a lesser level of purification. Many contain von Willebrand factor (VWF), which stabilizes FVIII and is needed for treatment of von Willebrand disease (VWD). Table 3 lists FVIII concentrates made by techniques allowing higher level of purification, including recombinant FVIII concentrates. Prothrombin complex concentrates, which are not highly purified, are described in Table 4.

Table 5 lists concentrates primarily intended for use in patients with inhibitors. At the present time, all are activated concentrates (bypassing agents). Concentrates of factor IX alone are described in Table 6. Concentrates for rare clotting factor deficiencies are listed in Table 7.

They are not widely available, and there are some deficiencies for which no concentrate is made. NovoSeven®, the recombinant activated factor VII concentrate, is increasingly used for patients with congenital deficiency of factor VII and now is licensed for that use in the USA. The FX/IX-concentrate Factor X P Behring® provides an up to two-fold higher content of FX compared to FIX and no FII or FVII. Therefore it is almost only used for patients with factor X-deficiency.

There is one concentrate of VWF virtually alone, LFB's Wilfactin®, Table 7. Another LFB product, Wilstart®, available only in France, combines 1000 IU of Wilfactin® and 500 IU of Factane®, for use in acute bleeding in VWD or as the initial surgical dose. Octapharma's Wilate®, in Table 2, was developed for use in VWD as well as in hemophilia A. Several other products, in tables 2 and 3, also contain VWF and are used in VWD as well as in hemophilia.

Concentrates for deficiencies of anti-thrombotic factors are listed in Table 8. The only plasminogen available is combined with streptokinase in the clot-lysing product, Eminase® (Roberts Pharmaceutical Corporation, New Jersey).

No shortages of factor VIII and factor IX concentrates were reported in the United States in 2007, nor were there any reports of breaches of safety. No HIV has been transmitted by any American concentrate since 1987. No hepatitis A, B or C has been transmitted by American concentrates since the Centers for Disease Control and Prevention began its broad surveillance of persons with hemophilia in 1998.

TABLE 1A: SEROLOGIC TESTS ON INDIVIDUAL DONOR PLASMA

PLASMA SOURCE	Syphilis	HIV 1-2	p-24 antigen	HTLV-1	HTLV-2	HBcAb	HBsAb	HBsAg	HCVAb	ALT[1]	B-19 parvovirus
US paid apheresis (Talecris, Grifols, others[4])	Yes[2]	Yes	No [3]	No	No	No	No	Yes	Yes	Yes	No
United States, recovered, unpaid	Yes[2]	Yes	No[3]	Yes	Yes	Yes	No	Yes	Yes	Yes	No
Baxter BioScience: United States, Austria, Germany	Yes[2]	Yes	No	No	No	No	No	Yes	Yes	Yes	No
CSL Behring: Austria, Denmark, Germany, United States	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No
Biotest: Austria, Belgium, Germany, United States	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	No
Intersero: Austria, Belgium, Germany	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	No
Germany unpaid	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	No
Octapharma: Sweden, Austria, Germany	Yes	Yes	No	No	No	Yes[5]	No	Yes	Yes	No	No
American Community Blood Centers, unpaid (Octapharma)	Yes	Yes	No	Yes[5]	Yes[5]	Yes[5]	No	Yes	Yes	No	No
Finnish Red Cross BS: Finland, unpaid	Yes	Yes	No	1st donation & q 3 yrs	1st donation & q 3 yrs	No	No	Yes	Yes	No	No
Sanquin: The Netherlands	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	No	No
LFB: France	Yes[6]	Yes	No	Yes	Yes	Yes[7]	Yes [8]	Yes	Yes	No	No
Grifols: Spain, Czech Republic, Slovakia	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	No
Kedrion: Italy	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	No
National Bioproducts Institute: South Africa[11]	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No
Australian Red Cross Blood Service [9]	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	No	No
New Zealand Blood Service [9]	Yes	Yes	No	1st donation	1st donation	No	No	Yes	Yes	No	No
Centre for Transfusion Medicine, Singapore [9]	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No
National Blood Center, Malaysia [9]	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No
Hong Kong Red Cross BTS [9]	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No	No
Japan	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Korean Red Cross: South Korea [10]	Yes	Yes	Yes	No	No	No	No	Yes	Yes [10]	Yes	No
Shanghai RAAS Blood Products Co: China	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	No

1. ALT testing is not required for release of plasma in the USA. The requirement in Europe is country-specific.
2. Performed every 4 months in accordance with the US Code of Federal Regulations.
3. Not required if a US FDA licensed HIV-1 NAT test, approved as an alternative to HIV-1 p24 Ag testing, is used..
4. US paid apheresis source plasma is used by several European fractionators, as indicated; US unpaid plasma (recovered from whole blood donations) is used by fractionators in other countries. US recovered plasma originates from the American Red Cross and other licensed US blood banks.
5. Only relevant for transfusion blood products but not for plasma for fractionation.
6. Not required for apheresis plasma intended only for fractionation.
7. Only in first time donors or for hepatic assessment after seroconversion.
8. Only performed when screening test for Hc Ab is positive.
9. CSL Bioplasma in Australia fractionates plasma on a contract (toll) basis for the Australian Red Cross Blood Transfusion Service, the New Zealand Blood Service, the Hong Kong Red Cross Blood Transfusion Service, the Center for Transfusion Medicine of Singapore and the National Blood Center of Malaysia, Kuala Lumpur.
10. NAT for HCV is performed on individual donations in Korea.
11. Since 2005, NAT tests for HCV, HBV and HIV-1 have been performed on individual donations of plasma supplied by SA Blood Transfusion Services

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
CSL Behring: United States, Germany	60+ days	512 or fewer	HAV, HBV, HCV, HIV-1, B-19 parvovirus	HAV, HBV, HCV, HIV, B-19 parvovirus	No
Baxter BioScience: United States, Austria	60+ days	512	HAV, HBV, HCV, HIV-1, B-19 parvovirus	HAV, HBV, HCV, HIV 1-2, B-19 parvovirus	
Talecris: United States	60+ days	96 or 480	HBV, HCV, HIV 1, B-19 parvovirus	HBV, HCV, HIV-1, B-19 parvovirus	No
Grifols: United States, Spain, Czech Republic, Slovakia	60+ days	512 or fewer	HAV, HBV, HCV, HIV, B-19 parvovirus	HBV, HCV, HIV, B-19 parvovirus	
BPL, UK: US plasma used	60 days	512	HAV, HBV, HCV, HIV 1-2, B-19 parvovirus	European requirement[1]	
Biotest: Germany	60 days	960	HAV, HBC, HCV, HIV 1, B-19 parvovirus	HBV, HCV, HIV	
Intersero: Germany	60+ days	960	HAV, HBV, HCV, HIV-1, B-19 parvovirus	HBV, HCV, HIV	
German Red Cross BSO NSTOB	2 months	48	HAV, HBV, HCV, HIV-1, B-19 parvovirus	European requirement[1]	
Octapharma: Sweden, Austria, Germany, USA	2 months[6]	16 - 512	(HBV,B-19 parvovirus,HAV, HCV, HIV-1.	European requirement[1]	No
Finnish Red Cross BS: Finland		1 or 96	HBV, HCV, HIV (individual) HAV, B-19 parvovirus (mini-pool)	FRC BS does not make plasma pools	
Sanquin: The Netherlands		480	HCV, HIV, HBV (individual) B-19 parvovirus (mini-pool)	HAV, HBV, HCV, HIV, B-19 parvovirus	
LFB: France	80+ days [4]	(1) 300; (2) 1000	(1) B-19 parvovirus; (2) HAV, HCV [5]	HAV, HBV, HCV, HIV-1, B-19 parvovirus	
Kedrion: Italy	60+ days	480 or fewer	HBV, HCV, HIV, B-19 parvovirus (HAV if required)	European requirement[1]	
National Bioproducts Institute, South Africa		1[2] and 216	HCV, HIV, HAV, B-19 parvovirus	HCV, HIV, HAV	
CSL Bioplasma, Australia		480	HCV, HIV (except ARCBS and NZBS plasma)	HCV, HIV (ARCBS and NZBS)	
Australian Red Cross Blood Service Fractionated at CSL Bioplasma		1[3] or 24[3]	HCV,HIV		
New Zealand Blood Service Fractionated at CSL Bioplasma		1[3] or 16	HCV, HIV		
Hong Kong Red Cross BTS Fractionated at CSL Bioplasma		24 (ARCBS), 480 (CSL)	HCV, HIV (at both ARCBS and CSL Bioplasma)		
Centre for Transfusion Med, Singapore Fractionated at CSL Bioplasma		1[2] (Singapore) 480 (CSL)	HCV, HIV (CSL)		
National Blood Centre of Malaysia Fractionated at CSL Bioplasma		480 (CSL)	HCV, HIV (CSL)		
GreenCross: South Korea	45 days	< 450	HAV, HCV	HAV, HBV, HCV, HIV	HAV, HBV, HCV, HIV
Japanese Red Cross: Japan	6 months	20	HBV, HCV, HIV-1	HBV, HCV, HIV-1	HAV, HBV, HCV, HIV-1, B-19 parvovirus
Kaketsuken: Japan	6 months	(1) 50, (2) 500	(1) HBV, HCV, HIV-1, (2) HAV, B-19 parvovirus	HAV, HBV, HCV, HIV-1, B-19 parvovirus	HAV, HBV, HCV, HIV-1, B-19 parvovirus
Benesis, Japan	6 months	50	HBV, HCV, HIV-1	HBV, HCV, HIV-1	HAV, HBV, HCV, HIV-1, B-19 parvovirus
Shanghai RAAS Blood Products: China	60+ days	48	HBV, HCV, HIV-1	HBV, HCV, HIV-1	HBV, HCV, HIV-1

1.The European Pharmacopoeia requires HCV testing by NAT.

2. Since October, 2005, NAT tests for HCV HBV and HIV are performed on individual donations.

3. "1" indicates single-bag testing.

4. A minimal 80 day observation period between the day of collection and thawing, and a minimal 90 day observation period between the day of collection and the first step of the manufacturing process

5. These tests are not performed by LFB when they are already carried out by the local testing centre during the biological qualification of the donation.

6. 60 days inventory hold performed on US Plasma only.

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

BRAND	COMPANY	SITE OF MANUFACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb FVIII IU/mg [1]	COMMENT
Factor 8 Y	BioProducts Lab.	Elstree, England	United States: paid apheresis	Both	Heparin/glycine ppt	Dry heat, 80° C, 72 hr	2.5 - 4	Contains VWF
Haemosolvate Factor VIII	National Bioproducts	Durban, South Africa	South Africa & United States: unpaid	Both	Heparin/glycine ppt	TNBP/ polysorbate 80	4-11	No albumin added; contains VWF
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)	CSL Behring	Marburg, Germany	United States, Germany, Austria: paid & unpaid	Both	Multiple precipitation	Pasteurization, 60° C,10 hr	38	Albumin added, contains VWF, ratio vWF/FVIII > 2.2
Humate P	CSL Behring	Marburg, Germany	United States: paid apheresis	To USA and Canada	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	Talecris	Clayton, NC, USA	United States: 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 Bioplasma	Melbourne, Australia	Australia, New Zealand, Malaysia, Singapore, Hong Kong: 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	Seoul, Korea	Korea: unpaid; United States: paid apheresis	Both	Ion exchange chromatography	TNBP/Triton X 100; Dry heat 100° C, 30 min	100+	No albumin added, contains VWF
Confact F	Kaketsuken	Kumamoto, Japan	Japan: unpaid	Domestic	Ion exchange chromatography	Dry heat, 65° C, 96 hr; 19 nm nanofiltration	50	Albumin added
Immunate	Baxter BioScience	Vienna, Austria	United States, Austria, Czech Republic, Germany, Sweden: mostly paid apheresis	Both	Ion exchange chromatography	Solvent-detergent ; vapor-heat, 60° C, 10 hr at 190 mbar	Mean 70, SD 30	Albumin added, contains VWF
Emoclot D.I.	Kedrion	Barga, Italy	Europe and United States: paid & unpaid	Both	Ion exchange chromatography	TNBP/polysorbate 80 & dry heat, 100° C, 30 min	> 80	No albumin added, contains 0.4 IU VWF:RCo per IU FVIII
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
Faktor VIII SDH Intersero	Intersero	Biotest, 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
Octanate	Octapharma	Vienna, Austria, Stockhom, Sweden & Lingolsheim, France	Sweden, Austria, Germany, United States	Both	Precipitations, ion exchange chromatography	TNBP/polysorbate 80 & Terminal dry heat, 100° C, 30 min at controlled residual moisture	> 100	No albumin added, contains VWF
Wilate	Octapharma	Vienna, Austria	Sweden, Austria, Germany, United States	Both	Precipitations, ion exchange and size exclusion chromatography	TNBP/Triton X 100, & terminal dry heat, 100° C, 120 min, at controlled residual moisture	>100	No albumin added; contains VWF and FVIII in the physiological ratio
FACTANE	LFB	France	Western European unpaid	Both	Adsorption on aluminium hydroxide gel Ion exchange chromatography	TNBP/ polysorbate 80 & 35-15 nm nanofiltration	> 100	No albumin added, contains VWF
Beriate P	CSL Behring	Marburg, Germany	USA, Austria, Denmark, Germany: paid & unpaid	Both	Ion exchange chromatography	Pasteurization, 60° C, 10 hr	170	No albumin, stabilized in amino acids & sucrose
Optivate	Bio Products Laboratory	Elstree, England	United States paid apheresis	Both	Cryoprecipitation, heparin and glycine precipitation, MPHS chromatography	Solvent-detergent and dry heat, 80°, 72 hr	800	Contains VWF

1. Specific activity minus any added albumin

TABLE 3. FACTOR VIII CONCENTRATES: AFFINITY CHROMATOGRAPHY, OR RECOMBINANT

BRAND	COMPANY	SITE OF MANU-FACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb FVIII IU/mg [1]	COMMENTS
Alphanate	Grifols	Los Angeles, CA, USA	United States: paid apheresis	Both	Heparin ligand chromatography	TNBP/polysorbate 80 & dry heat, 80° C, 72 hr	≥100	Albumin added, contains VWF; SA w/o alb & VWF = 1000-3000
Fanhdi	Grifols	Barcelona, Spain	1. USA: paid apheresis 2. Spain: unpaid recovered & apheresis 3. Czech Republic: recovered & apheresis 4. Slovakia, recovered & apheresis	1. Both 2.Domestic only 3. to Czech Republic 4. to Slovakia	Same as above	Same as above	≥100	Same as above
Monoclate P	CSL Behring	Kankakee, IL, USA	United States: 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	United States: paid apheresis	Both	Monoclonal Ab affinity & ion exchange chromatography	TNBP/ Octoxynol 9	Approx. 2000	Albumin added, no functional VWF
Replenate	Bio Products Laboratory	Elstree, England, UK	United States: paid apheresis	Domestic	Monoclonal Ab affinity & ion exchange chromatography	TNBP/ Triton X 100	> 2000	As above
Amofil	Sanquin OY	Sanquin, Amsterdam	Finland: unpaid recovered	To Finland	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	Amsterdam, Netherlands	Netherlands: unpaid	Domestic	Same as above	Same as above	> 2000	As above
GreenMono	Greencross Corp	Seoul, Korea	Korea: unpaid	Domestic	Same as above	TNBP/ Triton X 100	> 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

1. Specific activity minus any added albumin

Recombinant factor VIII concentrates:

BRAND	COMPANY	SITE OF MANU-FACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb FVIII IU/mg [1]	COMMENTS
Kogenate FS = KOGENATE Bayer (in EU)	Bayer	Berkeley, CA, USA	None, recombinant	Both	Recombinant: ion exchange & immunoaffinity chromatography	TNBP/ polysorbate 80	2600 - 6800	Full-length rFVIII; no VWF. Formulated with sucrose. Albumin not added during purification or formulation.
Helixate NexGen = Helixate FS	CSL Behring	Made by Bayer, Berkeley, CA	None, recombinant	Both	(Identical to Kogenate FS)	TNBP/ polysorbate 80	2600 - 6800	Same 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	Stockholm, Sweden	None, recombinant	Both	Recombinant	TNBP/ Triton X 100	13,000	B-domain-deleted FVIII, no VWF. No albumin added in formulation.

1. Specific activity minus any added albumin

TABLE 4: PROTHROMBIN COMPLEX CONCENTRATES ("PCC"; concentrates of prothrombin and factors VII, IX and X)

BRAND	COMPANY	SITE OF MANU-FACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb FIX IU/mg [1]	COMMENTS
Proplex – T	Baxter BioScience	Los Angeles, CA, USA	United States: 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
Prothroraas	Shanghai RAAS	Shanghai, China	China, paid/unpaid apheresis	Both	PEG precipitation, DEAE sephadex	Solvent/ detergent, nanofiltration		
Beriplex P/N	CSL Behring	Marburg, Germany	United States, Austria, Germany paid/unpaid	Both	DEAE-sephadex	Pasteurization at 60° C, 10 hr, & nanofiltration	3.5 – 5	Contains protein C 700-900 IU per 500 IU factor IX; anti-thrombin III, heparin & albumin added
Haemosolvex Factor IX	National Bioproducts	Pinetown, South Africa	South Africa: unpaid	Both	DEAE-sephadex	TNBP/polysorbate 80	0.9	No albumin added; heparin added
Profilnine SD	Grifols	Los Angeles, CA, USA	United States: paid apheresis	Both	Double DEAE cellulose chromatography	Solvent/detergent	4	No albumin, heparin or antithrombin III added
Prothrombinex-VF	CSL Bioplasma	Melbourne, Australia	Australia, New Zealand, Hong Kong, Malaysia, unpaid	Both	DEAE cellulose absorption	Dry heat, 80° C, 72 hr Nanofiltration	1 – 5	No albumin added
Prothromplex-T	Baxter BioScience	Vienna, Austria	United States, Austria, Czech Republic, 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	United States: paid apheresis	Export to USA	Same as above	Same as above		Heparin added
HT DEFIX	SNBTS	Edinburgh, Scotland	United States & Germany: unpaid	Both	Ion exchange chromatography	Dry heat, 80° C, 72 hr	2	Anti-thrombin III added
Octaplex	Octapharma	Vienna, Austria & Lingolsheim, France	Sweden, Austria, Germany & United States	Both	Ion exchange chromatographies	TNBP/ polysorbate 80 & nanofiltration	1 or more	Heparin added, no antithrombin or albumin added, low factor VIIa content
Facnyne	Greencross Corp	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 & 15 nm 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 & 15-19 nm	1	Anti-thrombin III & heparin added; no albumin added
UMAN Complex D.I.	Kedrion	Barga,Italy	Europe & United States, 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	Ion exchange chromatography	TNBP/ polysorbate 80	≥0.6	Heparin added, no albumin or anti-thrombin III added

1. Specific activity minus any added albumin

TABLE 5: CONCENTRATES PRIMARILY INTENDED FOR USE IN PATIENTS WITH INHIBITORS: Activated Concentrates (Bypassing agents)

FEIBA VH	Baxter Bioscience	Vienna, Austria	United States, Austria, Czech Republic, Germany, Sweden; mainly 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
NovoSeven = Niastase (in Canada)	Novo Nordisk	Copenhagen, Denmark	None	Both	Recombinant Factor VIIa	None	Also licensed for use in congenital deficiency of factor VII, in United States

TABLE 6: HIGHLY PURIFIED FACTOR IX CONCENTRATES

BRAND	COMPANY	SITE OF MANU-FACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb FIX IU/mg [1]	COMMENTS
Berinin-P = Berinin HS	CSL Behring	Marburg, Germany	United States, 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	United States, Austria, Czech Republic, 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
Octanine F	Octapharma	Vienna, Austria & Lingolsheim, France	Sweden, Austria, Germany & United States	Both	Ion exchange & affinity chromatographies	TNBP/ polysorbate 80 & nanofiltration	> 120	No albumin added
Nanotiv	Octapharma	Stockholm, Sweden	Sweden: Recovered & apheresis	Both	Ion exchange & affinity chromatographies	TNBP/ Triton X 100 & nanofiltration	150	No albumin added
MonoFIX-VF	CSL Bioplasma	Melbourne, Australia	Australia,New Zealand, Singapore, Hong Kong: Unpaid	Both	Ion exchange & heparin affinity chromatography	TNBP/ polysorbate 80 & nanofiltration	>50	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	Kedrion	Italy	Europe & United States: paid & unpaid	Both	Anion exchange, DEAE sephadex/sepharose & heparin affinity chromatography	TNBP polysorbate 80; dry heat 100° C, 30 min; nanofiltration 35 + 15 nm (registration pending for nanofiltration)	> 100	Anti-thrombin III & heparin added, no albumin added
BETAFACT	LFB	France	Western Europe, unpaid	Both	Ion exchange chromatography and 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
Factor IX Grifols	Grifols	Barcelona, Spain	1. United States paid 2. Spain recovered and apheresis, unpaid	1. Both 2. Domestic	Precipitation & multiple chromatography (including metal chelate affinity)	Solvent detergent, 15 nm nanofiltration	> 150	No albumin added
AlphaNine SD	Grifols	Los Angeles, CA, USA	United States: paid apheresis	Both	Ion exchange and dual polysaccharide ligand chromatography	Solvent/detergent, nanofiltration	210	No albumin added
Mononine	CSL Behring	Kankakee, IL, USA	United States: apheresis paid	Both	Immunoaffinity chromatography	Sodium thiocyanate & ultrafiltration	> 190	No albumin added
Nonafact	Sanquin	Amsterdam, The Netherlands	The Netherlands: unpaid	Both	Immunoaffinity & hydrophobic interaction chromatography	TNBP/ polysorbate 80; 15 nm 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	United States: paid apheresis	Both	Metal chelate chromatography	Solvent-detergent; 15 nm nanofiltration	200	No albumin added

1. Specific activity minus any added albumin

RECOMBINANT FACTOR IX CONCENTRATE

BRAND	COMPANY	MADE AT	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	SA s alb FIX IU/mg [1]	COMMENTS
BeneFIX	Wyeth	Andover, MA; USA	Both	Recombinant	Nanofiltration	200 +	No human or animal proteins used in manufacture; no albumin added
BeneFIX	Baxter SA (Switzerland)	Wyeth, Andover, MA, USA	Europe	Recombinant	Nanofiltration	200+	No human or animal proteins used in manufacture; no albumin added

1. Specific activity minus any added albumin

TABLE 7: OTHER CLOTTING FACTOR CONCENTRATES

BRAND	COMPANY	SITE OF MANU-FACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	COMMENTS
Clottagen (fibrinogen)	LFB	France	Western Europe, unpaid	Both	adsorption on aluminum hydroxide gel, Ion exchange chromatography and affininity 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; 35 nm nanofiltation	No albumin added
FIBRORAAS (fibrinogen)	Shanghai RAAS	Shanghai, China	China: paid & unpaid apheresis	Both	Multiple fractionation	TNBP/ polysorbate 80	
Haemocomplettan P = Haemocomplettan HS (fibrinogen)	CSL Behring	Marburg, Germany	United States, Austria, Germany; paid & unpaid	Both	Multiple precipitation	Pasteurization at 60° C, 20 hr	Albumin added
Factor VII	Baxter BioScience	Vienna, Austria	United States, 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	Elstree, England,	United States: paid apheresis	Both	Ion exchange chromatography	Dry heat, 80° C, 72 hr	S.A. 1.5 – 2 U/ mg protein
FACTEUR VII	LFB	France	Western Europe, unpaid	Both	Ion exchange chromatography	TNBP/ polysorbate 80	no albumin added
NovoSeven (=Niastase) (activated factor VII)	NovoNordisk	Copenhagen, Denmark	None	Both	Recombinant	Not applicable	Approved for congenital factor VII deficiency
Factor X P Behring	CSL Berhing	Marburg, Germany	United States, Austria, Germany; paid/unpaid	Both	DEAE-sephadex and precipitations	Pasteurization at 60° C, 10 hr	Contains high amount of factor X and some FIX, but no FII and FVII; antithrombin III and heparin added, no albumin added
Factor XI	Bio Products	Elstree, England, UK	United States: 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	Ion exchange chromatography, depth filtration	TNBP/ polysorbate 80 15 nm nanofiltration	Heparin, Anti-thrombin III added, C-1 esterase inhibitor added
WILFACTIN (Von Willebrand Factor)	LFB	France	Western Europe, unpaid	Both	Adsorption on aluminum hydroxide gel Ion exchange chromatography and affininity chromatography	TNBP/polysorbate 80; 35 nm nanofiltration; dry heat 80° C, 72 hr	S.A. (before addition of albumin) : > 50 units ristocetin cofactor (VWF:RCo) per mg; Albumin added
Fibrogammin P (=Fibrogammin HS) (Factor XIII)	CSL Behring	Marburg, Germany	United States, Austria, Germany: paid & unpaid	Both	Multiple precipitation	Pasteurization at 60° C, 10 hr	Albumin added

TABLE 8. CONCENTRATES OF ANTI-THROMBOTIC FACTORS: (A) Anti-thrombin concentrates

BRAND	COMPANY	SITE OF MANU-FACTURE	PLASMA SOURCE	EXPORT/ DOMESTIC	FRACTIONATION	VIRAL INACTIVATION	COMMENTS
ACLOTINE	LFB	France	Western Europe, unpaid	Both	affinity chromatography, depth filtration	Pasteurization, 60º C, 10 hrs 20-15 nm nanofiltration	
Anbinex	Grifols	Barcelona, Spain	1.United States paid apheresis 2.Spain unpaid recovered and apheresis	1.Both 2. Domestic	Double heparin ligand chromatography	Pasteurization, 60º C, 10 hrs; 15 nm nanofiltation	Specific activity 7.9 ± 0.4 IU/mg
Anti-thrombin	GreenCross	Seoul, Korea	Korea unpaid and United States paid apheresis	Both	Ion exchange and heparin affinity chromatography	Pasteurization, 60º C, 10 hrs	Specific activity more than 8.3 IU/mg
ATIII	BPL	Elstree, England	United States paid apheresis	Both	Cryosupernatant; heparin absorption, sepharose chromatography	Pasteurization 60º C, 10 hrs and dry heat, 80º C, 72 hrs	
Kybernin P	CSL Behring	Marburg, Germany	United States, Austria, Germany; paid and unpaid	Both	Precipitations and affinity chromatography	Pasteurization, 60º C, 10 hrs	No heparin added
Neuart	Benesis	Osaka, Japan	Japan, unpaid	Domestic	Ethanol fractionation	Pasteurization, 60º C, 10 hrs and 20 nm nanofiltration	Specific activity 9-10 IU/mg
Thrombate-III	Talecris	Clayton, NC, USA			Ethanol fractionation	Pasteurization, 60º C, 10 hrs	
Thrombotrol-VF	CSL Bioplasma	Melbourne, Australia	Australia, New Zealand, unpaid	Both	Heparin, sepharose and gel filtration chromatography	Pasteurization, 60º C, 10 hrs and 15 nm nanofiltration	

(B) Protein C concentrates

Anact C (activated protein C)	Kaketsuken	Kumamoto, Japan	Japan, unpaid	Domestic	Affinity and ion exchange chromatography	Dry heat 65º C., 10 hrs, and 15 nm nanofiltration	
Ceprotin	Baxter	Vienna, Austria	United States & Europe	Both	Cryosupernatant; ion exchange and immunoaffinity chromatography	Detergent; vapor heat, 60° for 10 ht and 80° for 1 hr	Albumin added
PROTEXEL	LFB	France	Western Europe, unpaid	Both	Ion exchange chromatography and affininity chromatography	Solvent/Detergent (TNBP/polysorbate 80)	

1425 René Lévesque Blvd. W., Suite 1010 Montréal, Québec H3G 1T7 CANADA
Tel.: +1 (514) 875-7944 Fax: +1 (514) 875-8916
www.wfh.org