Registry of Clotting Factor Concentrates Ninth Edition, 2012

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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 products available for export and clarifies differences among them. (There are many products manufactured for use in single countries that are not included in the registry.) 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.

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 and Biotest in Germany) 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.

In 2011, Talecris became a subsidiary of Grifols. Some Talecris products manufactured before the merger would still be within their labeled shelf life and Talecris-labeled products are still manufactured and available in some countries

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.

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, Sweden, Czech Republik, Switzerland, Norway	Yes[12]	Yes	No[3]	No	No	No	No	Yes	Yes	No	No
CSL Behring: Austria, Denmark, Germany, United States	No for Europe Yes[2,1]	Yes	No	No	No	No	No	Yes	Yes	No	No
Biotest: Austria, Belgium, Germany, United States, Switzerland	No	Yes	No	No	No	No	No	Yes	Yes	No	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	No	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
Taiwan Blood Services Foundation	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	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
Bio Products Laboratory, UK: US paid apheresis	Yes	Yes	No	Yes (recovered only)	Yes (recovered only)	Yes (recovered only)	No	Yes	Yes	No	No

1. ALT testing is not required for release of plasma in the USA. The requirement in Europe is country-specific.
2. Performed at first donation and 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 Biotherapies 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 Blood Services Group 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
12. The requirement is country-specific

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, Italy	60+ days	512 or fewer	HAV, HBV, HCV, HIV-1, B-19 parvovirus	HAV, HBV, HCV, HIV 1-2, B-19 parvovirus	No
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	
Bio Products Laboratory, UK	60 days	512 or fewer	HAV, HBV, HCV, HIV 1-2, B-19 parvovirus	European requirement[1]	
Biotest: Germany	60 days	960	HAV, HBC, HCV, HIV 1, HIV 2, B-19 parvovirus	HBV, HCV, HIV	No
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 or 6	HCV (6), HIV (6), HBV (6), B-19 parvovirus (480), HAV (480)	HBV, HCV, HIV, B-19 parvovirus	No
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		12 and 216	HCV, HIV, HAV, B-19 parvovirus	HCV, HIV, HAV	
CSL Biotherapies, Australia		480	HCV, HIV (see exceptions below)	HCV, HIV, B19[3] (see exceptions below)	
Australian Red Cross Blood Service Fractionated at CSL Biotherapies		480/512	HCV,HIV, B19[3] (optional)	HCV, HIV, B19[3]	
New Zealand Blood Service Fractionated at CSL Biotherapies		480/512	HCV, HIV, B19[3] (optional)	HCV, HIV, B19[3]	
Hong Kong Red Cross BTS Fractionated at CSL Biotherapies				HCV, HIV	
Blood Services Group, Singapore Fractionated at CSL Biotherapies		480/512	HCV, HIV (optional)	HCV, HIV	
National Blood Centre of Malaysia Fractionated at CSL Biotherapies		480 /512	HCV, HIV	HCV, HIV	
Taiwan Blood Services Foundation Fractionated at CSL Biotherapies		480/512	HCV, HIV, HBV, HAV, B19	HCV, HIV (optional HBV, HAV, B19)	
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. Applicable to Rh(D) plasma and recovered plasma for Rh(D) diluent.
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.

OTHER TABLES IN THE REGISTRY

Table 2: Factor VIII Concentrates Made by Precipitation (PPT), Gel Permeation or Ion Exchange Chromatography
Table 2A: Von Willebrand/factor VIII concentrates for the management of VWD
Table 3: Factor VIII Concentrates: Affinity Chromatography, or Recombinant
Table 4: Prothrombin Complex Concentrates ("PCC"; concentrates of prothrombin and factors VII, IX and X)
Table 5: Concentrates Primarily Intended for Use in Patients with Inhibitors: Activated Concentrates (Bypassing agents)
Table 6: Highly Purified Factor IX Concentrates
Table 7: Other Clotting Factor Concentrates
Table 8: Concentrates of Anti-Thrombotic Factors: (A) Anti-thrombin concentrates

Facts & Figures #6, Registry of Clotting Factor Concentrates is available at the WFH booth and at www.wfh.org

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