Plasma collection and immunoglobulin manufacturing

RARE DISEASE HUB

2–3 months

1. PLASMA COLLECTION

Plasma collection

Source plasma[1–3] (~80% of plasma)

Source plasma is collected from screened healthy donors via plasmapheresis, an automated process that separates plasma from the cellular components, which is then returned to the donor. Provides ~800 mL of plasma per donation.

Recovered plasma[1–3] (~20% of plasma)

Recovered plasma is derived from the whole blood of screened healthy donors. Blood components are separated, providing ~250 mL plasma per donation.

Takeda BioLife Plasma Services have >110 facilities across the US and >30 facilities in Europe, which meet or exceed standards of the IQPP developed by the PPTA, as well as QSEAL voluntary standards.[4,5]

~130: PID

~130 donations/year are needed to yield the 105 litres of plasma required to treat an average adult patient with PID.*[2]

2. PLASMA TESTING

To ensure its safety, plasma undergoes a series of testing and screening, including serological and nucleic acid testing (NAT) for HIV, HBV, HCV, HAV and parvovirus B19.[3,4,6]

Plasma is held for 60 days (inventory hold) prior to further processing.[4]

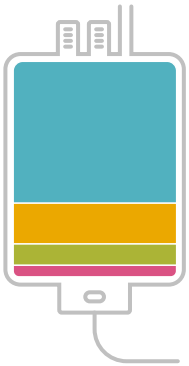
Plasma donation to in-market use ('vein-to-vein') takes approximately 7–12 months

3. PLASMA FRACTIONATION — 1 month

Pooled plasma undergoes fractionation, based on the process developed by Cohn *et al.* in the 1940s, to separate distinct proteins at different stages of the fractionation process. Fractionation combines manufacturing steps to isolate the crude fractions that are further purified into individual therapeutic products.[3,4,7]

Only 3–5 g of immunoglobulin can be obtained from a single 1 litre bag of plasma.[7,8]

Components within 1 litre of plasma[7,8]



Albumin (22–28 g)†
Burns, major incidents, major surgery, liver conditions

Immunoglobulin (3–5 g)†
Immunodeficiency diseases, specific neurological conditions, recurrent infections in certain conditions

Alpha-I antitrypsin (0.15–0.30 g)†
Alpha-I antitrypsin deficiency

Blood clotting proteins, e.g. factor VIII
Haemophilia and other clotting abnormalities

Listed under each component are factors that can influence the levels of each component in plasma.

4. PURIFICATION AND VIRAL REDUCTION/INACTIVATION — 2 months

Large-scale chromatography is used to improve the purity profile of extracted proteins.[3,4] Immunoglobulin fractionation involves three key safety steps for dedicated viral inactivation/removal:[4,9]

1. Solvent/detergent (S/D) treatment

Immunoglobulin is incubated in a solvent and 1–2 detergents for at least 1–6 hours at 25–35°C to remove enveloped viruses.[9–11]

2. Filtration

Nanofiltration of immunoglobulin removes lipid-enveloped viruses very effectively, non-lipid-enveloped viruses effectively and prions somewhat effectively.[9–11]

3. Low pH, high temperature incubation

Incubation of immunoglobulin at low pH and 30–32°C for >20 days inactivates a substantial dose of enveloped viruses. Complete inactivation (over 5–8 log) of HIV and other enveloped viruses is achieved. Efficacy against non-enveloped viruses is limited.[9]

2 months

5. FILL/FINISH — Formulation and packaging of the immunoglobulin product.[12]

6. DISTRIBUTION

7. PRODUCT TO PATIENT

*Based on 68 kg adult treated for 1 year; †Typical commercial plasma protein yields per litre of plasma.

HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQPP, International Quality Plasma Program; PID, primary immunodeficiency; PPTA, Plasma Protein Therapeutics Association; QSEAL, Quality Standards of Excellence, Assurance and Leadership.

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