Serum, Plasma & More

Human Products for Diagnostic Applications
For more than 20 years PAA Laboratories produces high quality cell culture media, reagents and sera. PAA features a worldwide raw material sourcing network and state-of-the-art GMP production facilities on three continents. They are located strategically in Europe, North America and Australia. Additionally PAA’s customers are served directly from seven subsidiary operations and local partners in more than 50 countries.

Besides animal sera and bovine serum albumin, also human serum and blood products are needed by the diagnostic industry. PAA is cooperating with reliable partners to source human plasma and serum of highest quality and safety. Benefit from our long lasting experience in the manufacture of sera and choose from our expanded product range for diagnostic applications.
Human Blood Products

Blood, often described as liquid tissue, is essential for almost all functions of the human body. The 4 – 6 litres of blood of an adult supply all organs with oxygen and enable transportation of substances, removal of metabolic waste, defence against pathogens, adjustment of temperature and fluid level and a lot more. Some of these important tasks are carried out by blood cells, namely oxygen-carrying erythrocytes, leukocytes which belong to the immune system and thrombocytes playing a key role in blood clotting.

Since blood plays such a vital role, the loss of already one litre can be life-threatening. Therefore, several million litres of blood are donated worldwide to save the lives of a multitude of patients. Not only blood loss can be treated with the help of these donations, also products to medicate severe diseases like haemophilia are based on donated blood.

All in all, the usage of blood and blood products can be divided into three categories described in the following.

**Therapeutics**

Improved techniques of blood separation are an essential part of modern blood donation. The partition of blood into the liquid part (plasma) or single cell types enables the optimum usage of every blood donation. Patients lacking thrombocytes for example can be treated with a concentrate consisting of these cells. On the other hand, erythrocyte concentrates gained from the same blood donation may be given to patients suffering from great blood loss. Finally, the residual plasma can be used to fractionate proteins, e.g. coagulation factors which are essential for the treatment of bleeding disorder.

**Diagnostics**

Blood products are not only used for the direct treatment of diseases or injuries. Human plasma, serum and albumin are also key products for the diagnostic industry. They are an integral part of most diagnostic test kits, used as negative or positive controls, standards, blocking reagents or diluents. A lot of diseases can only be correctly diagnosed by using these kits.

PAA offers a variety of products based on human plasma, serum and albumin exclusively intended for diagnostic usage only.

**Research**

Human serum, plasma and albumin are widely used in different fields of research. For the cultivation of human cells, human serum serves as a growth supplement to work within a homologous system. In addition to the expansion of our knowledge of cellular processes, these cells act as test systems to develop and optimize new therapies. Furthermore, human blood products are used as a blocking agent or control standard.

For these applications PAA provides different cell culture tested human products.
Plasma and Serum

Blood Clotting

To prevent blood loss after injuries, the coagulation cascade is activated by wounds or through contact to foreign surfaces. At the end of a complex series of reactions, the activation of thrombin results in the cleavage of fibrinogen to fibrin. Fibrin forms fibres and together with attracted thrombocytes they clot to close the wound.

Human Plasma

The surface of a collecting tube or bag would start the clotting cascade. Therefore anti-coagulants are included to avoid the formation of a clot during and after donation. These anti-coagulants are mostly based on citrate binding the calcium ions which are essential for most reactions in the clotting cascade. After separation of blood cells the remaining soluble part is called plasma.

Human Serum

If anti-coagulants are not added the clotting cascade will be activated and a blood clot forms shortly after donation. The clot consists of cells and fibrin and sediments at the bottom. Due to the fact that the soluble fraction of this material is then taken “off the clot” it is named off the clot serum.

In summary, the main difference between plasma and serum is the presence of coagulation factors and anti-coagulants in plasma (see figure 1).

Fig. 1: Difference in Plasma and Serum
Plasma Fractionation

45% of human blood consist of erythrocytes, leukocytes and thrombocytes. The major part of the residual volume is water containing electrolytes and proteins. The most abundant protein is albumin, followed by immunoglobulins and coagulation factors.

Cohn-Fractionation

The soluble part of blood contains proteins which are of importance for the treatment of certain diseases. The purification of single proteins is mostly performed according to a method established by Cohn in 1946. Today a couple of variations of this procedure exist.

In principle, Cohn-Fractionation utilizes the different solubility of albumin compared to other plasma proteins depending on ethanol concentration, pH and temperature. The main steps of the fractionation are illustrated in Figure 2.

Human Serum Albumin (HSA)

Albumin, present in fraction V, is a versatile product and suitable for different applications. It is used as a therapeutic for example after severe burns. Diagnostic kits contain HSA as a stabilizer or protein standard. Moreover, albumin serves as a growth supplement in cell cultures.

PAA offers high quality Human Serum Albumin in powder or liquid form in different concentrations for diagnostic purposes.
Donation

High demand for blood products
The growing world population and the improved health care situation in many countries result in a constantly increasing demand for blood products. Unfortunately the donation rates do not keep up with this development. Thus regular shortages occur even though about 60 million litres of blood and plasma are donated worldwide per year.

Selection of Donors
The selection of donors underlies strict regulations to ensure absolute safety for the patient. Depending on the country the criteria to be accepted as donor are slightly different. Among others they comprise the donor’s age, minimum weight and health status. Reasons for exclusion can be manifold such as pregnancy, recent residence in certain countries or the intake of drugs. Some of these reasons lead to a permanent, others only to a temporary rejection.

Donation Centres
Not only the selection of donors but also the reliability of the donation centre has great influence on the quality and safety of the product. Analogous regulations are valid for blood donations in Europe and the United States. The following issues describe the situation on example of Europe:

► Traceability
Donation centres must keep records over all donations for at least 30 years.

► "Look back"
An unfailing system must be established to track down the donor for any blood donation in the shortest time.

► Quality Assurance (QA)
European blood donation centres must comply with the stringent requirements laid down in the Good Clinical Laboratory Practise (GLP) and Good Manufacturing Practise (GMP) set by the European Community. This is absolutely essential to ensure highest standards for withdrawal, processing and storage of donations.

► Qualified Personnel
It is absolutely compulsory that a physician is present when the donation takes place. Furthermore, the leading physician of the donation centre has to be a specialist for transfusion medicine.
Whole Blood Donation vs. Plasmapheresis

There are different possibilities to donate blood or blood fractions. On the one hand, there is the classical whole blood donation in which up to 500 ml are given. It takes several weeks for the body to replace the blood cells. Thus a minimum of 8 weeks must lie between two donations.

In contrast to that, it is possible to leave the blood cells with the donor and only take the soluble part, the plasma. During this so-called plasmapheresis, the cellular components are separated from the liquid part outside the body. The cells are then transfused back into the donor. The advantage of this process is that a donation can be done every two days with up to 880 ml at a time. Especially the pharmaceutical industry greatly depends on plasma donated that way.

Strict Tests of each Donation

Part of the strict controls, which every accredited donation centre performs, is a thorough testing of every donation. Besides basic blood values, to detect a potential disease and determination of the blood group, extensive viral tests are carried out. With these tests, a past or present infection with HIV 1 or 2, Hepatitis B or C, and Syphilis can be detected (see box).

Additional measures such as the follow-up of the donor make sure that no blood products with latent infections below the detection limit are released.

PAA only sources raw material which is found negative for all mandatory virus and bacteria tests, carried out with validated test kits.

Viral Tests on every Donation

- Detection of antibodies against HIV 1 or 2
- Detection of antibodies against Hepatitis C virus
- Detection of Hepatitis B surface antigens
- Nucleic Acid Test for Hepatitis C genome
- Nucleic Acid Test for HIV 1 genome
- Detection of antibodies against Treponema pallidum

All test kits must be accredited and released by the respective national agencies.

PAA only works together with fully accredited blood donation centres. We set a high value on the safety of our products. Thus raw material is transported to PAA in controlled cool trucks and is stored in validated refrigerated warehouses to maintain the cold chain.
Processing

In our state-of-the-art facility we combine 20 years of experience with pharmaceutical production and quality control standards. PAA only uses human plasma and serum which is shipped under temperature controlled conditions from accredited blood donation centres.

Subsequent pooling of plasma or serum is strictly controlled and documented. This allows a traceability of every donation to the respective pool.

Every pool is then filtrated through 0.22 µm and either filled in sterile bottles or ready for further processing. These additional manufacturing steps include defibrination, dialysis, delipidation and charcoal stripping to meet the special demands of our customers.

The following overview of possible treatments of plasma or serum shall be a guide to decide on the most suitable product.

Untreated Plasma
Plasma can be distinguished by the way of sourcing. If plasma is taken from whole blood donations it is called Recovered Plasma. Whereas plasma donated separately, using plasmapheresis is called Source Plasma.
**Defibrination**

Plasma, in contrast to serum, still contains clotting factors and fibrinogen. Additionally, anti-coagulants are present, binding calcium ions being essential for the clotting cascade.

Since fibrinogen is unwanted in some applications the clotting cascade can be activated by the addition of calcium and thrombin. The resulting fibrin clot can then be removed.

**Dialysis**

A semi-permeable membrane with a defined pore-size may be used to alter the concentrations of small molecules or ions. This procedure allows the adjustment of electrolyte concentration to a physiological level. The method also allows the enrichment or depletion of certain factors according to customer specific requirements.

Dialysed defibrinated plasma can be found in our product portfolio under the name **Converted Serum**.

**Delipidation**

PAA offers plasma and serum with reduced lipid content since the presence of triglycerides and cholesterol can disturb measurements or may inhibit protein interactions. To lower the content of these lipids, fumed silica is used for binding and removal of these substances.

**Charcoal Stripping**

Activated charcoal has a very large surface area, thus it is ideal for adsorption and chemical reactions. In serum or plasma activated charcoal preferentially binds to steroid hormones. Due to this fact charcoal stripped material is also referred to as “hormone reduced”. Plasma or serum with low hormone levels can be utilized as negative control or diluent in assays determining hormone concentrations.

All untreated or processed plasma or serum can be charcoal stripped upon request.
GMP compliant Quality Control

**Extensive Analyses**

All blood products provided by PAA are tested according to the actual regulations and are collected in accredited blood donation centres. Every single donation is thoroughly tested with validated methods to detect a possible infection with HIV 1 or 2, Hepatitis B or C and Syphilis.

Every batch of PAA’s plasma, serum or HSA solution is filtered through 0.22 µm before the final filling. Extensive analyses are routinely performed on every end product by our comprehensive GMP compliant quality control.

**Chemical Analyses**

- Optical Appearance
- pH value
- Osmolality
- Endotoxin
- Calcium
- Chloride
- Creatinin
- Potassium
- Sodium
- Total Bilirubin
- Uric Acid
- Haemoglobin
- Glucose
- Cholesterol
- Triglycerides
- Folate

**Protein Concentrations**

- Total Protein
- Albumin
- α-Globulin
- β-Globulin
- γ-Globulin

**Micro Organisms**

- Aerobic Bacteria
- Anaerobic Bacteria
- Mycoplasma
- Fungi
- Sterility

**Cell Culture**

- Growth promotion
### Human Plasma

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<tr>
<th>Description</th>
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### Human Serum

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### Human Serum Albumin

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Other processing services (e.g. Charcoal Stripping) and/or other packaging sizes are available upon request.

All products are exclusively intended for diagnostic applications and not intended for therapeutic use.