Pharmaceuticals Policy and Law 7 (2005,2006) 273–282
IOS Press

Glossary of terms

Johan Prévot
Senior Manager, Public Affairs, PPTA Europe

This glossary contains definitions of terms commonly used in the field of blood and plasma protein therapies. These definitions may be helpful to better understand specific terminologies used throughout this book as well as in other documents on this subject matter.

Provided definitions may not apply in all situations. These definitions have been collected from various official sources (see *Sources*).

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Additive solution: a solution specifically formulated to maintain beneficial properties of cellular components during storage.

Albumin: the major plasma protein (approximately 60 per cent of the total), which is responsible for much of the plasma colloidal osmotic pressure and serves as a transport protein. Albumin stabilises circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

Allogeneic donation: blood and blood components collected from an individual and intended for transfusion to another individual, for use in medical devices or as starting material/raw material for manufacturing into medicinal products.

Alpha-1 Antitrypsin Deficiency (**AAT Deficiency or Alpha-1**)**:** is one of the most common serious hereditary disorders in the world and can result in life-threatening liver disease in children and adults or in lung disease in adults.

Apheresis: a method of obtaining one or more blood components by machine processing of whole blood in which the residual components of the blood are returned to the donor during or at the end of the process.

Autologous donation: blood and blood components collected from an individual and intended solely for subsequent autologous transfusion or other human application to that same individual.

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Batch (or *Lot*): a defined quantity of starting material, packaging material, or product processed in a single process or series of processes so that it could be expected to be homogeneous.

Biological product: Biological Products are defined as so because they are more difficult to characterise or control than standard chemically synthesised pharmaceuticals.

They include those where the starting material may be human or animal tissue or of microbiological origin. Also included are those where a complex bioassay system is required to monitor potency.

The two largest groups of biologicals are blood products and vaccines. Other products include hormones, larger peptides and a miscellaneous group of tissue derived products.

Biotechnology product: is one manufactured by recombinant DNA technology, one where genetic manipulation of cells is required, or a monoclonal antibody. Applications for these products are required to be submitted through the European centralised procedure. They comprise List A (the mandatory part) of the procedure.

Blood: whole blood collected from a single donor and processed either for transfusion or further manufacturing.

Buffy coat: a blood component prepared by centrifugation of a unit of whole blood, and which contains a considerable proportion of the leucocytes and platelets.

Chronic inflammatory demyelinating polyneuropathy (**CIDP**)**:** a rare autoimmune demyelinating polyneuropathy that can affect adults and children. Prolonged remission after treatment or cure is the exception. Long-term treatment is necessary, often for many years. Sometimes referred to as chronic Guillain-Barr é Syndrome.

Coagulation (**or clotting**) **factors:** a group of plasma protein substances (Factor I-XIII) contained in the plasma, which act in concert to bring about blood coagulation.

- **Factor VIII:** antihemophilic factor that is part of the factor VIII/von Willebrand factor complex. It is produced in the liver and acts in the intrinsic pathway of blood coagulation. It serves as a cofactor in factor X activation and this action is markedly enhanced by small amounts of thrombin.
- **Factor IX:** one of the proteins of the coagulation system. Deficiency of this protein causes haemophilia B.
- **Von Willebrand Factor:** plasma glycoprotein associated with Factor VIII; important in clotting and hemostatic plug formation.

Compatibility testing: the procedures performed to establish the matching of a donor's blood or blood components with that of a potential recipient.

C1 esterase inhibitor deficiency: Deficiency in C1 esterase inhibitor protein, the main function of which is inhibition of the complement system, causes intermittent angioedema (swelling of face and throat) and dermal swellings.

Control: having responsibility for maintaining the continued safety, purity, and potency of the product and for compliance with applicable product and establishment standards, and for compliance with current good manufacturing practices.

Cryoprecipitate: a plasma component prepared from plasma, fresh-frozen, by freeze-thaw precipitation of proteins and subsequent concentration and re-suspension of the precipitated proteins in a small volume of the plasma.

Cryopreservation: prolongation of the storage life of blood components by freezing.

Distributed:

(1) The blood or blood components have left the control of the licensed manufacturer, unlicensed registered blood establishment, or transfusion service; or
(2) The licensed manufacturer has provided Source plasma or any other blood component for use in the manufacture of a licensed biological product.

Distributor: any person engaged in the unrestricted distribution, other than by sale at retail, of products subject to license.

Facilities: any area used for the collection, processing, compatibility testing, storage or distribution of blood and blood components.

Fibrin: A protein involved in the clotting of blood. It is a fibrillar protein that is polymerised to form a "mesh" that forms a haemostatic plug or clot (in conjunction with platelets) over a wound site. Fibrin is made from its zymogen fibrinogen.

Fibrinogen: A soluble plasma glycoprotein that is synthesised by the liver. Processes in the coagulation cascade activate the zymogen prothrombin to the serine protease thrombin, which is responsible for converting fibrinogen into fibrin. Fibrin is then cross linked by factor XIII to form a clot.

Fibrin sealant: Plasma protein therapy used as surgical glue, to control bleeding. Its main ingredient is fibrinogen.

Good Manufacturing Practice: The part of the pharmaceutical quality assurance process which ensures that products are consistently produced and to meet to the

quality standards appropriate to their intended use and as required by the marketing authorization.

Granulocytes, apheresis: a concentrated suspension of granulocytes obtained by apheresis.

Guillain-Barré Syndrome (GBS): an acute disease of the peripheral nervous system in which the nerves in the arms and legs become inflamed and stop working. This causes sudden weakness leading to limb paralysis, and a loss of sensation, sometimes with pain.

Haematology: The science of the blood and blood producing organs

Haemophilia: Haemophilia is a lifelong bleeding disorder that prevents blood from clotting properly. People with hemophilia do not have enough clotting factor, a protein in blood that controls bleeding. The severity of a person's haemophilia depends on the amount of clotting factor that is missing.

There are two types of haemophilia: Haemophilia A and haemophilia B (sometimes called Christmas disease). Haemophilia A is caused by a deficiency of factor VIII (see coagulation factors), and haemophilia B is caused by a deficiency of factor IX (see coagulation factors).

Idiopathic Thrombocytopenic Purpura (ITP): An autoimmune blood disorder. Persons affected have reduced blood platelet levels, which are essential to the clotting mechanism.

Immunodeficiency: Inability to mount a normal immune response. Immunodeficiency can be due to a genetic disease or acquired as in AIDS due to HIV.

Immunoglobulins: Any of the structurally related glycoproteins that function as antibodies. They are divided into five classes (IgA, IgD, IgE, IgG, IgM) on the basis of structure and biological activity.

In-process control: Checks performed during production in order to monitor and if necessary to adjust the process to ensure that the material conforms to its specifications. The control of the environment or equipment may also be regarded as a part of in-process control.

Intermediate: Partly processed material that must undergo further manufacturing steps before it becomes a bulk product.

Kawasaki Disease: A childhood disease that primarily affects children under five years old. It is the leading cause of acquired heart disease in children. If not detected and treated immediately, it can result in heart damage and death.

Label: any written, printed, or graphic matter on the container or package or any such matter clearly visible through the immediate carton, receptacle, or wrapper.

Labelling: The action involving the selection of the correct label, with the required information, followed by line-clearance and application of the label.

Labile Blood Products: products that are extracted from donated blood, either directly or in one or few manufacturing steps, and which quickly loose their therapeutic potential (e.g. cell preparations and plasma)

Leukopheresis: the procedure in which blood is removed from the donor, a leukocyte concentrate is separated, and the remaining formed elements and residual plasma are returned to the donor.

Lot: *see batch.*

Manufacture: All operations of purchase of materials, production, quality control, release, storage, and distribution of pharmaceutical starting materials, and the related controls.

Manufacturer: any legal person or entity engaged in the manufacture of a product subject to license under the act; "Manufacturer" also includes any legal person or entity who is an applicant for a license where the applicant assumes responsibility for compliance with the applicable product and establishment standards.

Marketing authorization: an official document issued by the competent drug regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy and quality. It must set out, inter alia, the name of the product, the pharmaceutical dosage form, the quantitative formula (including excipients) per unit dose (using INNs or national generic names where they exist), the shelf-life and storage conditions, and packaging characteristics. It specifies the information on which authorization is based (e.g. "The product(s) must conform with all the details provided in your application and as modified in subsequent correspondence"). It also contains the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorization, and the period of validity of the authorization.

Master file: a data set that is:

– submitted by someone other than a finished product applicant, e.g. the supplier of an active ingredient or the supplier of a packaging component;
– a common feature of more than one product, e.g. sterility test procedures; or
– some other matter that is conveniently dealt with by means of a master file.

An applicant for a new marketing authorization or for a variation may make reference to a master file, but must have the permission of the person or company that submitted the master file.

Multifocal motor neuropathy (MMN): A rare slow progressing asymmetrical muscle weakness and muscle atrophy with autoimmune-mediated pathogenesis.

Myasthenia gravis (MG): A rare autoimmune neuromuscular disease characterised by severe muscular exhaustion which worsens after physical exercise and improves with rest.

Package: the immediate carton, receptacle, or wrapper, including all labelling matter therein and thereon, and the contents of the one or more enclosed containers. If no package, as defined in the preceding sentence, is used, the container shall be deemed to be the package.

Plasma: the liquid portion of the blood in which the cells are suspended. Plasma may be separated from the cellular portion of a whole blood collection for therapeutic use as fresh-frozen plasma or further processed to cryoprecipitate and cryoprecipitate-depleted plasma for transfusion. It may be used for the manufacture of medicinal products derived from human blood and human plasma or used in the preparation of pooled platelets, or pooled, leucocyte-depleted platelets. It may also be used for re-suspension of red cell preparations for exchange transfusion or perinatal transfusion.

Plasma, cryoprecipitate-depleted for transfusion: a plasma component prepared from a unit of plasma, fresh-frozen. It comprises the residual portion after the cryoprecipitate has been removed.

Plasma, fresh-frozen: the supernatant plasma separated from a whole blood donation or plasma collected by apheresis, frozen and stored.

Plasma Master File (PMF): The PMF is a stand-alone documentation, which is separate from the dossier for marketing authorisation, which provides all relevant detailed information on the characteristics of the entire human plasma used as a starting material and/or a raw material for the manufacture of sub/intermediate fractions, constituents of the excipient and active substance(s), which are part of medicinal products or medical devices incorporating stable derivatives of human blood or human plasma.

Plasmapheresis: the procedure in which blood is removed from the donor, the plasma is separated from the formed elements and at least the red blood cells are returned to the donor.

Plateletpheresis: the procedure in which blood is removed from a donor, a platelet concentrate is separated, and the remaining formed elements are returned to the donor along with a portion of the residual plasma.

Platelets, apheresis: a concentrated suspension of blood platelets obtained by apheresis.

Platelets, apheresis, leucocyte-depleted: a concentrated suspension of blood platelets, obtained by apheresis, and from which leucocytes are removed.

Platelets, recovered, pooled: a concentrated suspension of blood platelets, obtained by processing of whole blood units and pooling the platelets from the units during or after separation.

Platelets, recovered, pooled, leucocyte-depleted: a concentrated suspension of blood platelets, obtained by processing of whole blood units and pooling the platelets from the units during or after separation, and from which leucocytes are removed.

Platelets, recovered, single unit: a concentrated suspension of blood platelets, obtained by processing of a single unit of whole blood.

Platelets, recovered, single unit, leucocyte-depleted: a concentrated suspension of blood platelets, obtained by processing of a single whole blood unit from which leucocytes are removed.

Potency is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result.

Processing: any procedure employed after collection and before compatibility testing of blood and includes the identification of a unit of donor blood, the preparation of components from such unit of donor blood, serological testing, labelling and associated record keeping.

Production: All operations involved in the preparation of a pharmaceutical starting material, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished pharmaceutical starting materials.

Purity: relative freedom from extraneous matter in the finished product, whether or not harmful to the recipient or deleterious to the product. Purity includes but is not limited to relative freedom from residual moisture or other volatile substances and pyrogenic substances.

Quality assurance: A wide-ranging concept covering all matters that individually or collectively influence the quality of a product, including pharmaceutical starting materials. It is the totality of the arrangements made with the object of ensuring that pharmaceutical starting materials and pharmaceutical products are of the quality required for their intended use.

Quality control: All measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical starting materials conform to established specifications for identity, strength, purity and other characteristics.

Recall: A process for withdrawing or removing a pharmaceutical material from the distribution chain because of defects in the materials or complaints of a serious nature. The recall might be initiated by the manufacturer/importer/distributor or a responsible regulatory agency.

Recovered plasma: Plasma for fractionation recovered from whole blood donations and distinguished from Source Plasma by the mode of collection and the requirements for storage, pooling, dating and labelling of the product. Recovered plasma may be separated from individual units of Whole Blood by aseptic techniques up to 5 days after expiration or obtained from Fresh Frozen Plasma that has expired. Typically an average of 250 ml of recovered plasma is retrieved from a whole blood donation (450 ml).

Red cells: the red cells (erythrocytes responsible for the transport of oxygen in the body) from a single whole blood donation, with a large proportion of the plasma from the donation removed.

Red cells, apheresis: the red cells from an apheresis red cell donation.

Red cells, buffy coat removed: the red cells from a single whole blood donation, with a large proportion of the plasma from the donation removed. The buffy coat, containing a large proportion of the platelets and leucocytes in the donated unit, is removed.

Red cells, buffy coat removed, in additive solution: the red cells from a single whole blood donation, with a large proportion of the plasma from the donation

removed. The buffy coat, containing a large proportion of the platelets and leucocytes in the donated unit, is removed. A nutrient/preservative solution is added.

Red cells in additive solution: the red cells from a single whole blood donation, with a large proportion of the plasma from the donation removed. A nutrient/preservative solution is added.

Red cells, leucocyte-depleted: the red cells from a single whole blood donation, with a large proportion of the plasma from the donation removed, and from which leucocytes are removed.

Red cells, leucocyte-depleted, in additive solution: the red cells from a single whole blood donation, with a large proportion of the plasma from the donation removed, and from which leucocytes are removed. A nutrient/ preservative solution is added.

Safety: the relative freedom from harmful effect to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time.

Self-sufficiency: the ability to maintain oneself or itself without outside aid: capable of providing for one's own needs

Source Plasma: the fluid portion of human blood collected by plasmapheresis and intended as source material for further manufacturing use.

Stable Blood Products – Semi-stable and stable blood products have expiry term of more than a year and can tolerate less strict storage conditions without any impact on quality or safety.

Standards: specifications and procedures applicable to an establishment or to the manufacture or release of products, which are prescribed in this subchapter or established in the biologics license application designed to insure the continued safety, purity, and potency of such products.

Starting material: A starting material is an active ingredient or an excipient intended or designated for use in the production of a product.

Statistical process control: a method of quality control of a product or a process that relies on a system of analysis of an adequate sample size without the need to measure every product of the process.

Supplier: Person or company providing pharmaceutical starting materials on request. Suppliers may be distributors, manufacturers, traders, etc.

Unit: the volume of blood or one of its components in a suitable volume of anticoagulant obtained from a single collection of blood from one donor.

Validation: the establishment of documented and objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.

von Willebrand disease: an inherited bleeding disorder, similar to haemophilia, but the two disorders are not the same. vWD is the most common inherited clotting disorder, affecting both men and women. (also see *coagulation factors*) It has been estimated that vWD affects up to one percent of the population. However, it is generally the least severe of the clotting disorders.

Whole Blood: blood collected from human donors for transfusion to human recipients

Sources:

- Alpha 1 Foundation
- Code of Federal Regulation, US Food and Drugs Administration, Title 21 volume 7
- Core SPC for Human Albumin Solution, CPMP / PhVWP / BPWG / 2231 / 99/ Rev 1, Committee for Medicinal Products for Human Use, European Medicines Agency, 16 March 2005.
- CRISP (Computer Retrieval of Information on Scientific Projects) Thesaurus 2004
- Guideline on Requirements for Plasma Master File (PMF) Certification, CPMP/BWP/4663/03, Committee for Proprietary Medicinal Products, European Medicines Agency, 26 February 2004
- Guillain-Barré Syndrome (GBS) Support Group, UK.
- ITP Support Association, UK
- Kawasaki Disease Foundation
- Mode of preparation of labile blood products-available products, Lapierre V, Herve P. Presse Med. 1999 Jul 3–10;28(24):1314–1320
- Merriam-Webster dictionary
- Official Journal of the European Union, L 91/28 EN, 30 March 2004
- Online Medical Dictionary, http://cancerweb.ncl.ac.uk/omd/index.html
- UK's Medicines and Healthcare Products Regulatory Agency, http://medicines.mhra.gov.uk/
- Wikipedia Encyclopedia
- World Health Organization: Expert Committee On Biological Standardization, 52nd Report; Expert Committee on Specifications for Pharmaceutical Preparations, 38th report
- World Federation of Haemophilia, www.wfh.org