Glossary of Biotherapy and Related Terms

Association for the Advancement of Blood & Biotherapies

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Accreditation: Action or process of officially recognizing an entity as having a particular status or being qualified to perform a particular activity.

Accreditation Program (AABB): Promotes the highest standard of care for patients and donors in all aspects of blood banking, transfusion, biotherapies, and relationship testing. Our comprehensive quality systems approach encourages continuous improvement and is a mark of high quality—showing donors, patients, employees, and regulators that your organization is committed to optimizing its standards of care by managing risk and intentionally focusing on quality. Upon accreditation, organizations become an AABB institutional member, which confers valuable benefits: continuing education, regulatory updates, technical specialists available to answer questions, and access to AABB's highly regarded experts—all of which help facilities and leadership continue to maintain optimal performance. Visit website for more details/updates.

Allogeneic: Term to denote donor and intended recipient are different individuals.

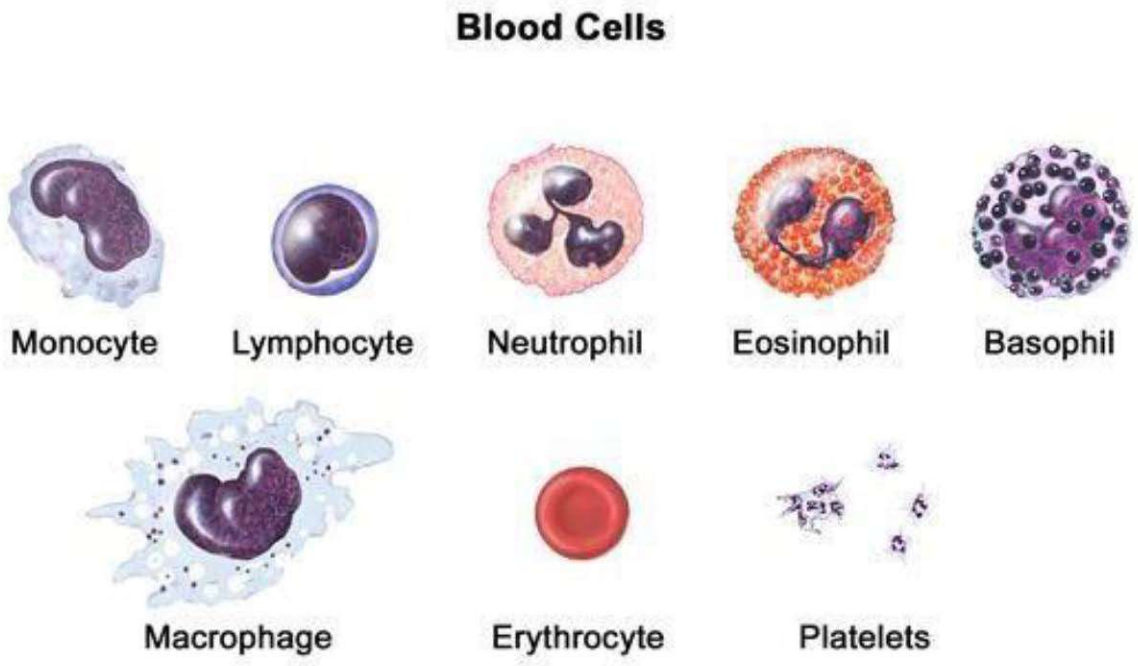
Antigen: Any foreign material that can stimulate an immune response and be bound by specific antibody or specific lymphocytes.

Apheresis: Process of removing a specific component of the blood, such as platelets, red cells, plasma (liquid part of the blood), or white cells and returning the remaining components to the donor. Apheresis can be used in three ways: 1) Therapeutic apheresis removes or reduces an element of the blood in patients whose health may be improved by the absence or reduction of the problematic element; 2) collection of a blood component for further use, allowing more of one element to be collected from a donor than could be separated from a unit of whole blood; and 3) collection of an element of blood that can be used or modified as cellular starting material for biotherapy research and application.

Autologous: Term to denote the implantation, transplantation, infusion, or transfer of human cells or tissue back into the individual from whom the cells or tissue were recovered.

Biotherapy: A type of treatment that uses substances made from living organisms to treat disease. Substances may occur naturally in the body or be made in the laboratory.

Blood: Substance that consists of a fluid (plasma) containing many types of cells: white cells (monocytes, lymphocytes, neutrophils, eosinophils, basophils, and macrophages), red cells (erythrocytes), and platelets. Blood circulates through the body in the arteries and veins.



Source: National Cancer Institute.

CABP Certification/Credential: The AABB Certified Advanced Biotherapies Professional (CABP) is a certification program that includes an exam designed to certify candidates have demonstrated the necessary knowledge to practice in the biotherapies field. This certification benefits the entire biotherapies field by establishing minimum standards of competence, identifying qualified and proficient professionals, and advancing safety and quality. Candidates must meet prerequisites, obtain a passing grade on the exam, and agree to the CABP Code of Conduct to earn the certification for a 3-year cycle.

Cell: Basic building blocks of all living things. The human body is composed of trillions of cells that provide structure for the body, take in nutrients from food, convert those nutrients into energy, and carry out specialized functions.

Cell therapy: General name for products that include cellular immunotherapies, cancer vaccines, and other types of both autologous and allogeneic cells for certain therapeutic indications, including hematopoietic stem cells and adult and embryonic stem cells.

Certificate: Method to educate individuals to achieve specific learning objectives. To earn a certificate, one participates in learning event(s) and passes an assessment demonstrating achievement of program learning objectives. There are no ongoing requirements. The certificate is not revoked; instead, one can earn a new certificate at specified intervals. [Compare to certification term. Important to note differences. AABB offers both an AABB Cellular Therapy Certificate Program (education) as well as the CABP certification (credential).]

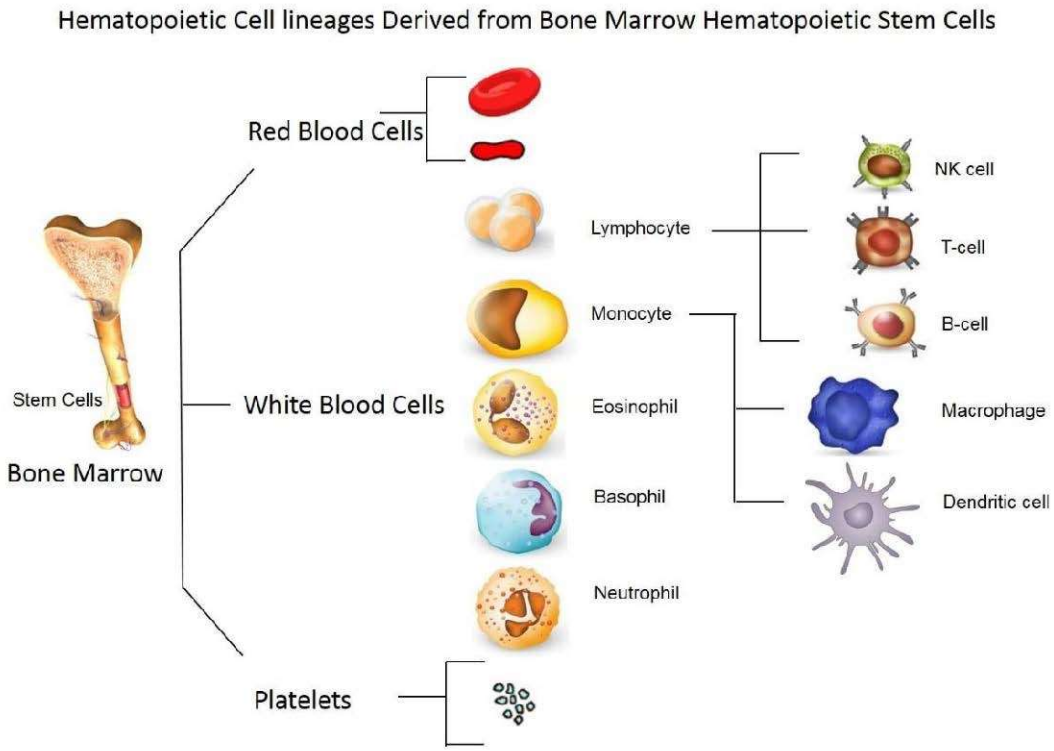
Certification: Method to assess current knowledge and skills; to earn credential by passing assessment demonstrating current knowledge and skills (per test content outline). To maintain credential, one must meet ongoing requirements (eg, code of ethics, work in the role, retesting or continuing education at specified intervals). Can be revoked if requirements are not met. AABB CABP credential is a certification.

Cord blood: Substance that remains in the placenta and in the attached umbilical cord after childbirth. It is collected because it contains stem cells, which can be used to treat hematopoietic and genetic disorders such as cancer.

Ex vivo: Experimentation or measurements performed in or on tissue from an organism in an external environment with minimal alteration of natural conditions.

Gene therapy: A type of treatment that seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use.

Hematopoiesis: Term used to describe the formation of blood cellular components.



Homologous: Method to repair, reconstruct, replace, or supplement a recipient's cells or tissues with a cellular therapy product that performs the same basic function or functions in the recipient as in the donor.

In vitro: A medical study or experiment performed in the laboratory, outside a living organism, (eg, within the confines of a test tube, laboratory dish, culture vessel).

In vivo: A medical test, experiment, or procedure that is performed on (or in) a living organism, such as a laboratory animal or human. In contrast to in-vitro studies, in-vivo studies are needed to see how the body will respond to a particular substance.

ISBT 128: The global standard for the terminology, identification, coding, and labeling of medical products of human origin (including blood, cell, tissue, milk, and organ products). It is used on six continents and widely endorsed by the professional community and disparate health-care systems.

Marrow: Soft spongy tissue found in the center of most bones, that contains hematopoietic stem cells (HSCs). (HSCs are also found in blood moving throughout the body.)

Minimal manipulation: 1) For structural tissue, processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement. 2) For cells or nonstructural tissues, processing does not alter the relevant biological characteristics of cells or tissues.

Regenerative: Methods to regrow, repair, or replace damaged or diseased cells, organs, or tissues.

Regenerative medicine therapies (RMTs): RMTs include cell therapies, therapeutic tissue engineering products, human cell and tissue products.

Sections 351 and 361 of the Public Health Service Act (PHSA): Provide the authority for FDA to establish regulatory requirements for marketing traditional biologics and human cells, tissues, and cellular and tissue-based products (HCT/Ps). ***Section 351*** of the PHSA identifies a set of products that will be regulated as biologicals. A biological product is a "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, applicable to the prevention, treatment, or cure of a disease or condition of human beings." These include blood-derived products, vaccines, in-vivo diagnostic allergenic products, immunoglobulin products, products containing cells or microorganisms, and most protein products. Biologics regulated under Section 351 of the PHSA and/or the FD&C Act include products FDA has determined do not meet all of the criteria in 21 CFR 1271.10(a) and are regulated as drugs and/or biological products. Examples include cultured cartilage cells; cultured nerve cells; lymphocyte immune therapy; gene therapy products; human cloning; human cells used in therapy involving the transfer of genetic material (cell nuclei, oocyte nuclei, mitochondrial genetic material in ooplasm, genetic material contained in a genetic vector); unrelated allogeneic hematopoietic stem cells; and unrelated donor lymphocytes for infusion. ***Section 361*** of the PHSA does not identify a specific class of products. Rather, it gives FDA the authority to make and enforce such regulations that are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the US. An HCT/P is regulated solely under Section 361 of the PHSA if it meets all of the following criteria:

- The HCT/P is minimally manipulated.
- The HCT/P is intended for homologous use only.
- The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage solution.
- Either: 1) the HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function or 2) the HCT/P has a systemic

effect or is dependent upon the metabolic activity of living cells for its primary function, and (a) is for autologous use; (b) is for allogeneic use in a first-degree or second-degree blood relative; or (c) is for reproductive use.

Examples of HCT/Ps regulated solely under Section 361 include bone (eg, demineralized bone), ligaments, tendons, fascia, cartilage, ocular tissue, skin, veins and arteries (not from preserved umbilical cords), pericardium, amniotic membrane (for ocular repair), dura mater, heart valve allografts, hematopoietic stem cells derived from peripheral or umbilical cord blood, reproductive cells (semen, oocytes), and embryos.

Standards: Describe the required way of doing something. It could be about making a product, managing a process, delivering a service, or supplying materials—standards cover a huge range of activities. Standards are the distilled wisdom of people with expertise in their subject matter and who know the needs of the organizations they represent—people such as manufacturers, sellers, buyers, customers, trade associations, users, or regulators. ***AABB Standards*** have been a forerunner in optimizing health and safety for the blood and biotherapies community since 1957. AABB standards incorporate both technical and quality systems requirements to ensure that all facets are reviewed, including specification of equipment, materials management, organizational structure, documents, resource management, and program assessment. All of this helps to ensure the highest level of quality and safety for donors and patients at all times. The AABB standards represent requirements that must be implemented by AABB-accredited facilities. A requirement contains the word "shall," which indicates that the statement is mandatory. Failure to meet the requirement would constitute a nonconformance under the AABB Accreditation Program. There are rare instances in which a standard uses the term "may." A statement that uses "may" is not a requirement.

Stem cell: Specific type of cell capable of evolving into many different types of specialized cells within the body. There are three primary types of stem cells: 1) embryonic stem cells (characterized as pluripotent in nature—capable of developing into the two hundred or so specialized cells of the adult organism); 2) adult stem cells [exist within certain tissues of the body (eg, blood and marrow) and carry out repair and regenerative functions]; and 3) induced pluripotent stem cells (iPSCs) (adult stem cells that have been genetically reprogrammed to behave like embryonic stem cells).

21st Century Cures Act: Signed into law on December 13, 2016, designed to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently.

Unapproved: not judged to be acceptable; not given official approval; not approved. Protecting patients is at the core of what is done at the US Food and Drug Administration. The FDA provides resources to help consumers understand the risks associated with unapproved stem cell, exosome, and other products marketed as regenerative medicine products and facilitates the reporting of side effects that may occur after their use. FDA warns consumers who have been treated with, or who are considering use of, unapproved stem cells, exosome, or other products marketed as regenerative medicine products, about their potential risk. These illegal products are often marketed by clinics under the umbrella term of regenerative medicine as being safe and effective for treatment of a wide range of diseases or conditions (eg, Alzheimer's disease and other neurologic disorders, orthopedic conditions), even though they have not been adequately studied

in clinical trials. FDA encourages patients and their health-care providers to report to the FDA any potential adverse events and complaints related to the use of these products using the FDA's MedWatch Adverse Event Reporting program. The FDA has posted a webpage for consumers that provides information about products marketed as stem cells, exosomes, or other regenerative medicine products, including the conditions for which they are approved, and which products are not approved at all.

Unproven Therapies: Treatments that (the) practitioner claims can alter the disease process although there is no proof to support the claim.

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