



## **Unproven Cellular Therapies – A Guide for Patients**

AABB, in harmony with its [mission](#), is committed to making cellular therapies (including stem cells and gene therapy) safe, available and effective worldwide. Advances in the development of new cellular therapy treatments could potentially lead to significant improvements in the health of patients and fulfill an unmet medical need. However, some cellular therapies may be offered to patients before they are proven to be safe or effective. Some medical professionals may overstate the potential benefit and understate the potential risks of these therapies, which may end up causing harm to a patient. Patients have the right to make their own decisions about whether to receive a certain therapy based on accurate information.

### **Summary**

The following Guide for Patients will provide basic information on cellular therapies including informed consent, clinical trials, regulatory oversight and marketing claims.

It is important for patients to know whether a therapy has been tested in humans and has been proven to be safe and supported by research and/or clinical evidence. As with other medical treatments, new cellular therapies are best evaluated using clinical trials. A [clinical trial](#) is a study in people to evaluate if a certain treatment or procedure is safe and effective. Clinical trials follow a scientific plan or protocol. This plan is reviewed and approved by independent committees, known as Institutional Review Boards or IRBs. IRBs are administrative bodies established within an institution to protect the rights and welfare of patients who participate in clinical trial activities conducted at the institution. IRBs are responsible for protecting patient rights. Some cellular therapies have not been adequately studied through clinical trials carried out following thorough IRB review.

The Food and Drug Administration (FDA), a federal agency, protects patient safety by regulating certain cellular therapies in the United States of America. The [FDA](#) can take action against providers of cellular therapies (such as stem cell clinics) for misleading patients or putting patients at risk. However, the FDA does not have the resources to continuously monitor and inspect all providers of stem cell therapies. Additionally, the FDA does not have jurisdiction over cellular therapies that occur in other countries. Regulations may vary between different countries.

In some instances, the media has over-hyped certain cellular therapies. Some of these cellular therapies are unproven and have not been tested in appropriately conducted clinical trials. As a result, these news stories may provide false hope to patients. Some healthcare providers may make untrue or exaggerated claims about the treatment or not fully explain the possible risks. Therefore, it is important that patients are given complete information to fully understand the possible risks and benefits of treatments.

## **What are Cellular Therapies?**

Stem cells may take on many different forms. There are two main types of stem cells, [adult stem cells](#) and [embryonic stem cells](#). An adult stem cell is only able to give rise to a limited number of cell types, depending on the tissue it was taken from. For example, stem cells from [cord blood](#) are considered adult stem cells that can give rise to cells that circulate in our blood such as red blood cells, white blood cells and platelets. An embryonic stem cell can potentially become any cell in the body. This guide focuses on adult stem cells.

Cellular therapy or stem cell therapy involves taking human cells and putting them into a patient to replace or repair damaged tissue or cells. When stem cells are used to replace the patient's existing bone marrow (where blood-forming stem cells are made), it is called a stem cell transplant. Adult stem cells used in cellular therapies can be collected from the patient and go back to the same patient. These are known as [autologous](#) cells. Cells that come from someone other than the patient who receives them are called [allogeneic](#) cells.

One specific cell type, hematopoietic or blood-forming stem cells (HSCs), are commonly used to treat some hematologic (blood) diseases such as leukemia. More than [25,000](#) hematopoietic stem cells transplants (HSCTs) are performed each year, with proven effectiveness for listed disease indications – that is, having the ability to produce a desired result. They have become the “standard of care” for disease indications such as leukemias, lymphomas, primary immune deficiencies and other inherited blood disorders such as sickle cell disease. The use of HSCs for other reasons and the use of other types of stem cells should generally be considered experimental – that is, unproven in controlled clinical trials. Their use should be studied in clinical trials to assess their risks and benefits. Although stem cell transplants can be life-saving treatment options for certain patients, similar to all medical procedures, there are [possible risks](#) with the therapy.

The field of [regenerative medicine](#) involves cellular therapies, gene therapies, tissue engineering, and other types of therapies or treatments to aid in treating a variety of diseases. Regenerative medicine may be defined as the process of replacing or "regenerating" human cells, tissues or organs to restore or establish normal function.

## **What is Informed Consent?**

Patients are required to give their [consent](#) before receiving a cellular therapy. This is known as informed consent. Informed consent has to be obtained from all participants of clinical trials. During the informed consent process, patients should be given complete information on the possible risks and benefits of the treatment or procedure. Physicians or other healthcare providers should discuss with patients if an unproven cellular therapy has not been proven safe and effective, and should fully explain the possible benefits and risks of the procedure. These healthcare providers should be able to provide data and scientific resources for use of the cellular therapy and advise if the patient is being asked to take part in a clinical trial. Patients should ask questions to ensure that they fully understand the potential side effects, costs and goals of a treatment to make an informed medical decision. Table 1 provides a list of items included in an informed consent and other questions to consider asking before receiving an unproven therapy.

## **What are Clinical Trials?**

Patients and their healthcare providers may want to find out whether a cellular therapy is being studied in a [clinical trial](#). A [clinical trial](#) is a research study in humans to help understand if a specific medication, cellular therapy or procedure is safe and effective. Clinical trials may end with any one of three results: improvement in patient health outcomes, no patient improvement, or unexpected patient harm. All clinical trial treatments are termed “investigational” and therefore the true risks are not known.

Clinical trials are often listed on [ClinicalTrials.gov](#). However, [not all trials](#) listed on the website comply with FDA regulations, have been approved by an IRB, or are considered scientifically accepted. Typically, proper clinical trial studies take place at institutions with an IRB, involve qualified personnel, and follow local and federal regulations (where applicable). This [website](#) explains how clinical trials help protect patients. An IRB is made up of professionals that include physicians, scientists, ethicists, and other experts. The IRB has many responsibilities such as scientific oversight, monitoring the trial as it progresses, protecting patient rights and ensuring the trial is conducted in an ethical manner. In addition to an IRB, novel cellular therapies that involve genetic modification of the cells should have the oversight of an Institutional Biosafety Committee or IBC. The IBC’s role is to assess and monitor any potential risk to the environment and/or public health.

## **Does the FDA Regulate Cellular Therapies?**

Medical facilities in the United States that conduct cell transplants follow FDA regulations. FDA [regulatory oversight](#) of these cellular therapies aims to protect patients and prevent communicable or infectious disease. A medical facility may be [registered](#) with the FDA, but that does not necessarily mean they are under FDA oversight. The FDA does not oversee all procedures performed in medical facilities. Therefore, treatments administered by physicians in their facilities or clinics in the United States may not be safe or effective. Cellular therapies administered outside of the United States are not monitored by the FDA and may or may not be monitored by regulators in other nations.

## **Why Should Patients Question Marketing Claims?**

Patients should question marketing claims related to the safety or efficacy of an unproven cellular therapy, since these claims may be [misleading or inaccurate](#). When therapies are given outside of clinical trials, the provider is not required to report any side effects to the FDA, known as adverse event reporting. Therefore, the available information on an unproven cellular therapy may not truly reflect the risks to patients. This limits the ability of patients and their medical team to weigh potential benefits and risks. Improper advertising of unproven cellular therapies can result in harm to the patient, including physical harm, psychological harm and financial loss.

## **Becoming an Informed Patient about an Unproven Cellular Therapy**

These are a few examples of questions patients may want to ask about a therapy.

**Table 1.**

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| <p>Is there a written, evidence-based plan for the procedure that has been approved by an IRB?</p>   | <p>Is the patient eligible for an existing cellular therapy clinical trial?</p>  |
| <p>If the use is not considered part of a clinical trial, what steps have been taken to protect the patient?</p>   | <p>Has the treatment been fully explained to the patient? Is it documented in the informed consent paperwork?</p>  |
| <p>Is the healthcare provider qualified to do the procedure?</p>   | <p>Does the healthcare institution have appropriate facilities (space, environmental conditions, equipment, etc.)?</p>   |
| <p>What is the plan for managing adverse events, or side effects, and making sure that patients receive timely and appropriate care and services?</p>    | <p>What are the possible benefits and risks of this therapy? Does the informed consent documentation contain this information?</p>   |
| <p>Does the patient’s health insurance cover the procedure, possible side effects or complications from the procedure?</p>                               | <p>What costs are the patient responsible for?</p>   |
| <p>If the treatment is investigational, is there an informed consent form for the clinical trial that has been reviewed and approved by an IRB?</p>      | <p>Does the informed consent form contain information on alternatives, if appropriate? Are other treatments available?</p>   |
| <p>Does the informed consent form mention how personal information will stay confidential and if and how patient data will be de-identified/blinded?</p> | <p>Does the informed consent form explain the purpose of the clinical trial?</p>   |
| <p>Does the informed consent form contain information on whether compensation for harm or other information is available?</p>                            | <p>Does the informed consent form identify the sponsor of the trial?</p>   |
| <p>Who is the contact person, regarding the patient’s rights or injury? Is this person listed on the informed consent form?</p>                          | <p>Does the informed consent form specify that participation in a trial and receiving treatment are voluntary and that the patient can withdraw his/her participation at any time without giving a reason?</p> |
| <p>If the patient is pregnant or planning to become pregnant, will this treatment potentially affect the fetus?</p>                                      | <p>Does the informed consent form clearly describe the procedure, state that the trial is for research, and identify what the patient can expect?</p>  |

For more information on informed consent, click [here](#).

## Additional Patient Resources

1. AABB. “International Competent Authorities.” [Available at: <http://www.aabb.org/advocacy/regulatorygovernment/ct/international/Pages/default.aspx>]
2. AABB. “Patient Advisory for Stem Cell Therapy and Medical Tourism.” (August 2013) [Available at: <http://www.aabb.org/aabbct/therapyfacts/Documents/Patient-Advisory-for-Stem-Cell-Therapy-and-Medical-Tourism.pdf#search=Medical%20tourism>]
3. American Cancer Society. “Informed Consent.” [Available at: <https://www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-financial-and-legal-matters/informed-consent.html>]
4. American Cancer Society. “Stem Cell Transplant Side Effects.” (May 2016) [Available at: <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant/transplant-side-effects.html>]
5. American Cancer Society. “Types of Stem Cell Transplants for Cancer Treatment.” (May 2016) [Available at: <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant/types-of-transplants.html>]
6. Be The Match / NMDP. “Cord blood donation frequently asked questions.” [Available at: <https://bethematch.org/support-the-cause/donate-cord-blood/cord-blood-faqs/>]
7. Be The Match / NMDP. “Diseases treatable by transplants.” [Available at: <https://bethematch.org/transplant-basics/how-transplants-work/diseases-treatable-by-transplants/>]
8. ClinicalTrials.gov. “Frequently Asked Questions.” [Available at: <https://clinicaltrials.gov/ct2/manage-recs/faq#board>]
9. ClinicalTrials.gov. “Learn About Clinical Trials.” [Available at: <https://clinicaltrials.gov/ct2/about-studies/learn>]
10. Dominici, Massimo, et al. “Positioning a Scientific Community on Unproven Cellular Therapies: The 2015 International Society for Cellular Therapy Perspective.” *Cytotherapy* (2015): 1664. Available with subscription from: [http://www.celltherapyjournal.org/article/S1465-3249\(15\)01081-6/fulltext](http://www.celltherapyjournal.org/article/S1465-3249(15)01081-6/fulltext)
11. FDA. “Guidance for Industry: Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) – Small Entity Compliance Guide.” (August 2007) [Available at: <https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/tissue/ucm062592.pdf>]
12. FDA. “FDA Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P’s) Product List.” (May 2009) [Available at: <https://www.fda.gov/biologicsbloodvaccines/tissueproducts/regulationoftissues/ucm150485.htm>]
13. FDA. “FDA warns US Stem Cell Clinic of significant deviations.” (August 2017) [Available at: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573431.htm>]
14. HHS – Office of Human Research Protections. “Informed Consent FAQs.” [Available at: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html>]

15. International Society for Cellular Therapy Presidential Task Force on the Use of Unproven Therapies. "Reference Guide." (2015:p43) [Available at: <http://www.celltherapysociety.org/?page=PTF2015>]
16. International Society for Stem Cell Research. "Guidelines for Stem Cell Research and Clinical Translation." (2016:p27) [Available at: <http://www.isscr.org/docs/default-source/all-isscr-guidelines/guidelines-2016/isscr-guidelines-for-stem-cell-research-and-clinical-translation.pdf?sfvrsn=4>]
17. JAMA. "Stem Cell Treatments." [Available at: <https://jamanetwork.com/journals/jama/fullarticle/2598269>]
18. NIH. "How Do Clinical Trials Protect Participants?" [Available at: <https://www.nhlbi.nih.gov/studies/clinicaltrials/protect>]
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20. NIH. "The Adult Stem Cell." (June 2001) [Available at: <https://stemcells.nih.gov/info/2001report/chapter4.htm>]
21. NIH. "The Basics." (June 2017). [Available at: <https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics>]
22. NIH. "What Are Clinical Trials?" [Available at: <https://www.nhlbi.nih.gov/studies/clinicaltrials>]
23. Mayo Clinic Video: How a stem cell transplant works. (June 2016) [Available at: <http://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/multimedia/stem-cell-transplant/vid-20084647>]