

THE ISSCR GUIDE TO STEM CELL TREATMENTS



INTERNATIONAL
SOCIETY FOR
STEM CELL
RESEARCH

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INTRODUCTION

Credit: McClendon, Pinto, Stupp,
Northwestern University and NIH.

The International Society for Stem Cell Research (ISSCR) is a global nonprofit professional society that promotes excellence in stem cell science and regenerative medicine and its applications to human health. It is central to the society's mission to share **scientifically accurate information** to inform patients and families about the current state of stem cell research and potential treatments. The ISSCR aims to further patient safety and public health through our efforts to **promote legitimate stem cell research and credible stem cell treatments**.

Many of us have heard about the extraordinary potential that stem cells hold for the treatment of a wide range of diseases and conditions. While stem cell research around the world has led to new discoveries with the potential to improve human health, considerable work is still needed to translate research into specific, effective, and safe therapies.

Most medical discoveries are based on years of research performed at universities and pharmaceutical and biotechnology companies. It is a lengthy process to progress laboratory discoveries to clinically safe and effective treatments. Like any new therapy, including traditional prescription drugs, stem cell treatments must be evaluated in clinical trials and be shown to meet certain standards before receiving approval from national regulatory bodies to treat patients.

The ISSCR is increasingly concerned by clinics and providers that are marketing and administering stem cell-based treatments that have not been tested for safety or approved by regulators. In actuality, many treatments sold by unscrupulous stem cell clinics have not been shown to be effective or safe by rigorous science, or - in many cases - have not even been shown to contain stem cells.

The majority of these “treatments” are unproven and have the potential to cause harm. While initial studies may appear to show potential, subsequent scientific testing in clinical trials is needed and may reveal that the approach being evaluated is ineffective or has unanticipated negative side effects. It is important that you know what to look out for before considering a stem cell treatment.

Stem cell treatments must be evaluated for efficacy and safety in regulated clinical trials before they receive approval.

What does this really mean for you as a patient, patient advocate, healthcare provider, friend, or family member? We hope to answer some of your questions about stem cells and stem cell treatments and provide the resources that you and your primary care physician or specialist need to make the best decisions regarding treatment.

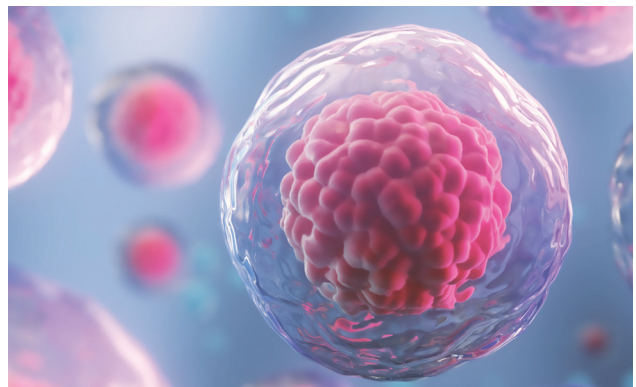


FIGURE 1. Unproven stem cell “treatments” are currently being marketed and administered by unscrupulous stem cell clinics and providers around the world. This guide will help patients understand what to look for when considering a stem cell treatment.

1. ABOUT STEM CELLS AND STEM CELL-BASED TREATMENTS

1.a. WHAT ARE STEM CELLS?

Stem cells* are unique cells that are defined by two properties - they can divide to make more of themselves and they can generate specialized cell types such as skin, muscle, or blood cells.

There are two types of stem cells: pluripotent stem cells and tissue-specific (or adult) stem cells.

Pluripotent stem cells are stem cells that can become any cell in the body. The types of pluripotent stem cells are: embryonic stem cells and induced pluripotent stem cells.

Embryonic stem cells (ESC) only exist at the earliest stages of embryonic development. They give rise to every cell type in the adult body. ESCs are derived from cells in the blastocyst, a very early stage of embryonic development (see Figure 1A).

Induced pluripotent stem cells (iPSC) are cells that have been made in the lab by converting tissue-specific cells, such as skin cells, into cells with the same properties as embryonic stem cells. Like embryonic stem cells, iPSCs can give rise to every cell type in the adult body (see Figure 1B).

Pluripotent stem cells are incredibly valuable because they can be grown in the laboratory in unlimited numbers and can be used to model development and disease, test the efficacy of new drugs, and develop cellular therapies for treatment. You can learn more about how pluripotent stem cells are donated and their uses in [Transforming Scientific Research](#).

Tissue-specific stem cells (also called somatic or adult stem cells) are stem cells that are found in many of our adult organs and tissues. They can generate some or all of the cell types in that organ tissue, but **cannot** give rise to every cell type in the adult body. This type of stem cell is responsible for replenishing the cells that make up the particular organ or tissue in which it is found. For example, blood stem cells constantly replace cells in the blood and immune system, and gut stem cells replenish the intestine and colon (see Figure 1C). While we already use certain tissue-specific stem cells in the clinic ([see question 2.a.](#)), scientists are also using this type of stem cell to learn about how our tissues develop, model diseases in the laboratory, and develop or test new treatments.

Visit [A Closer Look at Stem Cells](#) for more information on stem cells, stem cell research, how stem cells are being used to learn about and treat different diseases, and some of the challenges in the field.

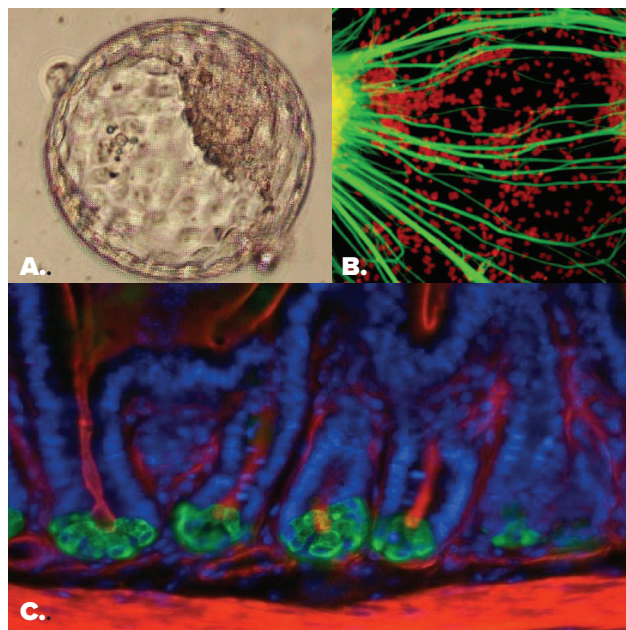


FIGURE 1. A. This is an early stage human embryo, known as a blastocyst. [Credit: Jenny Nichols, University of Edinburgh, UK.](#) **B.** Induced pluripotent stem cells were turned into neurons (green), which can be used to model diseases affecting the brain or identify new treatments. [Credit: Muotri Lab, University of California, San Diego, CA, USA.](#) **C.** This is a section of a mouse intestine. The green labeled cells represent the crypts of the intestine, the location where stem cells are present. [Credit: Paul Appleton, University of Dundee, UK.](#)

* Key terms in orange are defined in the [Glossary](#) at the end of the document.

1.b. WHAT ARE STEM CELL TREATMENTS?

A stem cell treatment uses stem cells or the specialized cell types that come from stem cells to replace or repair a patient's cells or tissues that are damaged or absent. The stem cells or cells derived from them may be from the patient or a donor. The cells may be manipulated in the laboratory, including adding or removing genes, before they are put into the patient's blood or transplanted directly into the damaged tissue. Stem cell treatments may also involve recruiting the stem cells within the patient's own tissues for self-repair. However, undifferentiated pluripotent stem cells are unsafe to inject into a patient as they could cause tumors to form.

Stem cell treatments are not one-size-fits-all.

Stem cell treatments are not one-size-fits-all. These treatments will be specific for the unique disease or condition and cell type, and potentially may be unique to the patient themselves. Potential patients should be wary of clinics marketing *one* stem cell treatment that can be used to treat a diversity of different diseases that affect different parts of the body.

This guide describes three main categories of stem cell treatments - approved, investigational, and unproven - and what you should consider before moving ahead.

Approved stem cell treatments are backed by convincing evidence of efficacy and safety, approved by the appropriate regulatory bodies (e.g. the European Medicines Agency (EMA), the Food and Drug Administration (FDA) in the United States, the Pharmaceutical and Medical Device Agency in Japan (PMDA), or the Therapeutic Goods Administration (TGA) in Australia) and are widely accepted by the global medical community. **The first conditions to**

be treated by accepted stem cell treatments were certain cancers of the blood and selected immunological conditions. There are currently active clinical trials using stem cell treatments for a number of conditions including diabetes, Parkinson's disease, age-related macular degeneration, and others.

Before a treatment becomes approved, it is considered an **investigational treatment**. An "investigational treatment" is a term used to describe stem cell treatments that are being tested in clinical trials but are not approved as effective and safe. To be proven effective and safe and receive proper regulatory approval, new uses of stem cells to treat disease must undergo rigorous testing through controlled clinical trials, be reviewed for scientific merit by independent experts, and approved by an ethics committee to ensure that the rights and well-being of the participants are respected. This process can take many years and involves numerous steps and multiple iterations of testing before a new treatment is considered effective and safe and is approved, or before it is determined to be ineffective or unsafe. Until formal approval, a stem cell treatment that is being tested in clinical trials is considered investigational. It is important to understand that testing a stem cell treatment in clinical trials does not guarantee that it will become an established therapy. Many stem cell treatments, as with drug products tested in clinical trials, are not approved and do not reach patients due to problems or shortcomings detected during clinical trials.

Unproven stem cell "treatments" have not been evaluated in a rigorous, multi-step clinical trial process and thus have not been shown to be effective or safe. **Unproven stem cell "treatments" are currently being marketed and administered by unscrupulous stem cell clinics and providers around the world and can cause physical, psychological, and/or financial harm.** For more information see [What You Need to Know About Unproven Stem Cell "Treatments."](#)

1.c. WHAT ARE SOME OF THE SPECIAL CONSIDERATIONS FOR STEM CELL TREATMENTS?

Treatments that use stem cells or stem cell-derived cells are largely new and there is a lot that we still need to learn.

There are particular challenges in preparing stem cells for therapeutic use. Unlike traditional prescription drugs which are synthesized from standardized chemical compounds, stem cell treatments are developed from living cells. Ensuring the uniformity, efficacy, and safety of the stem cell treatment requires new and specialized laboratory tests that in many cases are specific to the cell type being used.

For most diseases, it is still being determined which cells will work best to repair a particular damaged or diseased tissue, how to get those cells to the right place in the body, how many cells are needed, and how to ensure that they will survive in the body and perform the desired function.

Furthermore, side effects need to be documented and reported to regulators, and long-term safety must be determined, since transplanted cells may remain for many years, potentially a lifetime, in patients' bodies. **Potential patients should note that many clinics marketing unproven stem cell “treatments” [do not have rigorous standards](#) in place for monitoring and reporting side effects**, nor do they have long-term plans to monitor the health of their patients or determine whether they are experiencing [unanticipated side effects](#) as a result of the administered unproven stem cell “treatment”. **Careful monitoring and extended follow-up of patients who receive stem cell treatments is extremely important.** These studies are necessary to reduce physical, psychological, and/or financial harm for current and future patients.

2. APPROVED STEM CELL TREATMENTS

2.a. WHAT DISEASES OR CONDITIONS HAVE WELL ESTABLISHED STEM CELL TREATMENTS?

Approved stem cell treatments are limited. An established, approved stem cell treatment is **blood stem cell transplantation**, also known as **bone marrow transplantation** or **hematopoietic stem cell transplantation**. For more than 50 years, doctors have been transferring healthy blood stem cells to replace diseased ones to treat the patient. [Blood stem cell transplantation](#) has provided life-long

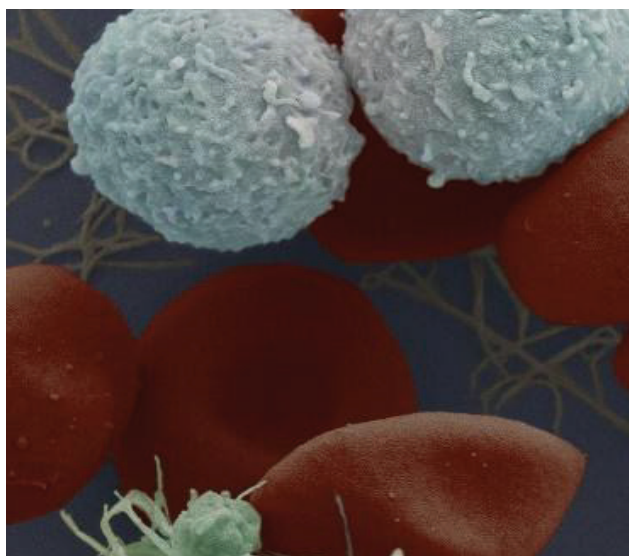


FIGURE 2. Blood stem cells can give rise to all cells of the blood and immune system. The round white cells in this image are immune cells, which will help fight infection, and the red cells are red blood cells that contain hemoglobin and transport oxygen around the body. [Credit: Anne Weston, Francis Crick Institute, UK.](#)

recovery for some patients with disorders of the blood and immune system, acquired loss of bone marrow function, and inherited metabolic diseases (see Figure 2). Learn more at [Treating Disease. What the Science Says](#).

Blood stem cells can be collected for transplantation from bone marrow, circulating blood, or umbilical cord blood. The use of blood (or hematopoietic) stem cell transplantation to treat blood cancer and some immune disorders is well established, efficacious, and fully regulated. **However, there are predatory clinics that offer unproven treatments that claim to treat a variety of other diseases using cord blood cells or cells derived from the placenta. These treatments have not been proven effective or safe.** To learn more, see [Cord Blood & Uses to Treat Disease](#).

Tissue-specific stem cells or adult stem cells like those found in the skin and cornea also play a role in tissue transplants and can contribute to long-term regeneration. For example, a stem cell treatment approved by the EMA in Europe uses stem cells found in the eye to [restore sight](#) after injuries to the cornea.

At this time, other stem cell treatments remain experimental and have not yet begun or completed clinical trials (see question 3.a.) or received the necessary approval for clinical use. Before additional stem cell treatments are fully approved, they must undergo rigorous scientific testing to prove that they achieve the desired result and are safe for the patient.



FIGURE 3: Developing a new medical treatment can take years to decades. This multi-step process begins in a laboratory where scientists perform preclinical studies before clinical trials in humans are conducted.

3. TESTING INVESTIGATIONAL STEM CELL TREATMENTS IN CLINICAL TRIALS

3.a. WHAT IS THE USUAL PROCESS FOR DEVELOPING A NEW MEDICAL TREATMENT?

Clinical translation is a multi-step process that can take years to decades. This process starts in a laboratory where scientists perform experiments to understand how living organisms work and what can go wrong in disease or injury. Scientists develop hypotheses (ideas that can be tested by experimentation), perform tests to determine whether the hypotheses are correct or incorrect, analyze the results, and make conclusions. These experiments underlie important medical discoveries and are pivotal for achieving real-world medical treatments. To learn more, visit [How Science Becomes Medicine](#).

To test how a new application might work for a particular disease or injury, studies are done on models of the disease in a laboratory (see Figure 3). These studies may be done on human cells grown in a dish or in animals with a relevant disease or injury that is similar to the human condition. These are referred to as preclinical studies. Preclinical studies should be reviewed by experts, protocols and results published in peer-reviewed journals and be reproduced, ideally by an independent laboratory, before a new experimental treatment is tested on patients in clinical trials.

After demonstrating through preclinical studies that the investigational treatment is likely to work and be safe, permission is sought from regulatory authorities

and ethical review boards to conduct clinical trials in humans, starting with a very small number of individuals. In some cases, new experimental treatments might be tested on a very small number of people before a clinical trial is started. Regulatory structures vary across jurisdictions and impact how investigational treatments are tested.

A **clinical trial** is a regulated research study designed to answer specific questions about a new investigational treatment or a new way of using a treatment that is approved for other uses. Clinical trials are used to establish whether a potential new treatment reliably produces the intended medical benefit and is safe.

Clinical trials formally compare the efficacy and safety of an experimental treatment or procedure with a control. A **control** may be an existing, approved treatment or a **placebo**, if no alternative exists. Ideally, someone entering a clinical trial is assigned randomly to receive the treatment or control (known as a **randomized trial**) and they will not know whether they receive the experimental treatment or the control (known as a **blinded clinical trial**). This reduces bias and improves the chances of obtaining meaningful results.



FIGURE 4: Clinical trials formally compare the efficacy and safety of an experimental treatment with a control. Before agreeing to participate in a clinical trial, patients should consult with a trusted and qualified physician or medical expert to ensure that your rights as a patient are being respected.

A well-designed trial will use one or more endpoints, which are outcomes that can be objectively measured to determine whether the investigational treatment is beneficial. These end points are determined in advance of the study and are used to generate credible evidence about efficacy and safety.

As efficacy, safety, and any side effects are better understood, and delivery methods are tested and reviewed, the number of patients in the trial is gradually increased.

Clinical trials determine whether a potential new treatment is effective and safe.

Once the trial data are collected, a national or regional regulatory agency, for example the EMA, FDA, PMDA, or TGA, will review the data to determine if the effectiveness and safety of the treatment was formally demonstrated, and should or should not be approved for clinical use for particular diseases or conditions.

To learn more, read [About Clinical Trials](#). Further information explaining and describing clinical trials written by the National Institutes of Health (US) can be found at ClinicalTrials.gov.

3.b. HOW CAN I LEARN ABOUT STEM CELL CLINICAL TRIALS?

Ask your primary care physician or medical specialist for advice on what clinical trials are available in your area for your specific disease or condition. Different clinical trials are offered at different institutions around the world. Remember that clinical trials have strict entry criteria to help ensure the safety of participants and to make sure that researchers will be able to answer their research question. **Credible clinical trials will have ethical and regulatory oversight and provide participants with clear details about what is involved and an informed consent form** ([see question 3.d](#)).

There are databases that allow you to search for registered clinical trials. For example, interested persons may search a database of clinical trials sponsored by the National Institutes of Health (US) at [ClinicalTrials.gov](https://clinicaltrials.gov). However, it is important to note that not all clinical trials are included in these databases, nor does the inclusion of a trial in a database indicate it is approved or cleared to proceed by a regulatory body.

Inclusion of a clinical trial in a database does not indicate that the treatment is effective or that it is approved or overseen by the organization or regulatory agency publishing the database.

3.c. WHAT SHOULD I LOOK FOR IF I AM CONSIDERING TRYING AN INVESTIGATIONAL STEM CELL TREATMENT THROUGH A CLINICAL TRIAL?

Consult with a trusted and qualified physician or medical expert to ensure that there are preliminary studies to indicate that the treatment is likely to be effective and safe, and that your rights as a patient are being respected. To begin, ask for evidence that:

- Preclinical studies ([see question 3.a](#)) have been published, reviewed, and repeated by experts in the field.
- The providers have approval from an independent committee, such as an Institutional Review Board (IRB) or Ethics Review Board (ERB), to ensure the risks are as low as possible, worth any potential benefits, and that your rights are being protected.
- The providers have approval or clearance from a national or regional regulatory agency, such as the EMA, FDA, PMDA, or TGA, for the safe conduct of clinical trials or medical use of a product for this disease.
- The investigators are qualified to conduct the study or studies in question.

Some smaller research studies may not need this level of regulatory approval but must have approval from an independent review committee and support from the clinical and administrative leadership where the procedure will be done.

It is not customary to pay to be in a clinical trial. Charging a research participant to participate in a clinical trial is often an indication of a problematic study or one that could have ethical, legal, or scientific shortcomings. Ethically, these so-called pay-to-play trials limit participants to only those who can afford the treatment and additionally, may not have control groups because patients are unlikely to want to pay for a placebo. Ultimately, these issues may severely limit the conclusions that can be drawn from such a study design. These “studies” may also be a disguise for charging patients for unproven products.

It is not customary to pay to be in a clinical trial.

3.d. WHAT IS AN INFORMED CONSENT FORM OR TREATMENT CONSENT FORM?

If you are offered an investigational stem cell treatment as part of a clinical trial or an unproven stem cell “treatment” outside of a clinical trial you should receive an **Informed Consent Form** or Treatment Consent Form. This document outlines your role as a patient and the possible implications of proceeding with the investigational or unproven treatment. It should provide a clear and detailed description of the treatment or procedure in language that you can easily understand. It should explain your options for treatment, the risks and potential benefit, and your and their responsibilities.

You should receive a consent form for any investigational stem cell treatment or procedure. It should emphasize the experimental nature of the treatment and outline the specific risks associated.

A consent form is a good way to get the information you need to determine if you want to move forward

with the treatment or procedure. **You are encouraged to have an open dialogue with your provider and make sure that all of your questions are answered** (see Figure 5). Once you have read and understood the consent form and had your questions answered through meaningful discussion with the provider, the form should be signed by you (or your legal representative) and the person providing the information. You should receive a copy of this form.

The informed consent or treatment consent form for a clinical trial should include answers to the following questions:

- How is participating in this clinical trial different from receiving the current standard of care?
- What is the investigational treatment or procedure that is being tested?
- What is the research question being tested and why is this research being done?
- What are the risks of the investigational treatment?
- What are your chances of receiving a different treatment (placebo or alternative treatment)?
- Is the clinical trial a [randomized trial](#)?
- How long will the trial last?

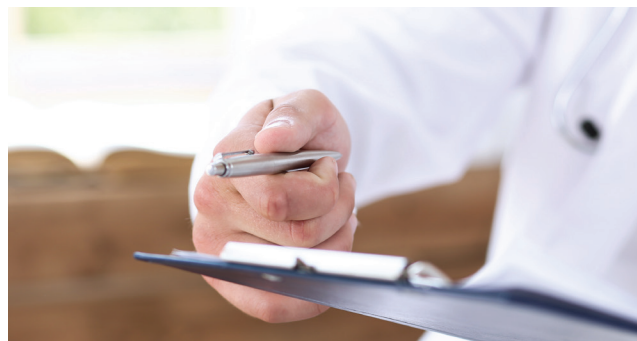


FIGURE 5: You should receive a consent form before participating in a clinical trial or receiving an unproven stem cell “treatment” outside of a clinical trial. This form should be in language that you can easily understand and provide you with information you need to determine if you want to move forward with the treatment.

- What is involved in the clinical trial before, during, and after treatment (including procedures like blood draws)?
- What are your rights and responsibilities as a participant?
- Who may see your research/medical data? What are your rights to confidentiality? How is the data stored and for how long, and what data will be shared with you?
- Will you be informed of any new information that may impact your decision to continue participating in the clinical trial?
- What are the circumstances under which you may be withdrawn from the trial?
- Who will perform the trial?
- What are the contact details of the point person, such as the Principal Investigator of the trial, and contact details of an independent organization that protects patient rights?
- How many participants are involved in the trial?
- Are there any costs associated with participating in the trial?
- Are there circumstances when clinical trial participants will be compensated or reimbursed for costs related to participating in the trial?
- Who will pay for medical expenses if there is an adverse medical event?

The consent form should also clarify your right to withdraw at any time without consequences and a disclosure of any relevant conflicts of interest. The documents should **not** include language that releases the investigator, the institution, the sponsor, or their agents from liability for negligence.



FIGURE 6. It is critical to have a meaningful discussion with your trusted healthcare provider and ensure that all of your questions are satisfactorily answered.

3.e. WHAT SHOULD I ASK WHEN CONSIDERING TAKING PART IN A CLINICAL TRIAL?

You should ask many questions about the treatment being offered and also seek a second opinion from a trusted healthcare provider with related qualifications, competency, and expertise who can give accurate and credible answers. **You should not be rushed to make a decision—make sure you understand the entire treatment plan and any associated risks.**

The doctors involved should specialize in your disease, describe alternative treatment options, and provide an Informed Consent Form or Treatment Consent Form that should address many of your questions ([see question 3.d.](#)).

Following are recommended questions to ask when considering taking part in a clinical trial:

THE TREATMENT

- Is the treatment routine for this specific disease or condition?
- Is the treatment part of a formal clinical trial?
- What are the alternative treatment options for my disease or condition?
- If I have this treatment, could it affect whether I get into another clinical trial in the future or exclude me from other potential treatments?
- What are the possible benefits I can expect? How will this be measured and how long will this take?
- Am I likely to experience personal benefit as a result of being in this study, or is my participation likely to benefit future patients rather than me?
- What other medications or special care might I need?
- How is this stem cell treatment or procedure done?
- What is the source of the stem cells?
- How are the stem cells identified, isolated, and grown?
- Are the cells differentiated into specialized cells before treatment?
- How are the cells delivered to the correct part of the body?
- If the cells are not my own, how will my immune system be prevented from reacting to the transplanted cells?
- Are there any advantages of being in a clinical trial that I should know about before I decide whether to participate?

- Are there any disadvantages connected to being in a clinical trial that I should know about before I decide whether to participate?

SCIENTIFIC EVIDENCE AND OVERSIGHT

- What is the scientific evidence that this stem cell treatment or procedure could treat my disease or condition? Where is this published? Is the journal credible? Are the findings credible?
- Have there been previous clinical trials? What was learned from these trials?
- Is there any independent oversight of the treatment plan, for example, an Institutional Review Board? Can you provide several names of qualified scientists and clinicians who can give independent advice?
- Is there any independent oversight or accreditation of the clinic where the treatment will be done and the facility where the cells are processed? Is this accreditation or oversight meaningful? Does it tell me anything about the credibility of this institution or the treatment I am considering?
- Has this treatment for this specific disease or condition received approval from a national or regulatory agency, such as the EMA, FDA, PMDA, or TGA?

SAFETY AND EMERGENCIES

- What are the risks of the treatment itself and the possible side effects, both immediate and long-term?
- Are there any other risks to me by participating in the trial?
- What will be done if an adverse reaction (bad side effect) develops? Who is the person to contact in an emergency or**

trial-related injury? Who will provide emergency medical care? What do I do if I cannot get in touch with someone from the clinic in the event of an emergency?

- Is the clinic adequately prepared to handle emergencies such as a serious allergic reaction?
- What will happen if I am no longer at the clinic when I experience a serious side effect?
- Will the clinic maintain communication with me and provide follow-ups for an extended period of time, potentially spanning months or even years, once I enroll in this trial?
- What follow-up treatment will be received, and for how long? What will I need to do?
- Who is the doctor in charge of the treatment? What specialized training does this doctor have? How well trained are the other doctors and the technical support staff?
- Who is responsible for paying the cost of care if I experience a medical emergency and subsequently require additional medical care?

PATIENT RIGHTS

- What are my rights as a participant? For example, in terms of confidentiality, my right to be informed of any new information that may arise, and the ability to withdraw from the treatment process?
- Who has access to my health data and how often can I access my own health data?
- What compensation am I entitled to if I am injured as a result of taking part in this trial?
- If I am injured, will researchers understand that it happened because I was in the trial or will the burden of proof be on me to make the case that the injury resulted from participating in the trial?

COST

- Are there any costs that I will have to pay if I participate? If so, what does this include? What other costs will I incur? Note, it is not customary for someone to pay to be in a clinical trial (other than perhaps travel and other personal expenses), and in fact, charging research participants fees to participate in a clinical trial is often a “red flag” of a problematic study or one that could have ethical, legal, or scientific shortcomings.
- What would be the cost of emergency treatment if something goes wrong? **Who would provide emergency care and who would pay for this?** Before traveling or agreeing to treatment, find out what costs your travel insurance, health insurance provider, or national health program will cover, in what circumstances, and in what countries.
- What happens if there is a serious complication that results in long-term disability? Who is responsible for paying associated costs?**
- If I have to go to court and seek remedies through litigation, who is responsible for paying legal fees?

4. UNPROVEN STEM CELL “TREATMENTS”

4.a. WHAT IS AN UNPROVEN STEM CELL “TREATMENT”?

An unproven treatment is an experimental treatment that is new, untested, or different from standard medical treatment and has not undergone the proper regulatory process. This is in contrast with investigational treatments which are being tested in clinical trials with proper regulatory oversight, and approved stem cell treatments that have been shown to be reasonably effective and safe for treating a particular disease or condition through a formal, regulated process of clinical trials ([see question 3.a.](#)).


The fact that a treatment is experimental does not automatically mean that it is part of a research study or clinical trial.

Patients should be aware that **many stem cell clinics and providers are currently marketing and administering unproven stem cell “treatments,” which are not supported by valid science and have not been shown to treat the particular disease or be safe.** Resources to help patients and family members identify unproven stem cell “treatments” and unfounded claims can be found at [What You Need to Know About Unproven Stem Cell-based “Treatments.”](#)

4.b. WHAT SHOULD I BE CAUTIOUS ABOUT IF I AM CONSIDERING AN UNPROVEN STEM CELL “TREATMENT?”

Although research is ongoing, most stem cell treatments are experimental and have not been shown to be effective and safe. There is certain information you should investigate if you are considering an unproven stem cell “treatment” outside of a regulated clinical trial, including a detailed description of the treatment, the science that supports it, the expected outcome, and the risks.

Several major warning signs of a company advertising an unproven stem cell “treatment” include:

 **Claims based on patient testimonials.** Be wary of clinics that rely on patient experiences rather than properly controlled studies. It is critical to evaluate a patient’s response to treatment in a [blinded study](#), where the patient does not know if they received the stem cell treatment or not. Patients can sometimes observe a perceived benefit after a treatment which may not be as a result of the treatment itself. Patients may also have experienced benefits unrelated to the treatment. **Unless there has been carefully evaluated clinical research, it is difficult to determine the effectiveness of the treatment and what a patient can expect.**

! Multiple diseases treated with the same cells. Stem cell treatments are not “one-size-fits-all”. Different diseases, such as Parkinson’s disease and heart disease, would be expected to be treated with different cell types, and therefore different stem cell treatments, that are appropriate for the respective disease. Also, your treatment should be provided by a doctor that is a specialist in your disease or condition.

! The source of the cells or how the treatment will be performed is not clearly documented. This information should be clearly explained in an Informed Consent or Treatment Consent Form ([see question 3.d.](#)). In addition, there should be a protocol, which can be thought of as the operating manual for the treatment, that outlines the treatment in detail to the medical practitioner. While it may not be made available to you automatically, you should be able to request the protocol. For a clinical trial or experimental treatment, protocols should have been reviewed for scientific merit by independent experts and approved by an ethics committee to ensure that the rights and well-being of the participants will be respected. When considering a stem cell treatment, ask who has approved this protocol and when the approval expires.

! Claims that there is no risk. There is always risk involved with treatment. Information about the possible risks should be available from preclinical or clinical research.

! High cost of treatment or hidden costs. It is not customary for someone to pay to be in a clinical trial. Consider what costs are involved in the “treatment”. Ask about additional costs beyond the fee for administering the “treatment”, such as costs of emergency medical care if something goes wrong, particularly if you are outside your

own country. Find out what costs your national health program or health insurance provider will cover, in what circumstances, and in what countries.

! Assurances that you can bank (store) your or your child’s stem cells for future therapeutic use. While there are a few legitimate uses for banked cells, you should be aware that there are unscrupulous stem cell clinics and blood/tissue banks that make false promises about stem cell treatments and promote banking stem cells for years, or even decades, for unproven future uses against a broad spectrum of diseases unrelated to the cell type stored. You and your family should be aware that storing cells for an indefinite time for a potential future “treatment” can be costly and there are no guarantees that the cells can be used or that the advertised future treatment will be shown to be safe and effective. To learn more, see [Should You Bank Stem Cells for Personal Use.](#)

! Claims that regulatory approval isn’t needed. In many jurisdictions, regulatory oversight is required if the cells are manipulated to a certain extent (see the TGA’s definition of [minimal manipulation](#), as an example) or if the cells will be used in a way that is different from how they would normally function (see the TGA’s [definition of homologous use](#), as an example). In these cases, stem cell treatments require regulatory oversight even if cells are being harvested and returned to the same patient.

4.c. WHAT SHOULD I ASK BEFORE CONSIDERING AN UNPROVEN STEM CELL “TREATMENT?”

You should ask many questions about the unproven stem cell “treatment” being offered and seek a second opinion from a trusted, qualified physician or medical expert with sufficient knowledge about stem cells and clinical research. You should not be rushed or financially enticed to make a decision—make sure you understand the entire treatment plan and any potential associated risks.

The physicians involved should specialize in your disease or condition, describe other treatment options, and discuss all of the risks that you will take on by receiving a procedure that has not been proven safe or effective. **You should be provided with an Informed Consent Form or Treatment Consent Form that should address many of your questions** ([see question 3.d.](#)). You should receive a consent form for any unproven stem cell “treatment,” even if it is not part of a clinical trial. It should emphasize the unproven nature of the treatment and outline the specific risks associated with the stem cell treatment(s). This form should be signed by you (or your legal representative) and the person providing the information. You should receive a copy of this form.

Following are recommended questions to ask when considering an unproven stem cell “treatment:”

THE “TREATMENT”

- Is the “treatment” routine for this specific disease or condition?
- What are the alternative treatment options for my disease or condition?
- If I have this “treatment,” could it affect whether I get into a clinical trial or exclude me from other potential treatments?
- What are the possible benefits I can expect? How will this be measured and how long will this take?
- What other medications or special care might I need?
- How does this fit in with my long-term treatment plan?
- How is this stem cell “treatment” done?
- What is the source of the stem cells?
- How are the stem cells identified, isolated, and grown?
- Are the cells differentiated into specialized cells before “treatment”?
- How are the cells delivered to the correct part of the body?
- If the cells are not my own, how will my immune system be prevented from reacting to the transplanted cells?

SCIENTIFIC EVIDENCE AND OVERSIGHT

- What is the current scientific evidence from preliminary tests using this “treatment?” Has this clinic conducted preclinical studies or clinical trials on this product themselves? What were the results? If not, why not?
- Is there any independent oversight of the treatment plan? Can you provide several names of scientists and clinicians who can give independent advice?
- Is there any independent oversight or accreditation of the clinic where the “treatment” will be done and the facility where the cells are processed? If so, is this oversight or accreditation credible? Should I rely on it in any way when making decisions about my health and health care?

- Is there approval from a national or regional regulatory agency, such as the EMA, FDA, PDMA, or TGA, of this treatment for this specific disease or condition?

SAFETY AND EMERGENCIES

- What are the risks of the procedure itself, and the possible side effects both immediate and long-term?
- What will be done if an adverse reaction (bad side effect) develops?** Who is the person to contact in an emergency or treatment-related injury? Who will provide emergency medical care? What do I do if I cannot get in touch with someone from the clinic in the event of an emergency?
- Is the clinic adequately prepared to handle emergencies, such as a serious allergic reaction?
- What follow-up treatment will be received, and for how long? What will I need to do?
- Who is the doctor in charge of the “treatment?” What specialized training does this doctor have? How well trained are the other doctors and the technical support staff?

PATIENT RIGHTS

- What are my rights as a participant—for example, confidentiality, my right to be informed of any new information that might come up, my right to withdraw from the treatment process?
- What compensation am I entitled to if I am injured as a result of receiving this “treatment?” What will I need to do to obtain this compensation? Will I have to go to court and sue?

COST

- Are there any costs to treatment? If so, what does this include? What other costs will I incur?
- What would be the costs of emergency treatment if something goes wrong?
- Who would provide emergency care and who would pay for this?
- What happens if there is a serious complication that results in long-term disability? Who is responsible for paying associated costs?**
- If I have to go to court and seek remedies through litigation, who is responsible for paying legal fees?
- Before traveling or agreeing to treatment, find out what costs your travel insurance, health insurance provider, or national health program will cover, in what circumstances, and in what countries.
- How can I get pre-approval from my insurer or health plan and take steps to avoid receiving unexpected and unwanted medical bills?

4.d. SHOULD I GET A SECOND OPINION?

You are encouraged to ask a lot of questions about the “treatment” being offered and to seek second opinions from independent qualified doctors. Your doctor should be supportive and help in the process of obtaining a second opinion. Primary caregivers should facilitate access to specialists to help patients make more informed decisions about their care. Medical records, research protocols, treatment protocols, and informed consent documents should be supplied to the person giving a second opinion.

For more information, visit [A Closer Look at Stem Cells](#).

GLOSSARY

Term	Definition
Approved stem cell treatments	Treatments that are backed by convincing evidence of efficacy and safety, approved by the appropriate regulatory bodies, and are widely accepted by the global medical community. At this time, beyond the treatment of various cancers of the blood and selected immunological conditions, there are very few conditions for which stem cell-based therapies are established as effective and safe treatments.
Blinded clinical trial	Participants do not know if they receive the treatment that is being assessed, a control treatment, or a placebo.
Blood stem cell transplantation/bone marrow transplantation	Bone marrow, blood stem cell transplantation, or hematopoietic stem cell transplantation is one of the only stem cell treatments that has been proven to be effective and safe. Through blood stem cell transplantation, healthy blood stem cells can replace diseased ones, potentially making all future blood and immune cells and treating the patient. Blood stem cell transplantations are most commonly used to treat blood diseases (such as cancers or red blood cell disorders), bone marrow failure diseases, and certain diseases that result from missing or dysfunctional immune cells. Inherited metabolic diseases (deficiencies in breaking down substances in the body) can also be treated by transplantation.
Clinical trial	A research study designed to answer specific questions about a new treatment or a new way of using a current treatment that also establishes whether potential treatments are effective and safe.

Term	Definition
Stem cells	Unique cells in our bodies defined by two properties; they can divide to make more of themselves and they can generate specialized cell types such as skin, muscle, or blood cells.
Pluripotent stem cell (PSC)	Stem cells that can differentiate to all of the cell types in the body. PSCs include embryonic stem cells and induced pluripotent stem cells.
Informed or Treatment Consent Form	Document that outlines a patient’s role in receiving an experimental treatment, and the possible implications of proceeding with the investigational or unapproved treatment. It should provide a clear and detailed description of the treatment or procedure in plain language and explain a patient’s options for treatment, their rights and responsibilities, and the risks.
Investigational treatment/Investigational procedure	Terms sometimes used to describe stem cell treatments that are being tested in clinical trials but are not approved as effective and safe. Until formal approval, a stem cell treatment that is being tested in clinical trials is considered investigational. It is important to understand that testing a stem cell treatment in clinical trials does not guarantee that it will become an approved and established therapy
Placebo	An inactive treatment that is used as a comparison to help researchers determine whether a treatment is more effective than no treatment at all.
Randomized clinical trial	Participants are randomly assigned to receive different interventions in order to reduce bias.
Unproven stem cell “treatment”	Treatment that has not been tested through formal or regulated clinical trials and has not been shown to be effective or safe. Unproven stem cell “treatments” are currently being marketed and administered by stem cell clinics and providers around the world operating outside accepted ethical standards. Administration of unproven “treatments” can cause physical, psychological, and/or financial harm.

ISSCR Resources

What You Need to Know About Unproven Stem Cell “Treatments”: <https://www.closerlookatstemcells.org/patient-resources/truth-about-stem-cell-treatments/>

The Clinical Applications of Donating and Banking Stem Cells: <https://www.closerlookatstemcells.org/the-clinical-applications-of-donating-and-banking-stem-cells/>

Cord Blood & Uses to Treat Disease: <https://www.closerlookatstemcells.org/cord-blood-just-the-facts/>

About Clinical Trials: <https://www.closerlookatstemcells.org/from-lab-to-you/about-clinical-trials/>

Types of Stem Cells: <https://www.closerlookatstemcells.org/learn-about-stem-cells/types-of-stem-cells/>

Transforming Scientific Research: <https://www.closerlookatstemcells.org/transforming-scientific-research/>

How Science Becomes Medicine: <https://www.closerlookatstemcells.org/from-lab-to-you/how-science-becomes-medicine>

Clinical Trial Resources

Clinical Trial Resources: <https://www.clinicaltrials.gov/>

Blinded Clinical Trial: <https://training.seer.cancer.gov/treatment/other/trial.html>

Clinical Trial Randomization: <https://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials/randomization/clinical-trial-randomization-infographic>

How Clinical Trials Work: <https://www.australianclinicaltrials.gov.au/what-clinical-trial/how-clinical-trials-work>

What is a Placebo and Why are Placebos Used in Clinical Trials: <https://health.ucdavis.edu/ctsc/area/clinicaltrials/documents/What-is-a-Placebo.pdf>

Common Terms You Should Know When Enrolling in a Clinical Trial <https://jcto.weill.cornell.edu/patients/clinical-trials-common-terms-to-know>

Additional Resources

Interpretation of Minimal Manipulation and Homologous Use:

AU: <https://www.tga.gov.au/method-preparation-interpretation-minimal-manipulation>

EMA: https://www.ema.europa.eu/en/documents/presentation/presentation-cats-views-classification-atmps-homologous-use-nicolas-ferry_en.pdf

FDA: <https://www.fda.gov/media/109176/download>

Europe approves Holoclar®, the first stem cell-based medicinal product: <https://www.eurostemcell.org/story/europe-approves-holoclar-first-stem-cell-based-medicinal-product>

What are Unproven Therapies?: <https://www.eurogct.org/what-are-unproven-therapies>

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