

Informed Consent
Standard for
Stem Cell-Based
Interventions
Offered Outside
of Formal
Clinical Trials



ISSCR

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www.isscr.org

Preface

The International Society for Stem Cell Research (ISSCR) is an independent nonprofit organization that fosters the exchange of information and ideas relating to stem cells, including professional and public education regarding the clinical application of stem cells. For many years, the ISSCR has been concerned about the premature administration and commercialization of unproven stem cell-based interventions outside of clinical research or medical innovation with oversight.

Concern for patient welfare underlies the Society's concern about the delivery of unproven stem cell-based interventions. While stem cell science and regenerative medicine hold enormous potential to yield new treatments for many diseases and conditions, most stem cell-based interventions are currently experimental. Prior to routine use in clinical practice, there should be evidence of their safety and efficacy from formal, approved clinical trials with the trial results published in the credible peer-reviewed literature.

The ISSCR has developed many resources to help patients learn about stem cell research, its potential to improve human health, and the risks of unproven stem cell-based interventions. These resources include the [Patient Handbook on Stem Cell Therapies](#) as well as 'A Closer Look at Stem Cells' website, which highlights "[Nine Things to Know About Stem](#)

[Cell Treatments](#)", and "[Stem Cell Treatments: What to Ask](#)." All of these resources are intended to help patients make informed decisions about stem cell-based interventions.

This document outlines a professional standard for the information that needs to be provided to patients (or their legally valid surrogates) to help position them to make an informed decision if offered stem cell-based interventions outside of a formal clinical trial. Stem cell-based interventions are complex and come with unique risks. The Consent Standard specifies the information that must be disclosed during the informed consent process, prior to administering any stem-cell based intervention outside of a clinical trial. Anyone offering stem cell-based interventions outside of a formal clinical trial should include these elements, along with anything else required by applicable laws, policies, practices, and regulations for informed consent.

The ISSCR does not endorse the administration of unproven stem cell-based interventions outside of formal clinical trials. Where such interventions are offered, however, any materials used during the consent process (including printed or digital media) should align with this Consent Standard in order for clinicians to meet their obligations for disclosure. In offering this Consent Standard, the ISSCR underscores that informed consent is a necessary, but not a sufficient condition for ethical medical practice. The fact that a patient or their proxy may have given informed consent to an unproven stem cell intervention does not alone justify the provision of the intervention.

Informed Consent Standard for Stem Cell-Based Interventions Offered Outside of Formal Clinical Trials

INFORMATION THAT SHOULD BE CONVEYED REGARDLESS OF JURISDICTION

This Consent Standard is not intended for use in clinical research (see Recommendation 3.3.2.6 of the [ISSCR Guidelines for Stem Cell Research and Clinical Translation](#) and Section 8 of the [ISSCR Patient Handbook](#)). In addition, the Consent Standard should be adapted to reflect local policies, practices, and regulations.

1. Rationale for treatment

Explain why the stem cell-based intervention is being offered and recommended.

2. Nature of the intervention

- a. Describe all surgical or invasive procedures, examinations, additional medications, devices, and timetable for the intervention.
- b. Explain whether the patient might need long-term special care, repeat interventions, or other medications.

3. Oversight

- a. Describe any relevant national policies or regulations as well as any type of independent or local oversight.
- b. Explain whether the stem cell-based intervention is approved by any governing or regulatory authority.
 - If so, which authority issued the approval?
 - If so, has it been approved for the patient's indication?

- If not approved for the patient's indication, what is the scientific rationale for the use in this case?
- If not approved for the patient's indication, is this intervention part of a regulated clinical trial?
- If it is not part of a regulated clinical trial, why not?

4. Benefits

Describe possible benefits of the stem cell-based intervention that is supportable with scientific evidence, and not just patient testimonies, including when the benefits would be expected to appear, what types of long-term monitoring would be offered, and how benefits will be measured.

5. Risks

Include a description of the nature of each risk, its potential severity, and its estimated likelihood. The potential risks of stem cell-based interventions include:

- a. Unique risks related to harvesting and processing cells (autologous or allogeneic).
- b. The reversible and potentially irreversible consequences of introducing a stem cell-based intervention.
- c. The possibility of reintroducing the disease.
- d. Unanticipated consequences that may possibly appear long after delivery of a stem cell-based intervention.
- e. Risks which are material to patients generally.
- f. Risks which the clinician knows, or should know, are material to the specific patient being treated.

6. Immunosuppression

Include an explanation as to how the immune system will be prevented from reacting to the transplanted cells and rejecting them should be provided along with the implications of immunosuppression.

7. Adverse events

- a. Describe what the patient should do in the event of adverse and unexpected complications associated with treatment.
 - How should the patient report adverse events?
 - Who should be contacted?
- b. Explain who will be responsible for patient care following an adverse event.
- c. Explain who is responsible for related costs.

8. Manufacturing method and related risks

- a. If cells are manipulated after they have been harvested, explain the associated risks of contamination with other cells or infectious agents.
- b. If the manipulation includes genome editing, explain the associated risks.
- c. Describe how safety and quality of the cells is assured.

9. Costs

Explain whether the treatment, follow-up and potential complications will be covered by the health system or the patient's insurance.

- a. If insurance or health providers won't pay, why not?
- b. If not, provide an estimate cost of that care.

10. Rights

The contents of the consent process should not include any suggestion that the rights of patients in the case of injury due to negligence or use of a defective product are limited or abridged.

11. Organization

- a. Describe the expertise and experience of the treatment facility and the team providing the intervention.
- b. Disclose any conflicts of interest, not including reasonable and customary payment for the delivery of medical services.

12. Alternatives

- a. Discuss the alternative proven treatment options for the patient's disease or condition at this stage of the illness.
- b. Discuss the alternative research options (i.e., approved clinical trials) for the patient's disease or condition at this stage of the illness.
- c. Discuss other reasonable alternatives for management of the patient's condition.

13. Data

Provide transparency regarding how the patient's information will be used and stored, and for how long.

EXAMPLE OF ADAPTATION SPECIFICALLY FOR USE IN THE UNITED STATES

This Consent Standard is not intended for use in clinical research or pay-to-participate, FDA-regulated trials that have gone through the IND review process (see Recommendations 3.3.2.6 and 3.3.2.9 of the [ISSCR Guidelines for Stem Cell Research and Clinical Translation](#) and Section 8 of the [ISSCR Patient Handbook](#)).

1. Rationale for treatment

Explain why the stem cell-based intervention is being offered and recommended.

2. Nature of the intervention

- Describe any surgical or invasive procedures, examinations, additional medications, devices and timetable for the intervention.
- Discuss whether the patient might need long-term special care, repeat interventions, or other medications.

3. Oversight

- Disclose whether the product is regulated as a biologic under Section 351 of the Public Health Service Act:
 - Is the intervention FDA-approved?
 - If not approved, explain that the intervention is experimental.
 - Is this intervention part of a clinical trial under an Investigational New Drug Application (IND)?
 - If under an IND, have all requirements for human subjects research [including Institutional Review Board (IRB) oversight] been fulfilled?
- If regulated under Section 361 of the Public Health Service Act, explain why the product is exempt from being regulated as a biologic.
 - Is it part of a clinical trial overseen by an IRB?
- Is there any other independent oversight of the intervention, including by state regulators?

4. Benefits

Describe possible benefits of the intervention that are supportable with scientific evidence, and not just patient testimonies, including when they would be expected to appear, what kind of long-term monitoring will be offered, how benefits will be measured.

5. Risks

Provide information about risks that include a description of the nature of each risk, its potential severity, and its estimated likelihood. The potential risks of stem cell-based interventions include:

- Unique risks related to harvesting and processing cells (autologous or allogeneic).
- The reversible and potentially irreversible consequences of introducing a stem cell-based intervention into patients.
- The possibility of reintroducing the disease.
- Unanticipated consequences that may possibly appear long after delivery of a stem cell-based intervention.
- Risks which are material to patients generally.
- Risks which the clinician knows, or should know, are material to the specific patient being treated.

6. Immunosuppression

Provide an explanation as to how the immune system will be prevented from reacting to the transplanted cells and rejecting them, along with the implications of immunosuppression.

7. Adverse events

- Discuss what the patient should do in the event of adverse and unexpected complications associated with treatment:
 - How should the patient report adverse events?
 - Who should be contacted?
- Discuss who will be responsible for patient care following an adverse event.
- Discuss who is responsible for related costs.

Note: As of June 2019, the only stem cell-based products that are FDA-approved for use in the United States consist of blood-forming stem cells (hematopoietic progenitor cells) derived from cord blood. These products are approved for use only in patients with disorders that affect the production of blood (called the "hematopoietic" system).

8. Manufacturing method and related risks

- a. If cells are manipulated after they have been harvested, discuss the associated risks of contamination with other cells or infectious agents.
- b. If the manipulation includes genome editing, discuss the associated risks.
- c. Describe how the safety and quality of the cells is assured.

9. Costs

Explain whether the treatment, follow-up and potential complications will be covered by the health system or the patient's insurance.

- a. If insurance or health providers won't pay, why not?
- b. If not, provide an estimate cost of that care.

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- a. Discuss the alternative proven treatment options for the patient's disease or condition at this stage of the illness.
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