

Experimental treatments for spinal cord injury:

What you should know.



- Why are clinical trials necessary?
- What makes a good clinical trial?
- What is informed consent?
- What treatments are available now?

Questions to Ask / Summary

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VERSION **THREE**

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Disclaimer: This guide is based on published scientific papers and the professional opinions of the authors as of the time of writing (2021). The fundamental purpose and content are similar to previous versions (2004, 2012) of this document. Earlier versions, including translations of the original version into French, Spanish, German, Japanese, Chinese and Turkish, are available at icord.org/research/iccp-clinical-trials-information. The recommendations are subject to change as new knowledge becomes available. This document is intended to be an additional resource for you, and is not intended to substitute for the advice and direction of your health care provider, or replace current clinical treatments. Users of this guide should periodically review the material to ensure that the advice herein is consistent with protocols of any experimental treatment being offered to improve functional outcomes after spinal cord injury. Unlocked versions are available for translation.

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What to ask before taking part in a clinical trial or human study? (your participation checklist)

Note: Most of these questions should be answered during the informed consent process.

Question	Yes	No	Additional Information
1. Safety			
a. Are there safety risks associated with this experimental treatment?			
b. Could my condition or my health get worse after this experimental treatment?			
c. If so, can you describe the possible risks associated with this experimental treatment?			
2. Possible benefits			
a. Can you describe the possible specific benefits of this experimental treatment?			
b. Can you describe the maximum level of recovery I might see after this treatment?			
c. Can you describe how any potential benefit will be measured?			
3. Clinical trial protocol			
a. Is this study being conducted under the oversight of an appropriate qualified regulatory body?			
b. Can you describe what clinical trial phase this particular trial falls within (Phase 1, 2, or 3), and what is the emphasis of study for this phase of the trial program?			
c. Is there a control group in this study?			
d. Could I be randomly assigned to the control group?			
e. Can you tell me how long I will be assessed for any change in outcome?			
f. Will I be blinded to whether I have received the experimental or control treatment?			
g. Will the investigators and examiners be blind to what treatment I have received?			
4. Payments and costs			
a. Do I have to pay for the experimental treatment?			
b. As a possible participant, are there other costs I have to pay to be involved in this study?			
c. Will my expenses associated with participating in this study be paid (e.g., travel to center for follow-up assessment)?			

Question	Yes	No	Additional Information
5. Participation in other trials			
a. Will my participation in this trial limit my participation in other SCI clinical trials?			
b. If I am assigned to the control group and the experimental treatment is subsequently shown to be an effective therapy for my type of SCI by this clinical trial program, will I be eligible to receive this treatment later?			
6. Preclinical or prior clinical evidence			
a. Can you describe the preclinical or prior clinical evidence that indicates this experimental treatment might be beneficial?			
b. Have these findings been independently confirmed by other researchers?			
c. Are there specialists that disagree with the validity of this trial? What are their objections?			
7. Independent assessment of the treatment and investigator			
a. Can you provide me several names of scientists and clinicians (not involved with this study) who can provide me independent advice about this treatment?			

What should the answers be?

So what do we, the authors, say should be the general answers to these questions? Please see below, but regardless of our opinion, it is a personal decision for which the individual living with SCI has to weigh the possible benefits against the possible risks in determining their course of action.

1. Safety

- a. Are there safety risks associated with this experimental treatment?

Answer: should be YES; no one can guarantee total safety, but some information should be available about possible risks based on either animal data or earlier Phase clinical trials.

- b. Could my condition or my health get worse after this experimental treatment?

Answer: should be YES again; if someone tells you there are no risks you should be wary. However small the chances, there is always the possibility of some problem.

- c. If so, can you describe the possible risks associated with this experimental treatment?
Answer: the investigator should be willing to discuss in detail the possible risks.

2. Possible benefits

- a. Can you describe the possible specific benefits of this experimental treatment?

Answer: the investigator should give you a range of possible benefits, from very subtle to more noticeable functional changes you might or might not experience.

- b. Can you describe the maximum level of recovery I might see after this treatment?

Answer: anyone who claims you are going to make a dramatic recovery with the return of almost full function should be avoided, as there is no evidence for any treatment having such striking outcomes.

- c. Can you describe how any potential benefit will be measured?

Answer: the investigator should be able to describe all the different kinds of tests you will undergo to evaluate your progress after treatment.

3. Clinical trial protocol

- a. Is this study being conducted under the oversight of an appropriate qualified regulatory body?

Answer: should be YES and the investigator should be able to provide you the details immediately. Be concerned if the answer is vague or consists of excuses why not.

- b. Can you describe what clinical trial phase this particular trial falls within (Phase 1, 2, or 3) and what is the emphasis of study for this phase of the trial program?

Answer: should be immediate, understandable, and in as much detail as you want.

- c. Is there a control group in this study?

Answer: should be YES for drug, cell therapy trials, especially. If not, is this a Phase 1 “open label” study (safety only)? If not, then you should be wary. However, in a rehabilitation study involving people who have lived with a SCI for many months or years, the focus may be on changes from a baseline for the individual established during the trial and a separate control group might not be included.

- d. Could I be randomly assigned to the control group?

Answer: should be YES for Phase 2 and 3 trials. If not, then this is likely not a scientifically strong clinical trial.

- e. Can you tell me how long I will be assessed for any change in outcome?

Answer: This could vary widely, from days or weeks to as much as a year or more, depending on the treatment and its expected effect on your recovery and safety. It is possible that you may have to commit the most time during the first few weeks, and this may include hospital stay as an in-patient. Subsequently,

you may be asked to return for assessments at defined times over the following months. Once you agree to participate, you should be willing to complete the full trial protocol, even if you feel you are not benefiting. Participants who withdraw from a study undermine the completion of the trial in a timely fashion and make it difficult to accurately interpret whether the treatment had any benefit.

- f. Will I be blinded to whether I have received the experimental or control treatment?

Answer: If physically and ethically possible in Phase 2 and 3 trials, the answer should be YES. If not, it could be an “open-label” Phase 1 trial or a rehabilitation or surgical trial where blinding is not possible or safe. In other cases, you should be wary. Sometimes you cannot help but know what group you are in, but the investigators should ask you not to tell the examiners which group you are in until the trial is over and all of the data is analyzed.

- g. Will the investigators and examiners be blind to what treatment I have received?

Answer: this should be a definite YES, for trial staff that can refrain from knowing the treatment being administered. If not, it may not be well-designed trial to determine the therapy’s effectiveness without bias, and you should be suspicious.

4. Payments and costs

- a. Do I have to pay for the experimental treatment?

Answer: this should be NO. If Yes, then this is not a clinical trial you can trust. You should be suspicious and should avoid the offered treatment.

- b. Are there any other costs associated with my participation in this study?

Answer: you should not have to pay for any procedure specifically related to a clinical trial program, but you, or your health care insurance provider, may have to pay for the current standard of medical care. You should be informed about whether the trial sponsor will pay for treatment of any complications you

might experience because of your participation in the trial.

- c. Will my expenses associated with participating in this study be paid (e.g., travel to center for follow-up assessment)?

Answer: should be YES.

5. Participation in other trials

- a. Will my participation in this trial limit my participation in other SCI clinical trials?

Answer: could be a possibility unless the potential effect of the treatment being tested is known to be temporary. The investigator should be able to outline which type of trials you may be excluded from in the future. For example, it is unlikely that participation in an acute treatment trial would later affect your potential participation in a study at a later (chronic) time point. Nevertheless, the number of inclusion and exclusion criteria for any two trials is difficult to predict and compare.

- b. If I am assigned to the control group and the experimental treatment is subsequently shown to be an effective therapy for my type of SCI by this clinical trial program, will I be eligible to receive this treatment later?

Answer: this a possibility, unless your SCI condition changed, or there was a limited time for treatment after SCI that will have passed. Generally, once an experimental treatment has been approved by a regulatory agency for clinical use, you would be eligible for treatment.

6. Preclinical or prior clinical evidence

- a. Can you describe the preclinical or prior clinical evidence that demonstrates this experimental treatment is beneficial?

Answer: the investigator should be able to describe the previous evidence in terms you can understand, including the strengths and limitations of the treatment approach. Evidence

may come from animal studies or a related human disorder. Remember that effects in animals, such as recovery of walking, cannot be expected to translate directly to effects in human beings.

- b. Have these findings been independently replicated?

Answer: this could go either way, but there should be some evidence that other researchers have obtained similar results, confirming the potential benefit when investigating this therapeutic target or treatment approach.

- c. Are there specialists that disagree with the validity of this trial? What are their objections?

Answer: the answer here may be YES, as there are almost always some difference in opinions about any proposed human treatment. Scientists are usually very critical of each other! The investigator should be able to provide you with a summary of the pros and cons for the treatment compared to any alternatives, but be wary of any treatment that is claimed to have no limitations. You, your friends and family will undoubtedly use the internet to look up information. If you run into biological or medical terms that you don't understand, we have tried to help by providing a glossary of some of the relevant terms (Appendix B). In any case, you should discuss your concerns and aspirations with your health care providers.

7. Independent assessment of the treatment and investigator

- a. Can you provide me several names of scientists and clinicians (not involved with this study) who can provide me independent advice about this treatment?

Answer: should be YES and you should be able to verify the credibility of the study and the credentials of the investigators via other sources or independent websites.

Experimental Treatments for SCI – Summary

Note: This section summarizes the most important aspects of the document. However, we **STRONGLY** recommend that you read the entire document to fully understand it. Reading this section alone will not provide you with the necessary knowledge to make an informed decision that could have consequences on your well-being.

What is the difference between a clinical trial and clinics offering unproven procedures?

Clinical trials are well-designed, objective tests of experimental treatments. They are regulated by local and governmental authorities and follow a defined scientific process to protect you from possible harm and to discover if the therapy is beneficial. Clinics offering unproven medical procedures do not follow these rules and cannot provide objective evidence the treatments they sell will work and not cause harm.

How do I tell whether an experimental treatment is part of a valid clinical trial program?

The document will explain the trial process and guide you on how to get more information. For a start, you should not be asked to pay for the experimental treatment being tested in a regulated, scientific trial. You may incur some expenses, such as insurance co-pay fees, deductibles or accessory costs (e.g., travel), but the cost for the treatment being tested is covered by the trial sponsors.

Why are clinical trials necessary?

Clinical trials are designed to provide clear evidence that a treatment is safe and beneficial. Every experimental therapy and trial poses some risk of causing unintended complications. Well-designed clinical trials document both benefits and unforeseen risks and are structured to determine if any benefit is due to the treatment rather than other factors, such as natural recovery or additional rehabilitation used along with the experimental treatment.

What makes a good clinical trial?

This depends on the trial phase (as explained in this section of the document). To test if a treatment is effective, a properly designed clinical trial follows a strict, scientifically accepted process that generally compares a group that receives the experimental treatment to a “control group” that gets an inactive (placebo) treatment. Other aspects of the trial should be as similar as possible for both groups. To remove bias or conflict of interest, trial assessors and participants may not be allowed to know which treatment has been delivered (this is called “blinding”).

How are clinical trials structured?

Each phase of well-designed clinical trials is governed by local, regional and/or federal agencies who review the evidence. They ensure that the requirements of each phase of the process have been followed, and that participants have not been harmed by the experimental treatment, before allowing the next phase to proceed.

What if I get assigned to the control group?

Trials are conducted because we do not yet know if an experimental treatment is beneficial or potentially harmful. Comparisons, e.g., between people who get a treatment or do not, help avoid bias so that impartial conclusions can be made. Volunteers participating in a trial, whether they are in the experimental or control group, should always receive the current best care available. Many trials will eventually offer the treatment to the control group if it is determined that the benefit to them, based on the current status of their injury, outweighs the risks.

What are the various trial phases?

Clinical trial phases are defined by regulatory authorities for testing, and ultimate approval, of new drugs, cellular therapies and devices. Testing usually requires a series of trials in sequential phases (Phase 1, 2 and 3), with results that

indicate both safety and meaningful benefit before a regulatory agency will consider approving an experimental treatment for use in regular care. Unfortunately, it is quite common to see an experimental treatment fail, even when early signs showed great potential. Short cutting these processes will likely result in a failure.

What are regulatory oversight and registration of clinical trials?

National authorities regulate trials testing new drugs, cellular therapies, tissue transplants, devices or technologies. Trials that test surgical procedures or rehabilitation activities may not be regulated by those agencies. However, all genuine trials should have approval from the local human research ethics committee. Treatments are approved for specific disorders, or segments of the population, so “off label” use is still a form of unproven therapy. An increasingly common practice is the registration of trials on a central, public website, which does not substitute for regulatory approval. The trial investigator will be able to inform potential participants about the registration details and agency approval associated with the trial.

What is required for participation in a clinical trial?

A well-designed trial, especially in the early phases, needs to limit testing to a group of participants who are similar to each other in order to have the best chance to show a benefit. Therefore, a person interested in participation must match a set of criteria (called inclusion and exclusion criteria) that is determined before the trial is allowed to proceed.

What is informed consent?

Before you participate in any trial activities, all aspects of the trial must be explained to you, including what is being tested and how, what is expected of you, and all potential risks and benefits, both short- and long-term. This occurs via a thorough discussion with the Investigator during which you may ask any and as many questions as you wish. Only when you feel all your questions have been answered to your satisfaction will you be asked to sign the form that says you have been informed and give consent to participate.

What if I have already received an experimental therapy?

Having already received an experimental therapy may, or may not disqualify you from receiving another experimental therapy. This depends on what the previous experimental therapy was, and how it might interact with the next experimental treatment. This can only be determined on a case-by-case basis, in discussion with the Investigator of the trial that you are considering.

How long will I be required to participate in the clinical trial?

You will become a volunteer participant (e.g. be enrolled) once you have given your informed consent. After that, the length of time you participate depends on the trial but typically involves several hours (during each of several visits) over several weeks, months, or even longer. You are free to withdraw your consent and stop participating at any time and for any reason.

What should I expect after a SCI clinical trial?

Even if a new treatment is shown to provide some functional benefit after completing a clinical trial program, it is still unlikely that it will provide a complete cure. Progress happens little by little and it is most likely that a combination of treatments will provide better outcomes in the future. With continued study, scientists and clinicians will refine the most appropriate combination treatments for SCI.

What treatments are available now?

Surgical procedures, rehabilitation, drug therapies, and assistive technologies, including some types of electrical stimulation are currently used in standard care. Surgical decompression and stabilization of the bones of the spinal column very soon after spinal injury are accepted best practices in many places around the world. Surgery is also indicated to treat complications including cysts expanding within the spinal cord (syringomyelia) that can cause loss of sensation or motor function, pain, and autonomic disturbances in 5-10% of people with chronic SCI. Many forms of rehabilitative strategies administered by trained therapists are standard

practice, some including assistive technologies or functional electrical stimulation to maximize functional recovery. SCIRE (www.scireproject.com) provides information about accepted rehabilitation strategies as well as drugs currently approved to treat spasticity, pain, metabolic functions and management of bladder, bowel, respiration, cardiovascular, sexual, reproductive activity, bone health, community mobility and quality of life.

What are some of the current experimental treatments proposed for SCI?

Current potential therapeutic interventions (e.g. new drugs, cell transplants, rehabilitation strategies or assistive devices) are focused on neuroprotection, repair / regeneration, neuroplasticity and replacement / assistance of function. More details can be found at SCITrialsFinder.net.

Should I STILL consider receiving an unproven treatment outside of a clinical trial?

This is a personal choice and the information provided here will help you to decide. If you choose to receive an inadequately tested treatment at a clinic claiming success, you may pay for a treatment that will most likely bring you no improvement and possibly cause adverse effects. You may need to undergo extensive travel with its attendant risks. Complications may create new health problems and there is a chance of losing further functions, causing pain or even life-threatening problems. You should discuss these with your healthcare provider(s) before making a final decision.

What if I read about it in the media?

Regulatory agencies strictly control marketing of experimental treatment trials; however, clinics that sell unproven treatments often advertise directly to patients through clinic websites, brochures and social media platforms. Positive results from trials of experimental treatments are published in peer-reviewed journals while clinics selling unproven treatments mainly provide selected testimonials, questionable data, and lack oversight by regulatory agencies.

Where can I get good advice?

Good advice is available through your medical professionals, non-profit organizations (professional societies, government and non-governmental organizations, foundations, academic or medical research centers, and advocacy groups), as well as published clinical and scientific literature in reputable medical journals.

Appendix A: What to ask before taking part in a clinical trial or human study?

A participation checklist, with questions that you can ask during the informed consent process, is available in Appendix A, along with information to help you understand the answers you might receive.