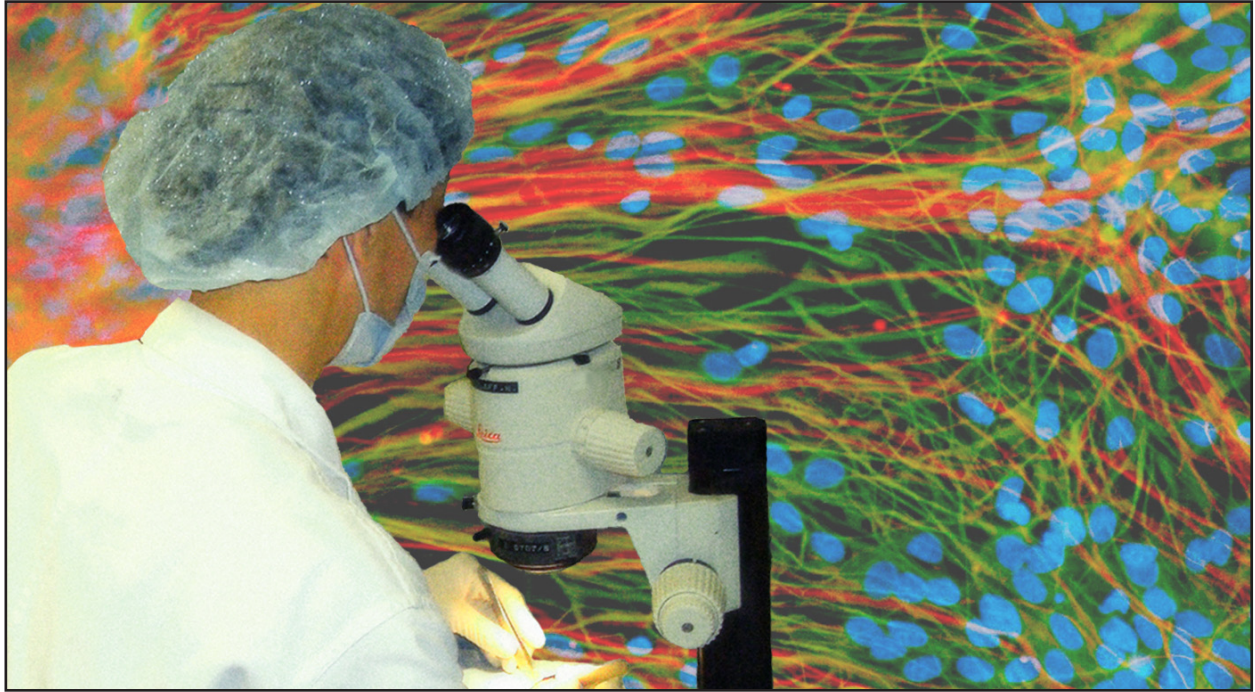


# Experimental treatments for spinal cord injury:



**what you should know  
if you are considering participation  
in a clinical trial.**

**A summary for people with spinal cord injury, their families,  
friends & caregivers.**

**Provided by**

**ICCP**  
International Campaign for Cures of spinal cord injury Paralysis

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Christopher and Dana Reeve Foundation (USA) • Institut pour la Recherche sur la Moëlle épinière et l'Encéphale (France) • International Spinal Research Trust (UK) • Fondation internationale pour la recherche en paraplégie (Switzerland) • Japan Spinal Cord Foundation • Miami Project to Cure Paralysis (USA) • Neil Sachse Foundation (Australia) • Paralyzed Veterans of America (USA) • Rick Hansen Foundation (Canada) • Neil Sachse Foundation (Australia) • Wings for Life (Austria)



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## Experimental treatment for spinal cord injury: what you should know if you are considering participation in a clinical trial.

After a spinal cord injury, patients are often told that there are no treatments available that will repair the damage. This is still true, and the advice is given to persuade people to focus on their rehabilitation rather than hoping for a miracle cure. However, great advances have been made in the science of spinal cord repair, and treatments that will improve the function of people with spinal injury are now coming, although a complete cure is still not feasible (a list of potential approaches currently being examined is provided in the full booklet).

As these new treatments move from the laboratory to the clinic, they will need to undergo clinical trials. This pamphlet offers advice to you should you consider participating in a trial.

This pamphlet is a summary of a more complete document. Both have been prepared by an international panel of scientists and clinicians, sponsored by the ICCP (International Campaign for Cures of spinal cord injury Paralysis), a confederation of the world's Spinal Injury not for profit organizations. The full document is available on the ICCP website, [www.campaignforcure.org](http://www.campaignforcure.org), and from the ICCP member organizations.



### Why are clinical trials necessary?

It can be surprisingly difficult to find out if a treatment is safe and if it really works. Patients often believe they have got better as a result of a new treatment, but the improvement may not really have been caused by the treatment. There are two main problems.

*The placebo effect.* People with spinal injury are desperate to get better. After being given a treatment their belief and hope usually leads them to report an apparent improvement. In clinical trials, patients receiving a sham or placebo treatment usually report a considerable improvement in their condition, and this may be just as large an improvement as is reported by the patients receiving the experimental (sometimes called active) treatment.

*Spontaneous recovery.* Immediately after a spinal injury patients are often completely paralyzed. Most people will recover to some extent without treatment, and for a few fortunate people the recovery can be dramatic, almost back to normal. The rate of recovery is greatest in the first three months, but recovery continues for a year or even more. It is very difficult to work out whether recovery in an individual is due to this spontaneous recovery, or due to the effects of a treatment, particularly if the treatment is given soon after the injury.

***There is a real danger that treatments that do not really work or might even do harm might become standard medical care because they were not subjected to a proper clinical trial.***

## Why should you think carefully before enlisting in a clinical trial?

People with spinal injuries are understandably desperate to get better. Scientists have been working extremely hard to develop new treatments, and want very much to see their treatments help people with spinal injuries as soon as possible. The urge for both groups to cut corners is considerable. The majority of clinical trials will be well planned and carefully conducted. However there may be a few that should be avoided.

This brochure, and the larger accompanying ICCP document should help you identify good clinical trials.

*A good clinical trial* will be testing a treatment that has undergone extensive investigation in animals and will have shown a strong and repeatable effect. The clinical trial will be carefully designed to compare a group of patients receiving the experimental treatment with others receiving no treatment or a placebo.

*Experimental treatments offered without having completed a trial.* Some possible treatments may be offered to patients, usually by doctors who believe strongly that they will work. In the absence of a clinical trial in which the effects of the treatment are

compared with a control group of patients receiving a placebo treatment, it is almost impossible to determine whether the treatment is really effective.

*Treatments offered for material gain.* Unfortunately, where patients are desperate for a cure, there is the opportunity for less scrupulous organizations to offer unproven treatments to those who can pay. You should not have to pay for any procedure specifically related to a clinical trial program, but you, or your health care insurance system, may have to pay for the current standard of medical care.

Creating new treatments for those with spinal injury is probably the most difficult thing that medicine has ever attempted.

There is a very small chance that a treatment offered prematurely without completing a properly designed clinical trial will work, but it is more likely that it will be ineffective or even do harm. We advise very strongly that you should only participate in properly designed and conducted clinical trials of treatments for which there is compelling evidence of efficacy from animal experiments.



## How are clinical trials structured?

It takes three clinical trial steps, or *phases*, to qualify a treatment for human patients.

*Phase 1* is to find out if the treatment is safe. A fairly small number of patients, usually between 20 and 80, are given the treatment, usually initially at a low dose, to see if there are side effects.

*Phase 2* is designed to look for positive treatment effects, comparing patients receiving the treatments with a control group.

If a useful effect is seen in Phase 2, the trial proceeds to *Phase 3*. Here a larger number of patients, usually in several clinics, are given the active treatment or a control treatment. If the treatment shows a clear useful effect and no serious side-

effects, usually in two separate Phase 3 trials, then it will be approved by the national regulatory agencies for clinical use.

### Design of clinical trials:

The key feature of most clinical trials is the comparison of a group of patients receiving the active (experimental) treatment with a control group, that either does not receive the treatment or receives an inactive placebo treatment. The only type of trial in which this is not the case is where patients whose condition is very stable (this would mean patients 1 year or more after spinal injury) who act as their own control group, and are given a treatment to see whether their condition improves compared with their



previous abilities. When the effect of a treatment on the experimental group is being compared with the outcomes from a control group, steps should be taken to make sure that the people doing the assessments are unaware of whether patients have received active or dummy treatments (this is known as blinding). In many trials the patients are also blinded to the group they have been assigned, although this type of blinding is sometimes hard to achieve with spinal injury treatments requiring surgery.

**How would participation in a clinical trial affect you?** Before anyone can be enrolled in a trial they must give informed consent. If a treatment has to be given very soon after spinal injury, some patients may not be fully conscious, and then their family can give consent on their behalf. Not all patients will qualify for a trial, because most trials will select particular groups of patients with particular types of injury. All trials have criteria because if the patients are too different from one another it may be impossible to find out if a treatment has worked. After enrollment, patients are randomly assigned to the active treatment or control group. After or during the treatment, there will be frequent follow up examinations, for which it will be necessary to attend the clinic. These examinations may include a full physical exam, blood tests, and tests of the ability to perform daily living tasks to assess spinal cord function. You should not have to pay for these visits.

**What if you get assigned to the control group?** Most patients would obviously prefer to receive the active treatment. However, as we described above, it is impossible to decide if a treatment really works unless there are control patients with whom to make comparisons. If by mischance the treatment has an undesirable side effect, then being in the control group is an advantage. Patients participating in a trial should all benefit by receiving the current best care. The trial investigators will have a policy on what to offer members of the control group at the end of the trial. Rapid enrolment in a second trial is sometimes a possibility, as is receiving some form of approved treatment. If this is not clear, you may need to enquire.

**What should you expect after a clinical trial?** At the end of the trial you are unlikely to be completely cured. Could you then obtain another treatment in a different trial? The enrollment criteria for some trials may exclude patients that have already received some types of experimental treatment. Those running the trial will have a policy on what to offer patients at the end. There is more information on this issue in the full document, and you can discuss it with the investigators running the clinical trial.



## You have been invited to participate in a clinical trial. How can you decide?

Before entering any trial you or your relatives will have to give informed consent. Here are some of the things about which you should satisfy yourself.

*Experimental evidence that the treatment works.* Any treatment reaching clinical trials should have been tested in animals with spinal injuries, and should have produced a clear improvement without toxic side effects. It is important that this positive result has been published and reviewed by other scientists, and has been repeated several times, in different

types of experimental spinal cord injury, and in more than one laboratory. If you ask you should receive a detailed account of this work.

*Evidence that the treatment is safe.* Before being applied to human patients any treatment should have gone through a series of safety tests. It may have already been tested in Phase 1 or 2.

*Design of the trial.* You should know whether you being enrolled in Phase 1, 2 or 3. The trial should be registered with an appropriate government regulatory



body. In a well conducted Phase 2 or 3 trial there will be a treatment and control group, and patients will be randomly assigned to one or the other. Steps should be taken to blind the assessors as to whether you

are in the treatment or control group. There will be a number of follow-up examinations over a period, often as long as a year after the treatment, conducted in the appropriate clinic. You should not have to pay for these. At the end of the trial there should be a clear policy on what can be offered to patients in both the active treatment and control groups.

## Where can you get advice?

You have several options:

- There are good websites run by the various spinal injury organizations that are members of the ICCP (see below). You can contact the foundations directly and ask for advice. Many of them are staffed by people who themselves have spinal cord injuries. Some government research agencies also have useful information on their websites (for instance the National Institutes for Health in the USA).
- Spinal injury researchers are generally pleased to offer advice if you ask them; it is best to do this by email. You can get names of researchers from the foundations.
- Most patients will have a regular physician, who will be prepared to offer advice or direct you to the most appropriate person.
- **Read the full document (available for download from the ICCP website):** it contains many more details about the information touched on in this

summary. We start with an overview of the ASIA scale and spontaneous recovery, and then look at the risks of unapproved treatments. We examine in-depth the anatomy of a clinical trial, from Phase 1 to Phase 4, as well as the basics of trial design and pre-clinical studies. We discuss the ethics of clinical trials, bias, controls, and the importance of informed consent. We review some scales that are used to measure functional benefits, and outline some concerns that might arise regarding the possibility of taking part in a future trial after already participating in a trial. We introduce you to some experimental approaches to SCI currently being studied. Finally, we provide you with a list of questions that you can pose to a researcher inviting you to participate in a human study. This checklist might assist you in your decision whether or not to participate in the trial.

**ICCP web site:** [www.campaignforcure.org](http://www.campaignforcure.org)

**Web sites of ICCP member organizations:**

Christopher and Dana Reeve Foundation: [www.christopherreeve.org](http://www.christopherreeve.org)

Institut pour la Recherche sur la Moëlle épinière et l'Encéphale: [www.irme.org](http://www.irme.org)

International Spinal Research Trust: [www.spinal-research.org](http://www.spinal-research.org)

Fondation internationale pour la recherche en paraplégie: [www.irp.ch](http://www.irp.ch)

Japan Spinal Cord Foundation: [www.jsf.org](http://www.jsf.org)

Miami Project to Cure Paralysis: [www.themiamiproject.org](http://www.themiamiproject.org)

Neil Sachse Foundation: [www.nsf.org.au](http://www.nsf.org.au)

Paralyzed Veterans of America: [www.pva.org](http://www.pva.org)

Rick Hansen Foundation: [www.rickhansen.com](http://www.rickhansen.com)

Spinal Cure Australia: [www.spinalcure.org.au](http://www.spinalcure.org.au)

Wings for Life: [www.wingsforlife.com](http://www.wingsforlife.com)

# What should you ask before agreeing to take part in a clinical trial? *(your participation checklist)*

Here are some questions to pose to the researcher inviting you to participate in a human study. This checklist may assist you in your decision whether or not to participate.

1. Safety	Yes	No	Additional in-depth information
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?			
d. Is this outcome measure accurate and sensitive as an assessment tool?			
3. Preclinical evidence			
a. Can you describe the preclinical evidence that demonstrates this experimental treatment is beneficial (i.e. in animals with SCI)?			
b. Have these findings been independently replicated?			
c. If they have been replicated, is there a consensus among the scientists that this treatment addresses a valid therapeutic target for improving my functional outcomes?			
d. Are there any dissenting opinions and do these arguments have some validity for not going forward with this treatment?			

4. Clinical trial protocol	Yes	No	Additional in-depth information
a. Is this human study registered as a clinical trial with an appropriate qualified regulatory body?			
b. Can you describe what clinical trial phase this particular human study falls within?			
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?			
<b>5. Participation in other trials</b>			
a. Will my participation in this clinical trial limit my participation in other SCI clinical trials?			
b. If I am assigned to the control group and the experimental treatment is subsequently validated as an effective therapy for my type of SCI by this clinical trial program, will I be eligible to receive this treatment later?			
<b>6. Payments and costs</b>			
a. Do I have to pay for this treatment?			
b. Are there any other costs associated with my participation in this study?			
c. Will my expenses associated with participating in this study be paid (e.g. travel to center for follow-up assessment)?			
<b>7. Independent assessment of the treatment and investigator</b>			
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 and your reputation?			



## So, 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 such risks from pre-clinical or earlier Phase clinical studies.

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

Answer: should be YES again; if someone states there are little or no risks you should be wary.

- c. *If so, can you describe the possible risks associated with this experimental treatment?*

Answer: the investigator should be able to discuss in detail the possible risks associated with this human study.

### 2. Possible benefits

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

Answer: the investigator should describe a range of possible benefits ranging from very subtle to modest functional improvements.

- 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, even in preclinical animal studies.

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

Answer: the investigator should be able to describe a number of different measures that will be used to evaluate your progress after treatment.

- d. *Is this outcome measure accurate and sensitive as a tool?*

Answer: the investigator should be able to describe the strengths and limitations of the evaluation procedures; once again, nothing is perfect.

### 3. Preclinical evidence

- a. *Can you describe the preclinical evidence that demonstrates this experimental treatment is*

*beneficial (i.e. in animals with SCI)?*

Answer: the investigator should be able to outline the evidence, including the strengths and limitations of the treatment approach.

- b. *Have these findings been independently replicated?*

Answer: this could go either way, but there should be evidence that other scientists have obtained similar results when investigating this therapeutic target or approach.

- c. *If they have been replicated, is there a consensus among the scientists that this treatment addresses a valid therapeutic target for improving my functional outcomes?*

Answer: this could go either way, but there should be some published discussion (e.g. a review) suggesting that the experimental treatment you are considering could alter or effect a valid target for improving functional outcomes after SCI.

- d. *Are there any dissenting opinions and do these arguments have some validity for not going forward with this treatment?*

Answers: the investigator should be able to provide you with a summary of the pros and cons for the treatment. If not, be wary of any treatment that is claimed to have no limitations; scientists are usually very critical of each other. Use the internet to look up the most recent publications on the proposed treatment ([www.pubmed.gov](http://www.pubmed.gov) is a good starting point). If you run into biological or medical terms that you don't understand, one of your health care providers should be able to help.

### 4. Clinical trial protocol

- a. *Is this human study registered as a clinical trial with an appropriate, qualified regulatory body?*

Answer: should be YES and the investigator should be able to provide you the details immediately. If the answer is vague on this point, you should be wary.

- b. *Can you describe what clinical trial phase this particular human study falls within (Phase 1, 2, or 3)?*

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

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

Answer: should be YES. If not, then this should be a Phase 1 "open label" study (safety only). If not, then this human study is unlikely to be a clinical trial and you should be wary.

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

Answer: should be YES for Phase 3 trials, If not,

then this is likely not a valid clinical trial.

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

Answer: should be anywhere from a minimum of 6 months to a year after treatment. It is possible that you may have to initially commit several weeks and this may include hospital stay as an in-patient. Subsequently, you may be asked to return for assessments at defined time points throughout the following months. Once you agree to participate, you should be willing to complete the full trial protocol, even if you feel that you are not benefiting. Participants who withdraw from a study undermine the completion of the trial in a timely fashion.

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

Answer: If at all physically possible, the answer should be YES. If not, it should be a Phase 1 trial. If not a Phase 1 trial then you should be wary that this is not a valid clinical trial. Sometimes you cannot help but know what group you are in, but you should be asked not to tell the examiners whether you are in the experimental or control group until the trial data is completely analyzed.

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

Answer: this should be a definite YES, unless it is a Phase 1 trial. If not, it is not a valid clinical trial and you should be wary.

## 5. Participation in other trials

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

Answer: should be YES, that this is a possibility. The investigator should be able to outline which type of trials you may be excluded from in the future.

- b. *If I am assigned to the control group and the*

*experimental treatment is subsequently validated as an effective therapy for my type of SCI by this clinical trial program, will I be eligible to receive this treatment later?*

Answer: should be YES, unless your SCI condition changed, or there was a limited time for treatment after SCI, which as now been exceeded. Generally, once an experimental treatment has been approved by a regulatory agency for clinical use you would be eligible for treatment.

## 6. Payments and costs

- a. *Do I have to pay for this treatment?*

Answer: this should be NO. If Yes, then this is not a valid clinical trial and you should be wary.

- 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 system, may have to pay for the current standard of medical care.

- 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.

## 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 and your reputation?*

Answer: should be YES and you should be able to verify the credibility of the study and the credentials of the investigators easily and readily via the internet.

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