**Saint Louis University Institutional Review Board**

**Human Gene Transfer Informed Consent Guidelines**

For specific gene transfer considerations in the informed consent document, see “Informed Consent Guidance for Human Gene Transfer Trials subject to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules” which is located online at <http://osp.od.nih.gov/sites/default/files/resources/IC2013.pdf>.

The most notable excerpts from the Guidelines are included or described below:

* [Describing gene transfer/vectors in the purpose section for general understanding](#Purpose)
* [Describing risks regarding gene transfer/vectors](#RISKS)
* [Reproductive Risk Considerations](#ReproductiveRisks)
* [Long-Term Follow-Up Considerations](#LongTerm)
* [Autopsy Considerations](#Autopsy)
* [Media Interest Considerations](#Media)

**PURPOSE SECTION [Section 1 of the Biomedical (Clinical) Informed Consent]**

**Describing Gene Transfer**: A brief description of the gene transfer intervention should be provided. The process of gene transfer is likely to be unfamiliar to most participants. Therefore, it is especially important that the investigator clearly and simply explain the gene transfer methodology used in the given study.

It is also important to use terms like "genes" and "DNA", especially if the gene transfer intervention is otherwise described by an acronym or other term that does not itself make an obvious connection to the introduction of new genes or new DNA into the body.

**Describing Vectors:** Most gene transfer requires a vector, often described as a transportation system to deliver the gene. For studies using a vector, descriptions using vivid analogies that compare the vector to a car and the gene to the passenger may be helpful to lay readers. For those few studies not using a traditional vector (e.g., naked plasmid DNA), the description should discuss the method of delivery in plain language.

Investigators should pay particular attention to how adenoviruses are described since they are not just a common cold. Adenovirus can be better described this way: "Adenovirus is a common virus found in humans. Normally, it can cause respiratory infections like a common cold, pneumonia, croup or bronchitis.”

**SAMPLE GENE TRANSFER DESCRIPTIONS**

* The gene transfer used in this study tries to provide corrected copies of one of your genes that does not work properly in your body [can be used in studies supplying corrected genes for monogenic diseases, or the p53 gene for some cancers]
* The gene transfer method used in this study tries to add copies of a gene that will change characteristics of the targeted cells [for example, when inserting the HSV-TK gene into tumor cells to make them susceptible to destruction by gangiclovir]
* The gene transfer method used in this study tries to add copies of a gene that increases the immune response against a tumor [use, for example, when inserting the gene for IL-2 or interferon gamma]

**SAMPLE VECTOR DESCRIPTIONS**

The study involves a virus called [adenovirus, adeno-associated virus, retrovirus, other virus, i.e. fowlpox, vaccinia], which has been changed in the laboratory so that it is not likely to cause an infection once it is in your body. [A short description of each virus used in the vector should be added.]

Method of delivery description samples:

• Loops of DNA containing the gene [naked plasmids].

• Loops of DNA associated with fat molecules [called liposomes] that help improve gene delivery.

**RISKS SECTION [Section 4 of the Biomedical (Clinical) Informed Consent]**

**Phase I Study**: Phase I trials involve the greatest uncertainty about risks of harm since existing evidence is limited to animal or laboratory studies or to results of the gene transfer intervention in a separate disease. All the expected and remote risks of harm that may foreseeably be associated with participation in the study should be listed and explained.

Previous experiences with the same or similar vector, or even a different transgene, should be included in the risks section, particularly in phase I studies. Experience with animal studies may be relevant, as well as other human experience, and possibly even in vitro experience, when the meaning and limitations of the findings are carefully described. A general statement that humans and animals respond very differently and a statement about the relationship between the dose levels used in animals and humans would be appropriate. Uncertainty about the likelihood of the occurrence of most risks of harm from the gene transfer intervention at this early stage of research should be acknowledged.

**Phase II Study**: The risks of harm from the intervention are better defined for a Phase II study. The consent form should include descriptions of risks of harm that were discovered in Phase I, such as reactions to the maximum tolerated dose. It should be acknowledged that the extent of experience is still limited and that unanticipated harms may develop.

**Phase III Study**: The risk statement of a Phase III trial should reflect the results of earlier trials. It should also acknowledge that with a greater number of enrolled participants, less-common side effects are likely to be recognized at this stage.

 **Types of Risks**: It may also be important to distinguish risks of procedures from risks of harm from investigational agents. Potential participants should be informed of the specific risks of harm from the vector and transgene used in the given study. The following risks of harm from gene transfer should be included whenever appropriate:

• The added vector and/or gene could create changes in cells that could lead to cancer

• The added vector and/or gene could create permanent changes in cells that could be passed on to children conceived and born during or after study participation

• The added vector and gene could go to unexpected cells or tissues in the body

• The added vector could become able to reproduce itself and the added vector and gene could be passed on to close contacts like an infection

**SAMPLE RISK LANGUAGE**

Sample 1 - Risks Associated with a Study Agent

The vector, which carries the gene into your cells, is considered harmless in humans. However, it is possible that the virus could grow and/or make the cells cancerous. There is a risk that the vector may enter the normal tissue surrounding the tumor, or other sites in the body. Another risk is that the vector might stay in your body and cause cancer or other diseases. Your immune system is expected to reject (kill) the vector in [time amount]. Thus, the vector should not be able to survive and grow in your body. The risk of causing a new cancer is probably very small. Although some vectors have caused cancers, no cancers have yet been found in any of the experiments in which genes have been transferred into monkeys and humans using this vector.

Sample 2 - Risk of Cancer Caused by Gene Transfer

Researchers have wondered whether a transferred gene might sometimes land in a place in a cell where it can cause harm. This happened to two children in another study. After getting the gene transfer, they developed leukemia (a type of blood cell cancer). A group of experts looked at all the test results. They found that gene transfer caused the leukemia by making some cells grow out of control. The children appear to be responding to treatment of the leukemia, but their long-term health is unknown at this time. There is a risk of unknown size of your child developing cancer, such as leukemia, should you volunteer your child to enter into this experimental study. This is a serious risk because cancers of the blood can lead to death.

**REPRODUCTIVE RISK CONSIDERATIONS [Section 4 of the Biomedical (Clinical) Informed Consent, Reproductive Risks]**

Some vectors used in gene transfer have the ability to integrate and alter the germ line. When data are inadequate to rule out the possibility of inadvertent germline alteration, non-sterile participants should be informed that the biological consequences of this procedure are not known and, therefore, unborn children, children who are breast- feeding, and mothers could be harmed (miscarriage or birth defects in future children, or changes that could be passed on to future generations). Use SLU template language for Reproductive Risks, found in the Sample Language section of the SLU template informed consent, but include that risks are unknown.

**LONG TERM FOLLOW-UP [Section 2 of the Biomedical (Clinical) Informed Consent]**

Because gene transfer is innovative and its long- term risks are not well understood, it is important to try to obtain long-term toxicity data on participants and to provide to participants any new significant clinical information that might affect their future care.

Gene transfer studies are subject to oversight by other Federal agencies, such as the Food and Drug Administration, which may have specific requirements for the duration of long-term follow-up. Investigators should know the current FDA policy regarding long-term follow-up, and the impact of these requirements on the participant should be discussed.

**REQUEST FOR AUTOPSY [Section 2 of the Biomedical (Clinical) Informed Consent]**

Participants should be informed that an autopsy will be requested in case of death. Investigators should explain that a participant's expression of autopsy wishes is not consent to autopsy and not required for study participation. Participants should express their wishes about an autopsy to their family, who will be asked permission for the autopsy in case of death, and encourage the family to take their wishes into account.

The autopsy request is one aspect of long-term follow up that is unique to gene transfer. Autopsies can yield important information that may enable a better understanding about the long-term effects of gene transfer intervention at the time of death.

**SAMPLE LANGUAGE**

Sample 1

If you die, no matter what the cause, investigators will ask your family if they can do an autopsy. An autopsy will help the investigators learn more about gene transfer. Please advise your family about your wishes regarding autopsy.

Sample 2

Because you are a study participant, study doctors will ask your family for permission to do an autopsy if you die, even if it is years after the study. This may help study doctors learn more about the effects of gene transfer. By signing this consent form, you are not forcing your family to agree to this. You should talk about this request with your family and advise them of your wishes.

**MEDIA INTEREST [Section 7 of the Biomedical (Clinical) Informed Consent]**

To alert subjects that others may have an interest in the innovative character of the protocol and in the status of the treated subjects, the subjects should be informed that the institution and investigators will make efforts to provide privacy protection from the media.