Guidelines
For
Gene Transfer Research in Humans

Ministry of Public Health
Department of Research

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Introduction

Human gene transfer has the potential to help improve monogenetic disorders such as sickle cell anemia, hemophilia, and cystic fibrosis. It also holds the promise to affect possible cure of polygenic diseases such as heart diseases, cancer, diabetes, Alzheimer and others. However, the uncertainty of its scope and application, and the consequent possibility for its potential side effects are of concern.

At present, gene transfer (also known as gene therapy) in humans is experimental and is being studied to determine whether it could treat diseases by introducing a therapeutic gene to the target cells compensating for the defective gene, or by triggering the immune system to fight the disease. Because the procedures and techniques being used are relatively new and their risks and benefits are not well established, human gene transfer research raises scientific, medical, ethical, and social considerations which require special attention.

The purpose of this document, when used in conjunction with Qatar Ministry of Public Health's policy "Guidelines, Rules and Policies for Research Involving Human Subjects" is to provide guidance for gene transfer research involving humans and to articulate standards for investigators and institutions to follow. This guideline document will be amended and updated as scientific advances and new knowledge of recombinant DNA research occurs.

The Qatar Health Research Ethics Committee has unanimously approved this document. A law to legally enforce this document is in process.

In developing these guidelines, the Ministry of Public Health consulted with guidelines developed by international organizations. A list of references is provided at the end of this document.

Definitions

Gene Therapy is defined as the insertion of genes into an individual's cells to treat a disease. It involves transplanting genes to a patient's cells to correct otherwise incurable diseases.

Germ line therapy, where germ cells (eggs or sperms) are modified by the introduction of functional genes, which are integrated into their genome. Therefore, the changes due to therapy would be heritable and would be passed on to later generations.

Somatic gene therapy, therapeutic genes are transferred into the somatic cells of a patient. Any modifications and effects that occur will be restricted to the patient only and will not be inherited by the patient's off-springs. In somatic gene therapy, the genetic modifications are carried out with a clear therapeutic intent, and the effects are confined to the treated subjects.

Gene marking studies, Gene marking studies provide crucial information on feasibility, safety, and efficacy of genetically modified cells as a prerequisite for gene therapy research trials. The marker (retroviral/adenoviral vectors) does not modify the cells, but allows them to be detected.

Monogenic disorder: disorders caused by mutations in a single gene. Examples of monogenic disorders include: Thalassemia, Sickle cell anemia, Hemophilia, Cystic fibrosis, and others.

Polygenic disorder: disorders caused by multiple gene defects. Examples include: diabetes, cardiovascular diseases, Alzheimer, cancer, and others.

Vector: A carrier molecule used to deliver the therapeutic gene to the patient's target cells. The most common vector is a virus that has been genetically altered to carry normal human DNA.

IBC: Institutional Biosafety Committee, a committee that provides local review, safety and oversight for nearly all forms of research utilizing recombinant DNA. The IBC focuses on the protection of research personnel, care givers, and the general public.

RAC: Recombinant DNA Advisory Committee, it is a subcommittee of the Qatar Health Research Ethics Committee. It focuses its reviews on the ethics and human safety of proposed gene therapy research.

Types of gene therapy:

Growing number of clinical studies have indicated that a major limitation of gene therapy research, other than safety, is to identify an ideal vector to introduce the therapeutic gene to the target cells and its optimal and durable expression in the recipients. Basic research and clinical investigations have been carried out, with varying degrees of success, using the following modalities:

(1) Viral gene therapy

(A) Retrovirus gene therapy
(B) Adenovirus gene therapy
(C) Adeno-associated virus gene therapy
(D) Herpes Simplex virus gene therapy

(2) Non-Viral gene therapy

(A) Physical approaches include needle injection of naked DNA, gene gun, electroporation, ultrasound, and hydrodynamic.
(B) Chemical approaches include cationic lipid-mediated gene delivery, cationic polymer-mediated gene therapy, and lipid/polymer hybrid gene therapy.

<u>The following guidelines are intended to provide guidance for clinical research using either viral and/or non-viral gene therapy in humans</u>

I. General guidelines for gene therapy research involving humans

All research investigations proposing to introduce into humans, DNA, RNA, or cells whose genetic material has been modified are considered experimental. Therefore, a research proposal must comply with the Ministry of Public of Health's "Guidelines, Regulations and Policies for Research Involving Human Subjects". Further, the Principle Investigator, Institutional Review Board Committee, the Bio-safety Committee, and Data Safety and Monitoring Board must observe the following:

• Clinical trials protocols involving human gene transfer require both governmental and institutional review and approval before any study participant can be enrolled.

• Institutional Review and Approval is performed by the Institutional Bio-safety Committee (IBC); Institutional Review Board (IRB), and all applicable regulatory authorization(s). These entities will be reviewing the gene transfer protocol as part of a formal approval process.

• Governmental review is performed by the Recombinant Review Committee (RAC) in the Department of Research at Ministry of Public Health. RAC review occurs before IBC approval. RAC review is required even if the gene transfer study is not supported by governmental fund.

• Studies in which genes are transferred into humans must be submitted to the Department of Research at Ministry of Public Health (DR-MOPH) for review. If the Department of Research finds the study to be "novel" it will be place the study the study on the next RAC meeting agenda. IBC approval must wait for the RAC's review. If, on the other hand, the DR-MOPH does not deem the study to be "novel" the IBC can act immediately.

• RAC review is a series of recommendations and advice from experts in the field. RAC review does not constitute a formal approval of the proposed gene transfer protocol.

• Institutional IRB may review the gene transfer protocol before or after RAC review, but will nonetheless be notified of the RAC recommendations

• The Department of Research at MOPH requires all institutions/laboratories proposing research involving recombinant DNA to register with their local Institutional Bio-safety Committee.

• Germ–line gene therapy research in humans is prohibited.

• Germ-line gene enhancement research in humans is prohibited.

II. Ethical Guidelines for Somatic Gene Therapy Research

(II-1) Application and Review Process

In addition to the responsibilities outlined in the MOPH's basic policy, the review boards and committees, the institution and the investigators should observe the following responsibilities:

(II-1-A) Responsibilities of the Review Boards and committees

No research participant shall be enrolled in the human gene transfer experiment until:

(1) The RAC review process has been satisfactory completed;
(2) Institutional Bio-safety (IBC) approval has been obtained,
(3) Institutional Review Board (IRB) approval has been obtained, and
(4) All applicable regulatory authorizations(s) have been obtained.

The review bodies are encouraged to address the following:

- Assess the purity, safety, and the undesirable adverse events associated with the vector delivery of the gene of interest, and that the vector carries no potential risk to the patient, the environment, and the health care workers.

- Compare the trial's protocol with currently available traditional therapies.

- The research protocol describes potential risks in detail and assesses their complications and that the investigators are prepared to handle unanticipated adverse events.

- Ensure that the proposals are supported by clear animal and pre-clinical data in order to demonstrate that the procedure is safe and is highly likely to provide knowledge of value. The principle investigators should provide evidence that such knowledge could not be obtained by non-gene transfer approaches.

(II-1-B) Responsibilities of the Principle Investigator:

The Principle Investigators (PIs) are responsible for full compliance with the MOPH guidelines during the conduct of gene therapy research. As part of his general responsibility, the PI should:

• Be adequately trained and capable to instruct and train laboratory staff in the practices and techniques required to ensure safety and the procedures for dealing with accidents.

• Propose physical and biological containment levels.

• Adhere to IBC -approved emergency plans for handling accidental spills and personnel contamination.

• Report any significant problems pertaining to the operation and implementation of containment practices and procedures to the IBC and other appropriate authorities.

Before conducting the gene transfer study, the PI must:

• Submit a research protocol to the IBC for review and approval.

• Seek the RAC review in addition to IBC and IRB approval, to conduct gene transfer experiment in humans

• Submit any subsequent changes (e.g., changes in the source of DNA or host-vector system) to the IBC for review and approval or disapproval.

• Remain in communication with the IBC throughout the duration of the study.

• Have no actual or perceived conflict of interest.

(II-2) Informed Consent

For all gene transfer experiments involving humans, no research participant shall be enrolled until an informed consent document has been legally signed that address the following information:

(II-2-A) General Requirements

• Detailed explanation in non-technical language of the purpose of the gene transfer study and the availability of alternative therapies and approaches.

• Clear assurance that participation in the study is voluntary and that failure to participate in the study or withdrawal of consent will not result in any penalty or loss of benefits to which the subjects are otherwise entitled.

• Clear itemization of all types of adverse experiences, their relative severity, and their frequencies.

• Any possible adverse medical consequences that may occur if the subjects withdraw from the study once the study has started.

• The availability of therapies and possibility of other investigational interventions and approaches.

• Information regarding the approximate number of patients who have previously received the genetic material under study.

• Warning to the subjects that, for genetic materials previously used in relatively few or no humans, unforeseen risks are possible, including ones that could be sever.

• For studies that are not expected to provide a therapeutic benefit to subjects, the Informed Consent document should clearly state that no direct clinical benefit to subjects is expected to occur as a result of participation in the study, although knowledge may be gained that may benefit others.

• For consistency in reporting, the following definitions are suggested: side effects that are listed as mild should be ones that do not require a therapeutic intervention; moderate side effects require an intervention; and severe side effects are potentially fatal or life threatening, disabling, or require prolonged hospitalization. Other verbal descriptions (e.g., “uncommon”, or “frequent” should be explained.

• Subjects should provide an explanation about the extent to which they will be responsible for any costs for medical treatment required as a result of research-related injury.

(II-2-B) Special Requirements

(1) Long –term follow-up

There are medical, scientific and ethical requirements to maintain a long-term follow-up of patients who participate in clinical trials of somatic gene therapy research. Medically, long-term follow-up allows new, unexpected adverse effects to be detected. Scientifically, long-term follow-up would provide information that may contribute to the improvement of the current gene therapy research. From an ethical standpoint, the benefit-risk balance of any clinical trial can be greatly enhanced by the investigator’s commitment to identify and manage any adverse events, even if they occur years after the treatment. Therefore, we recommend that all gene therapy protocols follow up subjects for up to 15-18 years.

(2) Request for Autopsy

To obtain information about the safety and efficacy of gene transfer, subjects should be informed that at the time of death, no matter what the cause, permission for an autopsy will be requested of their families and from the appropriate authorities. The principle investigator should ensure that material will be secured with written consent of the Pathologist charged with the autopsy.

(3) Reproductive Considerations

To avoid the possibility that any of the reagents employed in the gene transfer research cause harm to a fetus/child, subjects should be given information concerning possible risks and the need for contraception by males and females during the active phase of the study. The period of time for the use of contraception should be specified.

(4) Patient selection

It is recommended that gene therapy research should first be tested in patients with end-stage disease. However, there is no ethical reason to prohibit gene therapy research in subjects who do not have end-stage disease as long as the same process of risk-benefit consideration is applied and that the patient is fully aware of all consequences of the research. The review committees should ensure the absence of any biases as to gender, racial group, and other issues.

5) Disease selection

There is no ethical reason to discriminate between gene therapy research applications for Monogenic versus Polygenic disorders.

(6) Gene Therapy in pregnancy

The inclusion of pregnant women in gene therapy research carries theoretical risks of possible integration of the introduced gene into the growing fetus. Therefore, it is recommended that somatic gene therapy be deferred till the last semester of pregnancy or postpartum unless the perceived benefits of gene therapy to the mother clearly outweigh the risks to the fetus.

(7) Confidentiality of data

Specific safeguards must be employed to protect the confidentiality of data including:
• Coding or removal of identifiers.

• Case report forms should not identify subjects by name and must be stored in a secure area.

• Limitation of access to data.

• Use of locked file cabinets.

• Protection of computer-based data system

III. Special Requirements for Protocol Submission and Review of Gene Transfer Experiments

(III-1) Requirements for protocol submission

The following documentation must be submitted in printed or electronic form to the Department of Research, MOPH, PO # 42 (mail), 974-407-0800 (fax), e-mail: irb@moph.gov.qa.

• A cover letter on institutional letterhead, signed by the Principle investigator(s) and the research institution's highest authority (CEO, Dean of research, etc), that : (1) acknowledges that the documentation submitted to the DR-MOPH complies with the requirements (general, ethical, and special) set forth in this policy; (2) identifies the IBC and IRB at the proposed clinical trial site(s) responsible for the local review and approval of the protocol; and (3) acknowledges that no research participant will be enrolled until the RAC review process has been completed (see RAC review requirements); IBC approval (from the clinical trial sites) has been obtained; IRB approval has been obtained; and all applicable regulatory authorizations have been obtained.

• The scientific abstract.

• The non-technical abstract.

• The proposed clinical protocol, including tables, figures, and relevant manuscripts.
• Responses to the guidelines set forth in this policy.
• The proposed informed consent document.
• Curriculum vitae of the principle investigator(s)
• Description of the Proposal must include the following:
    A- Objectives and Rationale of the Proposed Research
    B- Research design, Anticipated Risks and Benefits
        • Structure and Characteristic of the Biological System
        • Preclinical Studies, Including Risk-Assessment Studies
        • Clinical Procedures, Including Research Participant Monitoring
        • Public Health Consideration
        • Qualification of Investigators and Adequacy of Laboratory and Clinical Facilities
C- Selection of Human Subjects

The DR-MOPH will confirm receipt within three working days after receiving the submission. If it appears that any portion of the necessary submission is missing, The DR-MOPH staff shall contact the Principle Investigator(s) immediately to request the missing materials.

Once the submission is complete, it is sent to members of the RAC for an initial review.

(III-2) RAC Review requirements

(III-2-A) Initial RAC Review

The initial RAC review process shall include a determination as to whether the human gene transfer experiment presents characteristics that warrant public RAC review and discussion. During the RAC's initial review, the RAC reviewers will examine the scientific rationale, scientific context (relative to other proposals reviewed by the RAC), whether the preliminary in vitro and in vivo safety data were obtained in appropriate models and are sufficient, and whether questions related to relevant social and ethical issues have been resolved. The DR-MOPH shall immediately notify the Principle Investigator(s) of RAC requests for additional information.

The outcome of the RAC review is a series of recommendations and advice from experts in the field. Investigators and sponsors should carefully consider these recommendations as part of optimizing the safe and ethical conduct of the trial.

These recommendations will be captured in summery letter sent by DR-MOPH. The Department of Research at MOPH shall notify, within 15 days after completion of the RAC meeting, the Principle Investigator(s) in writing with the results of the RAC's initial review.

Completion of the RAC review process is defined as: (A) receipt by the Principle Investigator(s) of a letter from DR-MOPH indicating that the submission does not present characteristics that warrant public RAC review and discussion; or (B) receipt by the Principle Investigator(s) of a letter from DR-MOPH that the protocol raises important scientific, safety, medical, ethical, or social issues that warrant in-depth discussion at the RAC's quarterly public meetings.

The summary letter will be sent to the IRB and IBC, as well as the funding body. For clinical trial site that is added after the RAC review process, see (section IV-3).

(III-2-B) Public RAC Review and Discussion

The process of public RAC review and discussion is intended to foster the safety and ethical conduct of human gene transfer experiments. It also informs the public about the technical aspects of the proposal, meaning and significance of the research, and any significant safety, social, and ethical implications in the research.

Review of gene transfer protocols by the RAC in an open forum shall continue in several areas of concern in which a particular protocol or new technology represents a significant departure from familiar practices. Such departures include, but not limited to: (I) novel vectors, particularly in cases in which modified human pathogens (such as herpes viruses or lentiviruses) are applied, (ii) new diseases, (iii) unique applications of gene transfer (such as gene transfer in utero), and (iv) other issues considered to require further public discussion.

Upon the initial RAC review and the determination that the gene transfer protocol has been selected for public RAC Review. The Principle Investigator will be asked to make a 15-20 minute presentation about the gene transfer proposal at the RAC meeting.

If a human gene transfer protocol is submitted less than eight weeks before a scheduled RAC meeting and is subsequently recommended for public RAC review and discussion, the review of the protocol by the RAC will be deferred until the next scheduled RAC meeting.

In order to maintain public access to information regarding human gene transfer protocols, MoPH/RAC will maintain all related Gene Transfer documentations. MOPH/RAC prefers that information provided contain no proprietary data or trade secrets, enabling all aspects of the discussion to be open to the public.

IV. Special Reporting requirements of Gene Transfer Protocols

All correspondences must be signed by the principal investigator and research institution official

(IV-1) Initiation of the Clinical Investigation

No later than 20 working days after enrollment of the first research participant in a human gene transfer experiment, the principle investigator(s) must submit the following documentations to the Department of Research at MOPH and Institutional Safety Committee:

i. Institutional Bio-safety Committee approval letter
ii. Institutional Review Board approval letter
iii. IRB approved Informed Consent document
iv. IRB approved Human Subject Protocol
v. Brief written protocol including the following elements:
    a. How the PI responded to each of the RAC's recommendations (if
    b. applicable)
    c. Any modifications to the protocol
vi. Curriculum vitae of the PI (in 2 pages biographical sketch format)
vii. (vii)Funding body grant number
viii. (viii)Investigational New Drug Registration Number
ix. (ix) Date of the initiation of the clinical trial

(IV-2) Investigational New Drug Application Reporting

Upon receipt of notification of permission to proceed with an Investigational New Drug application for a human gene transfer protocol, the Principle Investigator(s) shall submit a written report that includes the following information: (1) how the investigator(s) responded to RAC's recommendations on the protocol (if applicable), and (2) any modifications to the protocol as required by the Government Department under which the IND is registered.

(IV-3) Additional Clinical Trials Sites

No research participant shall be enrolled at a clinical trial site until the following documentations have been submitted to the Department of Research and approved by the MOPH and the funding body: (1) IBC approval (from the clinical trial site); (2) IRB approval; (3) IRB-approved informed consent document; (4) curriculum vitae of the principle investigator(s); and (5) funding body grant number(s) if applicable.

(IV-4) Annual Reports

Within 60 days after the one-year anniversary of the date on which the investigational gene product went into effect, and after each subsequent anniversary until the study is completed, the Principle Investigator (or delegate) shall submit to the funding body and the DR-MOPH the information set forth in (a), (b), and (c). When multiple sites are conducted under the single gene transfer protocol, the Principle Investigator (or delegate) may choose to submit a single annual report covering all studies, provided that each study is identified by its MOPH protocol number.

(a) Clinical Trial Information. A brief summary of the status of each trial in progress and each trial completed during the previous year. The summery is required to include the following information for each trial: (1) the title and purpose of the trial; (2) clinical site; (3) the Principle Investigator; (4) clinical protocol identifiers, including the MOPH protocol number, funding body grant number, and

the IND application number; (5) participant population (such as disease indication and general age group, e.g., adult or pediatric); (6) the total number of participants planned for inclusion in the trial; the number enrolled into the trial to date; and the number of subjects who dropped out of the trial with a brief description of the reasons; (7) the status of the trial, e.g., open to accrual of subjects, closed but data collection ongoing, or fully completed, and (8) if the trial has been completed, a brief description of study results.

(b) Progress Report and Data Analysis: Information obtained during the previous year's investigations, including: (1) a narrative or tabular summery showing the most frequent and most serious adverse experiences by body system; (2) a summary of all serious adverse events submitted during the past year. (3) a summary of serious adverse events that were expected or considered to have causes not associated with the use of the gene transfer product such as disease progression or concurrent medications; (4) if any deaths have occurred, the number of participants who died during participation in the investigation and causes of death; and (5) a brief description of any information obtained that is pertinent to an understanding of the gene transfer product's action, and information about bioavailability.

(c) A copy of the updated clinical protocol including a technical and non-technical abstract.

(IV-5) Safety Reporting

Principle Investigators must submit, in accordance with MOPH appendix "Guidance on reviewing and reporting unanticipated problems involving risks to subjects or others and adverse events", a written report on: (1) any serious adverse event that is unexpected and associated with the use of the gene transfer product (i.e., there is reasonable possibility that the event may have been caused by the use of the product; investigators should not await definitive proof of association before reporting such event); and (2) any finding from tests in laboratory animals that suggests a significant risk for the research participants including reports of mutagenicity, teratogenicity, or carcinogenicity. The report must be clearly labeled as a "safety Report" and must be submitted to the local institutional Bio-safety Committee, local institutional IRB committee, the funding body and the Department of Research/MOPH, within the timeframe set forth in safety reporting (IV-5-B). Principle investigators should adhere to any other serious event reporting requirements in accordance with MOPH regulations, state laws, and local institutional policies and procedures, as applicable.

Principle Investigators may delegate to another party, such as a corporate sponsor, the reporting functions set forth in this Guidance, with written notification to the MOPH/RAC of the delegation and of the name(s), address, telephone, and fax numbers of the contact(s). The Principle Investigator and the research institution are responsible for ensuring that the reporting requirements are fulfilled and will be held accountable for any reporting lapses. All submissions must be counter-signed by the research institution official.

The three alternative mechanisms for reporting serious adverse events to the Department of Research at MOPH are: by e-mail to irb@moph.gov.qa; by fax to 974-4407-0800; by mail to the office of DR, MOPH, P.O. 42, Doha /Qatar.

(IV-5-A) Content and Format

The reporting of a serious adverse event must include, but not limited to: (1) the date of the event; (2) designation of the report as an initial report or a follow-up report, identification of all safety reports previously filed for the clinical protocol concerning a similar adverse event, and an analysis of the significance of the adverse event in light of previous similar reports; (3) clinical site; (4) the principle investigator; (5) funding body's protocol number; (6) Investigational New Drug (if applicable) application number; (7) vector type ,e.g., adenovirus; (8) vector subtype, e.g., type 5, relevant deletions; (9) gene delivery method, e.g., *in vivo, ex vivo* transduction; (10) rout of administration, e.g., intra-tumor or intravenous; (11) dosing schedule; (12) a complete description of the event; (13) relevant clinical observations; (14) relevant clinical history; (15) relevant tests that were or are planned to be conducted; (16)date of any treatment of the event; and (17) the suspected cause of the event. These items may be reported by using the recommended Gene Transfer Adverse
Event Reporting Template available on DR-MOPH web site at: http://www.moph.gov.qa/

(IV-5-B) Time frame for Expedited Reports

Any adverse event associated with the use of the gene transfer product that is fatal, life-threatening, or unexpected must be reported to the SCH/RAC and the funding body as soon as possible, but not later than 7 calendar days after the sponsor's initial receipt of the information.

Serious Adverse events that are unexpected and associated with the use of the gene transfer product, but are not fatal or life-threatening, must be reported to the SCH/RAC and the funding body as soon as possible, but not later than 15 days after the sponsor's initial receipt of the information.

If, after further evaluation, an adverse event was initially considered not to be associated with the use of the gene transfer product is subsequently it was determined to be associated with the use of the gene transfer product, then the event must be reported to the Department of Research/MOPH and the funding body within 15 days of the determination.

Relevant additional clinical and laboratory data may become available following the initial serious adverse event report. Any follow-up information relevant to a serious adverse event must be reported within 15 calendar days of the sponsor's receipt of the information. If a serious adverse event occurs after the end of a clinical trial and is determined to be associated with the use of the gene transfer product, that event shall be reported to the Department of Research/MOPH within 15 calendar days of the determination.

Template for Reporting Adverse Events
In Human Gene Transfer Trials

Gene Transfer Adverse Event Reporting Template

PROTOCOL AND EVENT TYPE	
SCH (RAC) Protocol Number	
IND number (if applicable) Funding body grant number	
Date this report completed:	
Seriousness of the Adverse Event (AE) (choose one)	Death Life-threatening Initial or prolonged hospitalization Disability Congenital anomaly Required intervention to prevent permanent impairment/damage Other medically important condition Non-serious
Severity of Event	Minimal Moderate Severe Life- Threatening Fatal
Was this event expected in terms of its severity?	Yes No
Was this event expected in terms of its specificity?	Yes No
Relationship of Event to gene transfer product	Unrelated Unlikely Possible Probable Definite
Attribution of AE Attribution of AE, continued	Concomitant medication Product Intervention Underlying disease Route of administration Other suspected cause (describe)
Type of report	
DEMOGRAPHICS	
PI Name	
Name of Clinical Trial Site/Organization	
PI Telephone Number	
PI E-mail Address	
Reporter name	

Reporter Telephone number

Reporter E-mail address	
Research Participant's study identification number	
Research Participant's gender	
Research Participant's date of birth	
Research Participant's date of death	
Research Participant's weight in kgs	
Research Participant's height in cms	
Which Arm/Cohort/treatment group was the subject assigned to?	
Was subject dosed?	Yes No Information Not Available
What study agent was received:	IND agent Placebo Blinded Study Agent
Were there any Protocol Deviations/Violations/ Exceptions for this participant?	Yes:_____ _____ _____ No

DETAILED ADVERSE EVENT INFORMATION

Adverse Event Date
Description of Event
Relevant tests (e.g. x-rays) and results
Treatment (s) of Adverse Event (Include medications used to treat this event.)
Name of Concomitant Medications (Do not include medications used to treat this event.)
Pre-existing conditions/ relevant clinical history (if this is an oncology trial, please designate primary disease, e.g. ovarian cancer)
Date(s) of treatment(s) of the adverse event

Was autopsy performed?	Yes No
Date of autopsy	_____ or Not Applicable _____
Outcome of the event	Recovered/resolved Recovering/resolving Not recovered/not resolved Recovered/resolved with squeals Fatal Unknown
Documentation accompanying the report (e.g., Progress Notes, Discharge Summary, Lab or Autopsy Reports, Other, etc.)	
Description of any “other” documentation	
PRODUCT AND DOSING INFORMATION	
Name of gene transfer product	
Vector type (e.g. adenovirus)	
Vector sub-type (e.g. type 5, also include relevant deletions)	
Lot number	
Where the agent is manufactured?	
Route of administration	
Site of administration	
Did subject receive the dose specified in the protocol?	
If not, what dose was given?	
Date of first exposure to study agent?	
Date of most recent exposure to study agent?	
Total dose received prior to this event?	
Total dose quantity administered to subject to date	
Unit of measure for a single dose	

Dose quantity in a single administration
If courses used, how many were given prior to this event?
How many doses on the last course were given?

4- Gene Transfer Adverse Event Reporting Template Version

Was the administration of this product stopped because of this adverse event?
Name of other treatment (s) (medications, radiation, surgery) received by research participant as required by the protocol

References:

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http://oba.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm

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4. http://bioethics.georgetown.edu/publications/scopenotes/sn24.htm

5. Regional office for the Eastern Mediterranean of World Health Organization. Ethical issues related to gene manipulation and its effect on the health care delivery. Twenty-Sixth Meeting of Regional Consultative Committee (RCC), WHO/EMRO, Cairo, May 2002

6. World Health Organization. Genetics, Genomics and the patenting of DNA. WHO: Human Genetic Program. Chronic Diseases and Health Promotion. Switzerland: World Health Organization, 2005.

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8. Japan Society of Human Genetic guidelines.

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http://www.moh.gov.sg/mohcorp/uploadedFiles/Publications/Guidelines/NMEC_Guidelines/GeneGuidelines.pdf

10. UNESCO. Universal Declaration on the Human Genome and Human Rights, 1997.
http://unesdoc.unesco.org/images/0011/001102/110220e.pdf

11. Medical Research Center of Canada. Tri-Council Policy Statement: Ethical Conduct for Research involving Humans, 2003, (section 8: Human genetic Research).
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http://www7.health.gov.au/nhmrc/publications/humans/contents.thml

13. http://www.who.int/bulletin/volumes/86/8/08- 050724/en/index.html