



# Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies

**NHMRC**

National Health and Medical Research Council

**Guidelines for Ethical Review  
of Research Proposals  
for Human Somatic Cell Gene Therapy  
and Related Therapies**

Issued by the National Health and Medical Research Council in accordance with the  
*National Health and Medical Research Act, 1992 (Cth)*.

*PLEASE NOTE*

*These guidelines are effective from 1 January 2000.*

© Commonwealth of Australia 1999

ISBN 1 86496 097 3

Electronic ISBN 0 64242 236 2

This work is copyright. Apart from any use as permitted under the *Copyright Act 1968*, no part may be reproduced by any process without prior written permission from AusInfo. Requests and enquiries concerning reproduction and rights should be addressed to the Manager, Legislative Services, AusInfo, GPO Box 1920, Canberra ACT 2601.

The strategic intent of the NHMRC is to work with others for the health of all Australians, by promoting informed debate on ethics and policy, providing knowledge based advice, fostering a high quality and internationally recognised research base, and applying research rigour to health issues.

NHMRC documents are prepared by panels of experts drawn from appropriate Australian academic, (professional, community and government organisations. NHMRC is grateful to these people for the excellent work they do on its behalf. This work is usually performed on an honorary basis and in addition to their usual work commitments.

This document is sold through AusInfo Government Info Bookshops at a price which covers the cost of printing and distribution only. For publication purchases please contact AusInfo on their toll-free number 132 447, or through their internet address:

[http://www.ausinfo.gov.au/general/gen\\_hottobuy.htm](http://www.ausinfo.gov.au/general/gen_hottobuy.htm)

---

## CONTENTS

<b>Preamble</b>	<b>5</b>
<b>Introduction</b>	<b>7</b>
<b>Section 1 GUIDELINES FOR ETHICAL REVIEW OF RESEARCH PROPOSALS FOR HUMAN SOMATIC CELL GENE THERAPY AND RELATED THERAPIES</b>	<b>9</b>
1.2 Appendix to the Guidelines: bodies involved in the assessment of gene therapy proposals	11
<b>Section 2 HUMAN SOMATIC CELL GENE THERAPY – AN INFORMATION PAPER PROVIDING BACKGROUND TO THE GUIDELINES</b>	<b>13</b>
2.1 Preface	13
2.2 What are genes?	14
2.2.1 What do genes do?	15
2.2.2 The chemical composition of genes and the way they work	15
2.3 Genetic diseases	16
2.4 Gene therapy of genetic diseases	18
2.4.1 Techniques for inserting genes into cells	18
2.4.2 Weighing the risks and benefits of gene therapy	19
2.4.3 Benefits and limitations of gene therapy	19
2.4.4 Hazards of gene therapy	20
2.4.5 Selection of diseases for gene therapy	21
2.4.6 Experience to date	22
2.4.7 Is there a place for gene therapy of embryos?	22
2.5 Other experimental forms of treatment for genetic diseases	23
2.6 Cancer and gene therapy	24
2.7 Viruses and gene therapy	25
2.8 Genetic enhancement	26
2.9 Bibliography	27

---

## PREAMBLE

Somatic cell gene therapy is an innovative form of therapy and is under systematic investigation to determine its safety and efficacy. It is thus considered to be research. This document contains guidelines for ethical review of research proposals for human somatic cell gene therapy and related therapies, and an accompanying background information paper. The guidelines identify the following as matters for Human Research Ethics Committee (HREC) consideration: assessment of risks and benefits for those to be treated; the objectives and rationale of the research; the method to be used for gene modification; how the effects of treatment will be measured; the process for obtaining consent; the proponent's capacity to perform the research; the purity of the material to be administered; information gathered from previous similar research which is relevant to the proposed research; assessment of the likelihood that the administered DNA or RNA will enter germ cells or result in harm to others; and the approvals required before the research can proceed.

Section 1 comprises the *Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies*, and replaces Supplementary Note 7 of the NHMRC *Statement on Human Experimentation and Supplementary Notes* (1992). Section 2 provides background information about human gene therapy and replaces the NHMRC information paper *Human Gene Therapy and Related Procedures* (1994).

Guidelines on human genetic research, and research in general, are provided by the NHMRC's *National Statement on Ethical Conduct in Research Involving Humans* (1999), known as the *National Statement*. *Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies* should be read in conjunction with the *National Statement*.

---

## INTRODUCTION

Somatic cell gene therapy involves the introduction of DNA (deoxyribonucleic acid) or RNA (ribonucleic acid) into the somatic (non-reproductive) cells of humans, or the introduction into humans of cells whose genetic material has been modified, in order to provide an alternative form of treatment to improve the health of individuals.

As originally conceived, it involves the use of a gene carrier or 'vector' (often a defective virus) to carry a gene into cells with a view to integration of the gene into chromosomal DNA and its long term expression. However, additional novel and varied strategies for introducing or modifying gene expression in humans have been devised which make the boundary between gene therapy and other treatment strategies hazy. Consider immunisation with a virus expressing a particular protein, or immunisation with naked DNA, to treat or prevent a chronic viral infection such as HIV, or as part of cancer treatment. These methodologies overlap with the traditional concept of gene therapy in that DNA is introduced into somatic cells, but could also be thought of as modifications to standard immunisation strategies in which DNA, rather than protein, is used to generate the immune response.

Sometimes there may be uncertainty about whether a proposed research project should be considered to fall under the heading of 'gene therapy'. For this reason these guidelines address 'gene therapy and related therapies' though, for the sake of simplicity, the term 'gene therapy' is used in this document to cover both gene therapy, and related therapies. Where there is doubt as to whether a research proposal falls into the category of gene therapy, researchers should seek guidance from the NHMRC's Gene and Related Therapies Research Advisory Panel (GTRAP) on whether to treat the proposed research as a gene therapy proposal.

For the present, somatic cell gene therapy remains an experimental procedure, directed towards demonstrating the feasibility, efficacy and safety of this approach to treatment. Human somatic cell gene therapy experiments have been conducted to improve treatment for individuals with: genetic (inherited) diseases of a serious nature, cancers, viral infections such as HIV, and a number of other serious human diseases. Immunisation using DNA vaccines is another form of therapy that is being evaluated. It can be anticipated that if somatic cell gene therapy proves to be both effective and safe, it will be tried for diseases that are less serious and may ultimately have a role in preventing diseases.

DNA or RNA can also be introduced into somatic cells to mark their distribution and fate. Although no therapeutic benefit is expected, such studies are important for understanding the underlying basis for diseases or as first steps in the development of some somatic cell gene therapies for serious diseases.

There may be other justifiable therapeutic or non-therapeutic reasons for introducing DNA or RNA into human somatic cells.

While the introduction of DNA or RNA into somatic cells is ethically acceptable, the introduction of DNA or RNA into germ (reproductive) cells or embryos is ethically













































