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<h1>Applications to the Gene Therapy Advisory Committee (GTAC)</h1>	
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Version 1.0	11 Jul 2006	Annual review
Version 2.0	27 Jun 2006	Change of office name and annual review
Version 3.0	26 Jun 2008	Annual review and change to JRO
Version 4.0	08 Feb 2010	Content review and addition of controlled document statement
Version 5.0	14 Jul 2011	Annual Review
Version 6.0	30 Nov 2012	Annual Review
Version 7.0	18 Feb 2015	Scheduled Review
Version 8.0	25 Oct 2017	Schedule Review
Version 9.0	19 Oct 2020	Schedule Review Template removed and administrative changes to SOP. JRCO name change to RGIT.

Table of Contents

1. PURPOSE	3
2. INTRODUCTION	3
3. PROCEDURE FOR OBTAINING A GTAC APPROVAL	4
3.1. Procedure for applying for a GTAC approval for a clinical trial	4
4. REFERENCES	7
5. APPENDICES.....	7

1. PURPOSE

This SOP describes the procedure for applying to a Gene Therapy Advisory Committee (GTAC) for the approval of research which involves gene therapy in human subjects.

2. INTRODUCTION

A GTAC is an ethics committee under the oversight of the National Research Ethics Service responsible for ensuring that studies involving gene therapy are safe. GTAC is the UK national REC for gene therapy clinical research according to regulation 14(5) of The Medicines for Human Use (Clinical Trials) Regulations 2004. There are four UK ethics committees empowered to approve clinical trials of gene therapy products according to the definition given in Part IV of Directive 2003/63/EC (amending Directive 2001/83/EC). GTAC's remit is to consider and advise on study proposals that involve gene therapy research on human subjects on ethical grounds, taking account of the scientific merits of the proposals and the potential benefits and risks. The four committees are - London – West London and GTAC; South Central – Oxford A; North East – York; or Scotland (A) REC (based in Edinburgh).

Definition of a Gene Therapy Medicinal Product:

Gene therapy medicinal products are defined in Part IV of Directive 2003/63/EC (amending Directive 2001/83/EC) as follows:

"...[a] gene therapy medicinal product means a product obtained through a set of manufacturing processes aimed at the transfer, to be performed either in vivo or ex vivo, of a prophylactic, diagnostic or therapeutic gene (i.e. a piece of nucleic acid), to human/animal cells and its subsequent expression in vivo. The gene transfer involves an expression system contained in a delivery system known as a vector, which can be of viral, as well as non-viral origin. The vector can also be included in a human or animal cell."

In addition to its legal responsibility for trials of gene therapy medicinal products, a GTAC committee also reviews the following types of research:

- Trials of other Advanced Therapy Medicinal Products (ATMPs), i.e. somatic cell therapy and tissue engineered products
- Trials of stem cell therapy involving cells derived from stem cell lines
- Trials of vaccines involving recombinant vectors or vectors with potentially immunoregulatory mediator molecules
- First in human trials of vaccine vectors (or variants of vectors in use) or of engineered antigen molecules
- Other non-CTIMP gene therapy research (e.g. non-interventional trials).

Research studies involving well-established adult stem cell therapies (for example, bone marrow transplantation) or types of vaccine may be reviewed by any appropriate REC.

The 1992 report of the Committee on the Ethics of Gene Therapy (the Clothier Committee) recommended that gene therapy (genetic engineering in humans) should be limited to life threatening diseases or disorders. GTAC approval must be sought before somatic cell gene

therapy (i.e. on any cell other than the sperm or egg cells) or gene transfer research is conducted on human subjects. This includes both therapeutic and non-therapeutic research. GTAC's do not currently consider research proposals for germ line cell (egg or sperm) gene therapy.

Guidance on gene therapy ethical review requirements can be found at [Gene Therapy Advisory Committee](#) (cited on 30 May 2020)

It is the responsibility of the Chief Investigator (CI) to ensure that GTAC approval is obtained prior to initiating the trial.

All other regulation and guidance governing the use of gene therapy must also be adhered to. For example, the Human Tissue Act or EU Clinical Trials Directive.

3. PROCEDURE FOR OBTAINING A GTAC APPROVAL

The procedure for obtaining a GTAC approval differs depending on the type of gene therapy trial proposed:

1. Clinical trial of gene therapy
2. Named patient use of gene therapy products

3.1. Procedure for applying for a GTAC approval for a clinical trial

Applications are made via the Integrated Research Application System (IRAS) found at: [RGIT Integrated Research Application System \(IRAS\)](#) (cited on 30 May 2020) which combines the ethics application with other regulatory forms such as MHRA applications. The IRAS application form now replaces the GTAC form. All UK studies must apply through this system. Applications can be made via the online booking service [RGIT Website HRA NHS Online Booking Service](#) (cited on 30 May 2020)

From 1st May 2008, amendments to the Clinical Trials Regulations have come into force. Included in these are new arrangements for the way a GTAC operates. GTAC is able to transfer gene therapy proposals to other Research Ethics Committees, if the proposal is deemed to be 'low genetic risk.' This frees up a GTAC to fulfil a change in its remit as a result of recommendation 8 of the UK Stem Cell Initiative ('The Pattison Report') to oversee the ethical conduct of stem cell clinical research. (A decision tree is included in Appendix 1).

The Health Research Authority (HRA) Board, in its capacity as the Appointing Authority for the Gene Therapy Advisory Committee (GTAC), agreed new arrangements for ethics applications to GTAC at its Board meeting on 25 October 2012. As well as providing an opportunity for ethical review across a wider geographical area, they will now be able to offer at least 30 meeting dates per year. The new processes mean that the review of applications will follow [RGIT Website NRES Standard Operating Procedures](#) (cited on 30 May 2020), with clear roles for the MHRA and RECs, and that any concerns will be addressed through the Memorandum of Understanding between the HRA and MHRA.

3.1.1 R&D Capacity and Capability Approval

In addition to a GTAC approval, Capacity and Capability approval must be sought from the local NHS Trust Research and Development office for each site where the research will take place. Applications should be made using the HRA local document pack to all sites involved in the study. See SOP RGIT_SOP_031 for approvals at ICHNT.

Imperial College AHSC has a Joint Clinical Research Safety Committee which must approve gene therapy, genetic modification and wild type non-medicinal biological agent research projects occurring at this site before submission to GTAC.

Contact Details:

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3.1.2 MHRA approval

In addition to a GTAC approval and Capacity and Capability approval, the Chief Investigator is required to submit a Clinical Trials Authorisation to the MHRA as gene therapies are classed as investigational medicinal products in law. For advice on how to undertake this, please consult SOP ref JRO/SOP/008.

3.1.3 When to apply

Applications can only be submitted once sponsorship approval for the research study is in place. Applications to conduct clinical trials involving gene therapy must be submitted via the Integrated Research Applications System (IRAS) as part of the standard national ethics application process. The site can be accessed at *RGIT Website* [IRAS - Integrated Research Application System](#) (cited on 30 May 2020).

Advice before submission can be provided by Professor Andrew George at London- West London REC and GTAC. Initial contact should be made via nrescommittee.london-westlondon@nhs.net and the email marked for the attention of Andrew George.

3.1.4 Notification of the Committee's Decision

The applicant will be notified of the Committee's decision. Reasons in writing will be given for the decision and will stipulate any conditions of approval as appropriate. GTACs are required to give an opinion within 90 days of receiving a valid application (under the UK clinical trials regulations).

3.1.5 Reports

Successful applicants will be asked to provide a Progress Report and Safety Report annually to the approving GTAC. These reports should be submitted on the standard NRES report forms and are accessible online via *RGIT Website* [HRA NHS - Progress Reports](#) (cited on 30 May 2020).

3.1.6 Amendments

To make an amendment to an already approved gene therapy clinical trial the online amendment tool must be completed. This can be generated in IRAS. Further details can be found in SOP reference RGIT_SOP_006.

4. REFERENCES

[UK Policy Framework for Health and Social Care Research](#) *(cited on 30 May 2020)*

[UK Medicines for Human Use \(Clinical Trials\) Regulations 2004](#) *(cited on 30 May 2020)*

[EU Directive 2003/63/EC – Amendment to 2001/83/EC Code relating to medicinal products for human use](#) *(cited on 30 May 2020)*

[Mental Capacity Act 2005](#) *(cited on 30 May 2020)*

[Human Research Authority Website](#) *(cited on 30 May 2020)*

[MRC Data and Tissues Tool Kit](#) *(cited on 30 May 2020)*

RGIT_SOP_006 Amendments to healthcare research

RGIT_SOP_008 How to submit a CTA to the MHRA

RGIT_SOP_031 Imperial College Healthcare Trust Approval

5. APPENDICES

The following Appendices list the following Templates associated to this SOP which can be found on the [SOP, Associated Documents & Templates page](#).

Appendix 1: Decision tree - RGIT_TEMP_011