gene ethics
working for a GM-free future
ABN 67 104 140 918
A: 60 Leicester St, Carlton Vic 3053
T: 03 9347 4500 / 1300 133 868
F: 03 9341 8199
E: info@geneethics.org
W: www.geneethics.org

Gene Ethics comments on OGTR Proposed Regulatory Amendments

Introduction

Gene Ethics is a citizen advocacy group which has several concerns about the proposed amendments to the OGTR regulations.

Gene Ethics wants the OGTR to provide referenced scientific evidence in support of the proposed regulatory amendments. Gene Ethics considers that the proposed regulatory amendments are substantial and raise serious safety concerns, and therefore requests the OGTR to provide further opportunities for public consultation and discussion before the proposed amendments proceed.

The OGTR's proposed amendments and discussion are insufficiently supported by evidence. We seek scientific evidence to support all the proposed amendments and to substantiate the OGTR's proposals.

In particular, Gene Ethics submission seeks substantiation and further scientific evidence regarding:

1. Exempt dealings

What evidence can OGTR provide that:

- genetic manipulations produced using viral vectors can be safely classified as 'non vector systems'?
- none of the exempt host/vector systems will be able to affect humans?
- the 'vector is no longer present in, or able to be remobilised from, the host'?
- the viral vectors are completely cleared from the animal subsequently after innoculation and/or that 'the replication defective viral vector is no longer in the animal'?
- 'in time any remaining unincorporated vector will be cleared from the animal through the action of its immune system'?
- animals which have had somatic cells modified by viral vectors do not become subsequently infected with any virus which is able to remobilise the vector?
- existing viral particles in animals will not subsequently remobilise the vector or recombine with the vector?
- no germ-cell lines have been modified in animals?
- the nucleic acid is 'stably incorporated into the somatic cells'?

- 'the somatic cells cannot give rise to infectious agents as a result of the genetic modification'?
- 'the animal is not infected with a virus that can recombine with the genetically modified nucleic acid in the somatic cells of the animal'?
- *'once the viral vector is no longer present, the dealing no longer poses such risks'?*

Oncogenic modifications

What evidence can OGTR provide:

- that oncogenic modifications, which OGTR acknowledges pose some risk of causing cancer in human, should be included in exempt dealings and for 'removing relevant prohibiting clauses in Schedule 2 Part 1 and Schedule 3 Part 1'?
- for the necessity and advisability of departing from the historical precedent of precautionary regulation in dealings with oncogenic modifications?
- to support the statement that the 'potential for in vivo expression of an oncogene in a laboratory worker following exposure to a gene construct or GMO would be extremely low'?
- on more precise figures on the likelihood of the potential for in vivo expression of an oncogene in a laboratory worker
- on how OGTR have arrived at the conclusion that the risk is 'extremely low'?
- that laboratory workers working with dealings classified as exempt will all be sufficiently trained and/or informed about the dangers of working with potentially oncogenic materials?
- that if such dealings are classified as exempt, OGTR will be able to regulate for a laboratory worker using sharps suffering a needlestick injury when handling oncogenic manipulations and viral vectors?
- that laboratory workers will not develop cancer working with oncogenic modifications under the exempt classification?
- that 'with the proposed removal of avipox vectors (see proposal 1.3 above) none of the host/vector systems permitted for use in exempt dealings will be able to transduce human cells'?
- that any oncogenic modifications will not be able to recombine with viral vectors and/or give rise to any oncogenic viruses?
- that any animals infected with oncogenic modifications will not subsequently become infected with viruses capable of recombining with/remobilising any oncogenic modifications?
- these viral vectors are unable to regain replication competence or to remobilise?
- the viral vectors have been removed from animals?
- 'replication competence has been disabled'?
- that for oncogenic cell lines produced using GM the transforming gene is 'stably integrated' and cannot be subsequently remobilised in any way?
- that the 'risk to the operator is negligible once the transforming gene is stably integrated' when using cell lines with oncogenic transformations produced using genetic modification?
- why these GM cell lines are not currently being properly labelled?
- why the OGTR finds it necessary to significantly expand the definition of tissue culture classified as exempt in the regulations?
- whether the definition of 'any of the following that cannot spontaneously generate a whole animal' would include allowing classification as exempt GM plants whose flowering and/or fertility mechanisms have been disabled using any genetic use restriction technologies?
- what evidence OGTR can provide that laboratory facilities are adequate and laboratory workers will be sufficiently trained to be able to safely handle the increased volume(s) in GM cultures for exempt and NLRD dealings?

2. Notifiable Low Risk Dealings

Gene Ethics seeks clarification:

- does the OGTR consider that 'biologically contained' for NLRDs includes the use of genetic use restriction technologies (GURTS)?
- on the necessity and advisability of expanding the list of GM animals able to be classified as NLRDs to include GM rabbits and guinea pigs.

Gene Ethics notes the Feral Animal CRC experiments with mouse pox which unintentionally resulted in a virulent strain of mouse pox which killed all the experimental animals. The scientists published their results which subsequently led to global concerns about the potential for bioweapons production using GM techniques.

What evidence can OGTR give:

- that the genetic modification will 'not lead to the production of infectious agents'?
- that there are no rabbit or guinea pig diseases which may, interacting with genetic modifications, pose new threats to humans or animals?
- if animal-human hybrids would be classified as NLRDs under the proposed amendments? As any animal-human hybrids would pose significant ethical questions, Gene Ethics strongly recommends that these be disallowed under the regulations as NLRDs.
- that any GM rabbits which may escape containment will not allow the escape of GM material(s) to Australia's invasive rabbit population, other species including native species, or allow GM rabbits to interbreed with wild rabbit populations?
- that rabbits carrying potentially oncogenic viral elements do not subsequently escape and transfer any oncogenic viruses or any other GM material or diseases to wild rabbits or other species including native species?

GM plants containment

The proposed amendments include a proposal that the regulated community be subject to a specific requirement not to compromise containment. Gene Ethics considers this good, but it must not substitute for full regulatory oversight, monitoring and enforcement by OGTR.

Gene Ethics does not support the deletion of specific wording in the regulations which specifies containment requirements for GM plants.

Gene Ethics also notes that GM eucalyptus trees have been granted environmental release in the USA. GM trees pose unique threats to native forests and biodiversity and are poorly understood, the lifecycle of a tree being much longer than that of agricultural crops. GM trees are among the areas of GM identified by parties to the UN CBD as requiring further expert advice.

Gene Ethics considers that the regulations ought to retain specific requirements for the containment of plant propagating material, and that these should not be deleted from the regulations. Gene Ethics considers that the phrase 'appropriate facilities' is too vague and gives too much scope for varied interpretations among those conducting GM experiments.

Gene Ethics recommends that specific regulatory requirements for the containment of GM plants remain in the regulations and that these be fully enforced by OGTR, in addition to the proposed explicit requirement for the regulated community not to compromise containment.

What guarantees can OGTR give:

- that GM plants will not escape containment?
- that all laboratory workers will be properly trained and facilities properly equipped and maintained to prevent escape of GM plants into the environment?

Somatic cell gene therapy – introduction of a GMO into a human

Gene Ethics is extremely concerned that somatic cell gene therapy in human beings is proposed to be de-licensable. Somatic cell gene therapy overseas resulted in many illnesses and some deaths, including American Jesse Gelsinger. We consider that the proposed changes provide insufficient safeguards.

What evidence can OGTR provide that:

- the somatic cells which are to be introduced into a patient 'are incapable of secreting any infectious agents'?
- for the necessity of removing the licensing requirement for 'dealings involving introduction into a patient of genetically modified human somatic cells'?
- a patient who has undergone somatic cell gene therapy and is not considered under the regulations to be a GMO and is therefore not subject to any regulation will pose negligble risk to human health and safety in the wider population?
- somatic cell gene therapy poses 'negligible risk to human health and safety?
- 'somatic cell gene therapy poses negligible risk to human health and safety' under specific conditions 'when human somatic cells are isolated from a patient (or a compatible donor), genetically modified and reintroduced into the patient'?
- such somatic cell gene therapy poses negligible risk regardless of the the nature of the genetic modification?
- the introduced human GM somatic cells 'are incapable of secreting any infectious agents into a human being'?
- the somatic cell gene therapy will not result in any germ-line cells being genetically modified?
- the introduction of the GM somatic cells will not result in any insertion mutagenisis?

Somatic cell gene therapy projects are dangerous and definitely should not be classified as NLRDs.

Gene Ethics draws the OGTR's attention to the following quote from UK Institute of Science in Society's website:

> "Last year in the US, gene therapy clinical trials ground to a halt amid scandalous reports of deaths and conflicts of interest [2]. The US National Institutes of Health (NIH) set up a special telephone hot line for victims that counted 652 cases of serious adverse events along with six unexplained deaths. Effects included high fevers, infections and severe changes in blood pressure, all of which went previously unreported to the NIH Recombinant DNA Advisory Committee (RAC). David Baltimore, Nobel laureate and president of Caltech, a gene therapy based biotech company, said " I disagree we've had any benefit from gene therapy trials so far, many of us are now asking, what the hell are we doing putting these things into people?" 'Gene Therapy Oversold by Scientists Who Disregard Risks' http://www.i-sis.org.uk/isisnews/i-sisnews9-27.php

How does the OGTR respond to:

- the large number of serious adverse effects and deaths resulting from somatic cell gene therapy as identified by US NIH in the above quote?

- the fact that these adverse effects included 'high fevers' and 'infections'

- what guarantees or assurances can OGTR provide that the proposed NLRD somatic cell gene manipulations will not result in any fevers or infections which may pose a risk to the general public or to the environment once the patient is released (provided the patient survives or from the dead body if the patient dies)?

- what evidence can OGTR provide of the demonstrated benefits of somatic cell gene therapy?

- Gene Ethics contacted Dr Mae Wan Ho last week at Institute of Science in Society UK to ask if our regulator was correct in saying somatic cell gene therapy posed negligible risk. Mae Wan's answer: "Definitely not. These procedures are risky, insertion mutagenesis, cancer being the top risks. Germline modification is also a potential."

- What scientific evidence can OGTR provide that somatic cell gene therapy does not pose any of the risks identified by Dr Mae Wan Ho, including insertion mutagenisis, cancer and germline modification?

3. Viral Vectors

What evidence can OGTR provide that:

- the retroviral and non-retroviral vectors are 'replication defective' and cannot regain replication competence in any way?
- for dealings involving 'higher risk genes' and retroviral or non retroviral vectors, it is necessary, advisable and justified to reclassify them as PC2 NLRDs, as exempt from licensing requirements
- to support the assertion that "Dealings with viral vectors unable to transduce human cells pose negligible risk to laboratory workers because the vector cannot efficiently enter human cells and therefore is unlikely to express genes or integrate into the worker's genome even in the event of unintended exposure.'
- on an estimation or any figures on the likelihood of the vectors expressing genes or integrating into the worker's genome in the event of unintented exposure, including that from a needlestick injury?
- to support the assertion that the 'vector cannot efficiently enter human cells'?
- on published scientific evidence other than 'ongoing regulatory experience' that dealings with higher risk genes and replication defective viral vectors pose negligible risk to human health and safety and the environment?
- on published scientific evidence concerning the 'uptake of newer viral vectors with improved safety features' and 'an increase in scientific knowledge regarding these vectors'?
- to support their conclusions that dealings involving replication defective viral vectors any 'higher risk genes' including immunomodulatory molecules and oncogenic modifications will pose 'negligible risk to human health and safety and the environment' or to laboratory workers?
- on evidence and published scientific research about the 'safety features' of these vectors.
- on any figures or estimation of the actual reduction in likelihood of replication competence being regained? Gene Ethics notes particularly that the proposed amendments concern dealings with 'higher risk genes' and so would like some more precise estimation of the likelihood of replication competence being regained in dealings with viral vectors and higher risk genes.

4. Oversight of NLRDs

What assurances can OGTR give that facilities will be properly equipped and staff will be properly trained and monitored not to compromise containment?

The discussion paper argues that the explicit requirement not to compromise containment of GMOs will provide for more stringent regulation. We support this explicit requirement. However as mentioned above, we do not support the deletion of specific criteria for the containment of propagating GM plants.

Conclusion

Gene Ethics seeks OGTR's comprehensive scientific evidence and answers to all the above questions, to support the proposed amendments to the regulations. We are ready to meet OGTR personnel to discuss our concerns.

Prepared by Gene Ethics, June 2010:
T:1300 133 868 E: info@geneethics.org W: www.geneethics.org