

3 Gaps in HSNO Act Coverage

3.1 Summary

This section addresses two gaps in coverage of the HSNO Act highlighted by the Royal Commission.

Genetic modification of human cell lines

A cell line is an established population of cells derived from tissues that will grow and divide indefinitely in the laboratory given the appropriate growth medium and space. Although the genetic modification of animal cell lines currently requires approval under the HSNO Act, the same modification of human cell lines does not. This is because humans, their tissues and their cells are specifically exempt from coverage under the HSNO Act through being excluded from the definition of an organism. Similarly, the Medicines Act covers clinical trials of new medicines involving human participants, but does not currently include laboratory research using human cell lines.

Two options have been identified to ensure that genetic modification of human cell lines for research purposes is subject to appropriate regulation. The first option would involve amending the HSNO Act to include applications for the development (genetic modification) of a human cell line or the importation of genetically modified cell lines. The other option is to address this matter in the Ministry of Health's current review of human cell and tissue research, possibly with guidelines to cover the genetic modification of human cell lines in the interim.

New organisms regenerated from tissues

Neither the importation of tissue samples nor any development activity (other than genetic modification) requires a HSNO approval. Improvements in cloning and related technologies since the commencement of the HSNO Act mean that it is now possible to produce an animal not currently in New Zealand (a new organism) from imported tissue using a surrogate mother, without a HSNO approval, thereby bypassing the usual requirements to fully evaluate the effects of introducing that new species of organism into New Zealand.

In addressing this gap it is proposed that the focus of the HSNO oversight remain the same; that is, on the nature of the new animals produced and their potential effects on the environment, not on the technologies themselves nor on any other direct use of the tissues.

Two options have been identified for amending the HSNO Act to include new animals produced using cloning and related techniques: either amend the definition of 'develop' to cover the regeneration of new organisms, or broaden the definition of 'new organism' or 'organism' and include a power to make regulations to provide that things are not 'organisms' or 'new organisms' for the purposes of the Act. It is proposed that the amendments extend to the artificial regeneration of organisms from all tissues, including plant and fungal tissues that are not capable of replicating themselves.

The proposed amendments would **not** extend to human cloning as the term organism in the HSNO Act specifically excludes human beings.

3.2 Genetic modification of human cell lines

The Royal Commission on Genetic Modification recommended that the HSNO Act be amended to clarify that research involving genetic modification of human cell lines or tissue cultures is covered by the Act. The Government agreed to accept the *intent* of the recommendation, which is to ensure that the genetic modification of human cell lines and tissue cultures is subject to appropriate regulation.

3.2.1 Nature of the issue

A cell line is an established population of cells, derived from human, animal or plant tissues, that will grow and divide indefinitely given the appropriate growth medium and space. The culturing of such cells *in vitro* (in a test-tube or other laboratory environment) is therefore often referred to as 'tissue culture'. Cell lines allow in-depth research into the properties of such cells, as well as research into numerous human and animal diseases and their treatment. They may also be used in the production *in vitro* of certain biological products.

The genetic modification of animal cell lines, including the insertion of human DNA into an animal cell, currently requires approval under the HSNO Act. The same modification of human cell lines does not require comparable approval. This is because humans, their tissues and their cells are specifically exempt from coverage under the HSNO Act through being excluded from the definition of an organism. The Medicines Act covers clinical trials of new medicines involving human participants, but does not currently include laboratory research using human cell lines.

The objective is therefore to provide appropriate regulatory oversight for research involving genetic modification of human cell lines. There are two main options.

- **Option 1:** Amend the HSNO Act to cover the genetic modification of human cell lines.
- **Option 2:** Address this matter in the Ministry of Health review.

3.2.2 Discussion of the options

Under *Option 1* the HSNO approvals that might be obtained would be for developing a GMO in containment or importing a GMO into containment. The approvals would be limited to the cellular level; that is, to the development (genetic modification) of a human cell line or the importation of a genetically modified cell line.

It is expected that appropriate experiments would be approved as low-risk genetic modifications by IBSCs. However, the types of genetic modification procedures that are categorised as low risk may also have to be considered and the regulations modified.

It is proposed that the scope of the amendments would cover:

- genetic modification of cell lines *in vitro* in containment in the laboratory (as well as importation of genetically modified human cell lines)
- genetic modification only and *not* activities such as nuclear transfer and cloning, stem-cell research, gene therapy, assisted reproductive technologies, and xenotransplantation (other than those parts of such activities that involve genetic modification)
- cell lines derived from somatic cells and possibly germ cells; but *not* gametes (sperm or ova), embryos or any subsequent reproductive stage capable of leading to a human individual.

At present ethical approval is not required for research involving human cell lines in containment. Ethical approval would, however, be required prior to collecting the initial human tissue sample from which the cell line is derived. This consent would specify the research for which the donor is prepared to have their tissue sample used. Any research not covered by the initial consent of the donor would need to be approved by an ethics committee.

Under Option 1 it is proposed that the HSNO Act be amended to cover the genetic modification of human cell lines, and that the HSNO (Low-Risk Genetic Modification) Regulations be amended to include human cell lines as host organism for low-risk genetic modification.

Option 2 arises as a possibility because the Ministry of Health has begun a review of all aspects of human cell and tissue research, including the collection, storage, use and disposal of bodies, organs, tissues and tissue samples, with a view to updating relevant legislation. Rather than address the genetic modification of human cell lines by way of an amendment to the HSNO Act, this matter could be addressed in the Ministry of Health review.

The advantage of this option is that the decision on exactly what is covered by the HSNO Act could be decided as part of a comprehensive review, thus ensuring that there are no future gaps or unnecessary overlaps in regulatory oversight. However, it would mean that the genetic modification of human cell lines remained unregulated until the Ministry of Health review.

- 3a Is it necessary to include genetic modification of human cell lines in the HSNO Act at this stage? If so, what do you think would be the best way of doing this? Please fully explain your comments and illustrate them with examples, where necessary.**
- 3b Should consideration of the control of genetic modification of human cell lines be done as part of the Ministry of Health's wider consideration of all aspects of human cell and tissue research? Would guidelines be sufficient in the interim?**
- 3c What is the likely impact to existing practice of the changes outlined in the options given above?**

3.3 New organisms regenerated from tissues

The Royal Commission recommended that the HSNO Act be amended to cover procedures used in mammalian cloning, such as nuclear transfer or cell fusion. The Government agreed to accept the intent of the recommendation, to the extent that it ensures that new species of mammals (or other animals) cannot be imported as tissues and subsequently regenerated by cloning and released without an appropriate HSNO Act approval.

This section discusses options for amending the HSNO Act to cover the regeneration of animals that are not currently in New Zealand from tissues using cloning and related techniques. The purpose of the proposed changes is to ensure that new technology cannot be used to bypass the usual requirements to fully evaluate the effects of introducing a new species of animal into New Zealand. The cloning of animals that are already in New Zealand – such as cows and sheep – is not affected.

3.3.1 How did this issue arise?

This issue arose because neither the importation of tissue samples nor any development activity (other than genetic modification) requires a HSNO approval.

The importation into containment of tissues is regulated by the Biosecurity Act.² However, while a HSNO approval is required to import a new organism, the definition in the Act of an ‘organism’ does not include biological material such as tissue, which is itself incapable of unassisted self-replication, but which originates from a new organism. Therefore, because a tissue is not an organism, no HSNO approval is required.

Similarly, while a HSNO approval is required to develop a new organism, the Act restricts the meaning of ‘develop’ to the genetic modification of an organism. The current definition therefore excludes development in the sense of regenerating or creating an organism where no genetic modification is involved.

Cloning and related technologies have progressed significantly since the HSNO Act and associated regulations came into force. The advances in these technologies mean that it is now possible to produce an animal not currently in New Zealand (a new organism) from imported tissue using a surrogate mother, without a HSNO approval.

Although this regulatory gap has not caused problems so far, the use of cloning and other technologies is likely to increase in the future. In order to ensure unapproved new organisms are not developed and/or released in New Zealand there needs to be regulatory oversight in this area.

² Animal tissues are classed as risk goods and their importation is controlled by permit. Animal tissues are directed to a laboratory approved as a transitional facility for biological products operating under the standard for biological products (MAF Reg Std:154.02.17).

It is proposed that the focus of the HSNO Act remains the same: to look at the nature of the new animal produced rather than the technology that was used to produce it. This would focus HSNO oversight on those animals that were new organisms and their potential effects on the environment.

Possible approaches for amendment

Two options identified for amending the HSNO Act to include non-GM animals produced using cloning techniques are as follows.

- **Option 1:** Amend the definition of ‘develop’ to cover regeneration of new organisms. (This would, however, require a new framework for dealing with the development of new [non-GMO] organisms.)
- **Option 2:** Broaden the definition of ‘new organism’ or ‘organism’ and include a power to make regulations to provide that things are not ‘organisms’ or ‘new organisms’ for the purposes of the Act.

3d How should the HSNO Act be changed to best cover new organisms produced using cloning technologies?

3e What other ways might there be to regulate these organisms?

Please fully explain your answers by setting out possible illustrative examples and by relating your suggestions to the HSNO Act’s present requirements.

3.3.2 At what stage in the process should the HSNO assessment be carried out?

When a tissue from an organism not present in New Zealand is imported, there may be no intention to regenerate an organism from that tissue. Regulation at this stage is imposed by the Ministry of Agriculture and Forestry (MAF) under the Biosecurity Act.

Any tissue sample is subject to the requirements of an import health standard issued under the Biosecurity Act. The importer is required to obtain an import permit before importing the tissue. Tissue for *in vitro* use is directed to a transitional facility and held there. Permission must be obtained from the Director of Animal Biosecurity if the researcher wishes to do any *in vivo* work. Regeneration techniques are included, which means that the Director of Animal Biosecurity would be aware of any regeneration work, even if it was not stated as a purpose in the original application.

If a new category of approval was introduced for developing non-genetically modified new organisms in containment, and an approval was required before the regeneration work started, this would be a good stage to carry out an assessment under the HSNO Act, since for regeneration techniques this would be the stage at which a new whole organism is developed. If the new organism was later released from containment, it would undergo an assessment in the same way as any other new organism under the HSNO Act. Obviously if the tissue was imported expressly for the purposes of regeneration, an approval would be required before importation was permitted.

An alternative would be simply to assess the organism at the point of release from containment. However, this could mean that the level of containment may not be correct for the organism once regenerated, and that a new organism would be present in a containment facility without a HSNO approval and any HSNO controls prior to release.

3f At what stage do you think a regenerated new organism should be assessed under the HSNO Act?

Please explain your answer by setting out possible illustrative examples and by relating your suggestions to the HSNO Act's present requirements.

3.3.3 Regeneration of other new organisms

The Royal Commission recommendation refers to procedures used in 'mammalian cloning'. In its initial response the Government agreed that regulatory oversight should be provided for all animals that are new organisms, rather than just mammals. However, the same issues apply to all organisms, including plants and fungi.

Plants and fungi are commonly regenerated from tissues. In many cases this can happen naturally, in which case the tissue would fall under the definition of 'organism' ("a genetic structure capable of replicating itself") and would already require a HSNO approval. In other cases, special laboratory techniques would be required to produce the organism (for example, tissue culture). The possible approaches for amendment to the HSNO Act would similarly apply to all potential new organisms, and would therefore clarify regulatory coverage of all new organisms regenerated from imported tissue.