New Zealanders for HEALTH RESEARCH
Ngā Tāngata o Aotearoa mō te Rangahau Hauora

"New Zealand's peak body representing the entire health and medical research pipeline"

Submission on Hazardous Substances and New Organisms (HSNO) (Hazardous Substances Assessments) Amendment Bill[1]

Introduction

New Zealanders for Health Research (NZHR) was established in November 2015 to bring about increased investment in health research from government, industry and philanthropy. We believe that health research is the catalyst for bringing about the best possible health for all New Zealanders, and we're on a mission to increase investment in health research as an essential and embedded component of all parts of New Zealand's health system, responsive to New Zealanders' unique health imperatives. We are therefore committed to ensuring that health research is carried out as efficiently as possible, that results of health research are translated into policy, practice and individual decision making, and for there to be a level of investment in health research to enable this to happen as optimally as possible.

Recommendations

The HSNO Amendment Bill be amended to facilitate the efficient conduct of clinical research by:

1. exempting genetic modification of donor cells prior to reinsertion into a patient from section 42 of the HSNO Act (1996), and introducing a fit for purpose regulatory framework based on the approach adopted by the Australian Office of the Gene Technology Regulator

2. providing clarity as to the sort of review which would be required for a GMO medicine.

3. including statutory timelines for the pre-application process, in addition to those already in the HSNO Act for the application process itself.

Overview

Despite references in the HSNO Act (1966) to "rapid assessment" the reality is that the process of gaining approval to develop and use genetically modified organisms (GMOs) typically takes months. This often means that clinical research organisations which are developing new GMO based therapies for hitherto untreatable or hard to treat conditions, and who have secured the funding and specialised research staff to undertake the work, find themselves in the position of having to "cool their heels" awaiting the outcome of their applications.

This delays opportunities for clinical trials patients to potentially benefit from, and in some cases have their lives saved by, the new therapy. It can also be a waste of resources as

[1] Hazardous Substances and New Organisms (Hazardous Substances Assessments) Amendment Bill 54-1 (2021), Government Bill Contents - New Zealand Legislation

research staff continue to be paid while awaiting the outcome of the application, but without actually undertaking the research they were hired to do, risking funding running out before the research has been completed.

Such delays could be safely mitigated if the HSNO Amendment Bill were to be amended in respect of both genetic modification of donor cells prior to reinsertion into a patient (such as for CAR T therapy), and genetic modification of foreign organisms into a therapeutic product for human use (such as for vaccine development).

Submission

Genetic modification of donor cells prior to reinsertion into a patient

The genetic modification of donor cells prior to reinsertion into a patient is covered by Section 42 of the Hazardous Substances and New Organisms Act (1996)[2], ***rapid assessment of adverse effects for development of genetically modified organisms***, which states:

(1) Where the Authority receives an application under section 40 to develop a genetically modified organism in containment, the Authority may make a rapid assessment of the adverse effects of developing that organism.

(2) If the Authority is satisfied that any development meets the criteria for a low-risk genetic modification specified in regulations made under section 41, the Authority may approve the application and impose such controls providing for each of the matters specified in Schedule 3 as the Authority thinks fit.

Because of the often months long processes associated with the granting of such approvals NZHR recommends that the HSNO Amendment Bill amends Section 42 of the HSNO Act so that genetic modification of donor cells prior to reinsertion into a patient becomes exempted.

One way to do this would be to adopt the approach of the Australian Office of the Gene Technology Regulator (OGTR), which represents a simpler - yet still controlled - process for GMOs (like CAR T-cells for example).

The OGTR states that introduction of a GMO into a person is a licensable dealing, according to Schedule 3 Part 3.1 (n) of the Australian Gene Technology Regulations 2001, unless the GMO meets the exclusion specified in that clause. This clause is as follows (with exclusions highlighted in red):

(n) a dealing involving the intentional introduction of a GMO into a human being, unless the GMO:

(i) is a human somatic cell; and

(ii) cannot secrete or produce infectious agents as a result of the genetic modification; and

[2] https://www.legislation.govt.nz/act/public/1996/0030/latest/DLM381222.html#DLM382998

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(iii) if it was generated using viral vectors:

(a) has been tested for the presence of viruses likely to recombine with the genetically modified nucleic acid in the somatic cells; and

(b) the testing did not detect a virus mentioned in sub-subparagraph (A); and

(c) the viral vector used to generate the GMO as part of a previous dealing is no longer present in the somatic cells;

If the product meets all of the requirements for exclusion specified in this clause then:

- The dealings with the modified cells prior to introduction into a patient are exempt dealings. The only legislative requirement for exempt dealings is no intentional release into the environment – as per regulation 6, and no approval from the Gene Technology Regulator (the Regulator) is required. (Please see the OGTR's Guidance Notes for the Containment of Exempt Dealings for reference); and
- Once the cells are introduced into the patient they are no longer covered by the Gene Technology Act 2000 , as the definition of a GMO in Part 2 Division 2 clause 10 of the Act specifically excludes people who have undergone somatic cell gene therapy from being considered GMOs.

NZHR therefore recommends that the HSNO Amendment Bill be amended by exempting genetic modification of donor cells prior to reinsertion into a patient from section 42 of the HSNO Act (1996), and introducing a fit for purpose regulatory framework based on the approach adopted by the Australian Office of the Gene Technology Regulator

Genetic modification of foreign organisms into a therapeutic product for human use

In the experience of NZHR members genetic modification of foreign organisms into a therapeutic product for human use (such as for vaccine development) have been considered under section 34 of the HSNO Act.

The significant delays in getting clinical trials underway under this section have been partly attributed to unclear EPA criteria for determining the type of assessment that would be required for this class of GMO. This is not clear from information provided on the EPA website, and indeed one NZHR member has reported that even the EPA itself was not able to provide a firm commitment in this regard.

Significant delays have also been attributed to the length of the pre-application process as set out by the EPA here: www.epa.govt.nz/industry-areas/new-organisms/applying-for-approval/the-application-process. We note that the Australian OGTR has addressed this problem by introducing statutory timelines for the pre-application process. Furthermore, in Australia there is a requirement for sponsors to utilise the review of an Institutional Biosafety Committee prior to OGTR submission. This ensures the quality of the submission thereby eliminating unnecessary review time for the OGTR. Up front risks are identified and issues discussed with the sponsor prior to the submission, thereby setting the pathway for guaranteed compliance.

NZHR therefore recommends that the HSNO Amendment Bill be amended to:

- Provide clarity as to the sort of review would be required for a GMO medicine.

- Include statutory timelines for the pre-application process, in addition to those already in the HSNO Act for the application process itself.

Oral submission

This submission was presented orally on 28th October to Parliament's Environment Committee by Chris Higgins and Malaghan Institute staff Robert Weinkove and Giulia Giunti, as follows:

Chris Higgins

Thanks for the opportunity for New Zealanders for Health Research to meet the Environment Committee and present our submission in person.

As well as myself as Chief Executive our submission today is co-presented by Malaghan Institute of Medical Research staff Dr Robert Weinkove, and Dr. Giulia Giunti, Malaghan's Clinical Director and Malaghan's Quality Manager respectively.

We imagine that it might be unusual for the Environment Committee to be hearing from the medical research community and that it will be therefore useful to provide some background.

Over the last five years we've been arguing for a three to four fold increase in government investment in health research. Given the very low current levels of investment we are especially concerned to ensure that the money that is made available is used as efficiently as possible in order to maximise opportunities for translating the results of health research into life improving and life saving new therapies and services.

When we saw that the Hazardous Substances and New Organisms Act was the subject of an amendment Bill we took that as an opportunity to convey concerns that had been expressed to us by our stakeholders that Environmental Protection Authority processes were unnecessarily delaying the carrying out of - literally life saving - medical research.

What we've been witnessing is unnecessary wasting of precious resources as research staff continue to be paid while awaiting the outcome of the application, but without actually undertaking the research they were hired to do.

This not only risks funding running out before the research has been completed, but also puts at risk the lives of very ill clinical trials participants who are waiting for the opportunity to try out a new therapy which is often their last hope for an effective treatment or cure.

Our submission in response to these concerns is to recommend safe efficient alternatives which won't risk environmental exposure to Genetically Modified Organisms (GMOs) based on the regulatory approach adopted by the Australian Office of the Gene Technology Regulator.

Specifically we are proposing that the HSNO Amendment Bill be amended in respect of both genetic modification of donor cells prior to reinsertion into a patient (such as for CAR T-cell therapy), and genetic modification of foreign organisms into a therapeutic product for human use (such as for vaccine development).
I'll now hand over to Robert and Giulia.

Robert Weinkove and Giulia Giunti

Chimeric antigen receptor T-cells, known as CAR T-cells, are increasingly a standard-of-care treatment to treat people with certain lymphomas, leukaemia and other cancers.

CAR T-cell therapies are not new. The very first trial started in 2010, the first product was licensed for routine use in 2017 in the USA, where 5 CAR T-cell products are now licensed. CAR T-cells are also now licensed and routine in Australia, the UK and Europe.

The Malaghan Institute is running a clinical trial of a CAR T-cell therapy in Aotearoa New Zealand at present, and we hope to facilitate more trials of this potentially-life saving type of treatment in future.

Members of the Select Committee may want to view the recent Prime TV documentary called, "A Mlld Touch of Cancer" featuring David Downs, and two other NZ CAR T-cell recipients for the impact of this type of treatment

In the current Act, CAR T-cells are classified as a GMO. However we contend that CAR T-cells cells are not an organism, because they cannot grow except within the body of the intended recipient. There is no risk of them forming a self-sustaining population or growing in the environment. As such, there is no risk foreseen of the GMO to the environment or risk of the GMOs on the relationship of Māori and their culture and traditions with their ancestral lands, water, sites, waahi tapu, valued flora and fauna and other taonga, and the principles of the Treaty of Waitangi.

In Australia, the manufacture and release of patient-specific CAR T-cells for treatment and safety testing are classified as 'exempt low risk dealings'. This much more **pragmatic** approach contributes to Australia's lead in uptake of these treatments.

We contend that the HSNO Act needs to be updated to anticipate this modality of treatment, which is important for the health of New Zealanders with cancers that cannot be treated with conventional means. Our proposal is consistent with the Australian regulatory approach, and remains safe.

Of course, individual treatments would still be assessed for safety by the Gene Technology Advisory Committee and/or Medsafe, and trials assessed by the ethics committees.

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NZHR constituency

In developing this submission we have consulted with our Platinum to Bronze partners and members as set out below (and from whom we derive 100% of our funding).

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