Working Paper 2020/06

Letter to the Minister on AgResearch's approval for GM animals in light of pandemic risk

MCGUINNESS INSTITUTE
TE HONONGA WAKA

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15 July 2020

Hon David Parker
Minister for the Environment
Parliament
New Zealand

Dear Minister,

Request Government to revoke AgResearch's approval for GM animals in light of pandemic risk

The primary purpose of this letter is to ask the New Zealand Government to apply a precautionary approach and revoke AgResearch's approval to undertake outdoor genetic modification (GM) experiments, namely ERMA 200223. As at 30 June 2018, there were 76 GM animals (37 cows and 39 goats) (EPA, 2018, pp. 6–7).

Of particular concern is that the types of experiments carried out under ERMA 200223 have a risk (albeit a very low probability) of causing an epidemic or pandemic. The current pandemic is an example of how a species barrier breakdown can cause global damage to human health and environmental and economic wellbeing. We consider AgResearch's GM experiments are New Zealand's equivalent to Asia's wet markets; while their purpose and level of regulation are very different, both settings create the possibility for viruses to cross the species barrier. This risk can occur when modifying the genetic make-up of an animal using foreign genetic material (in AgResearch's case from a human and/or another animal) and in Asia's wet markets this can occur when humans, wild animals, fish and meat are in close proximity. Although we believe the probability of accidently creating a novel human disease is very small, there would be serious and irreversible consequences. We consider the likelihood of this risk occurring increases when GM experiments occur outside a laboratory and in the field. This can happen if the EPA (previously ERMA) approves an outdoor development (GMD) or a field trial (GMF).

The Institute is also concerned that AgResearch has not met many of the controls specified in the 2010 decision (ERMA, 2010b, pp. 42–44) (see Attachment 1). The Institute has reviewed the latest ERMA 200223 annual report (for the 12 months ending 30 June 2018) against these controls and found that many of the operational controls (ERMA, 2010b, pp. 3–4) have not been actioned or have only been partially audited (see Attachment 2).

The approach taken by ERMA in 2010 in terms of accepting and then approving the application was unique. It created a category called outdoor development (rather than a field trial), which enabled the applicant to combine a number of species (including human DNA) (ERMA, 2010b, pp. 3–4). It also moved all retrospective AgResearch outdoor experiments approved by ERMA under this new broader combined approval (being ERMA 200223) (ERMA, 2010a, p. 12). In the Institute's view, this approach went against the case-by-case assessment initially intended under the Hazardous Substances and New Organisms Act 1996, which aimed to assess the more risky experiments (e.g. those conducted in the outdoors) based on each experiments unique profile. We consider that ERMA's 2010 acceptance and approval of AgResearch's application in effect licenced the applicant rather than the application (in effect operating outside the existing law).

Due to ERMA's unique approach, the ERMA committee added two further controls as a type of handbrake to manage the limitations inherent in their new, largely hands-off, approach. However these controls have not been actioned:

- Control 12 put in place a mechanism for ERMA (now the EPA) to reassess the decision midway through the consent period (ERMA, 2010b, p. 43). We believe the committee intended this control to address the high degree of uncertainty they had in 2010 regarding risks, costs and benefits. The ability to reassess the approval was to be triggered on receipt of the 'ten year report' from AgResearch (ERMA, 2010b, p. 43). Importantly, it forms the basis for the EPA to review whether grounds for reassessment exist. This ten year report was due 31 August 2019 and covers the annual reporting period 1 July 2018 to 30 June 2019 as well as requiring information on the proof-of-concept, adverse effects (including effects that relate to the principles of the Treaty) and any beneficial effects to date or that might occur in the next ten years (ERMA, 2010b, p. 43) (see Attachment 1). We are concerned that the ten year report is now ten months overdue.
- Control 13 put in place a mechanism for iwi/Māori cultural matters to be addressed through the establishment of an ERMA 200223 Iwi Liaison Group (ERMA, 2010b, p. 43). We believe the committee intended this control to address concerns that they were unable to resolve in 2010. The fact that the EPA is both aware the group had not met since 2011 and have not altered the experiments accordingly; indicates both parties are treating this control as irrelevant.

About ERMA 200223

The Environmental Risk Management Authority (ERMA), now EPA, approved AgResearch's GMD application on 13 April 2010, which allowed for the mixing of human and animal genetic material (with controls) to develop

genetically modified goats, sheep and cows in order to produce human therapeutic proteins (or with altered levels of endogenous proteins) for the study of gene function, milk composition and disease resistance. The application received 1545 written submissions. The approval expires on 15 April 2030 (ERMA, 2010b, p. 44).

Box 1: Application: ERMA 200223 Host organism
Source: (ERMA, 2010b, p. 45)
Ovis aries Linnaeus, 1758, cells [sheep]
Bos taurus Linnaeus, 1758, cells [cattle]
Capra aegagrus hircus Linnaeus, 1758, cells [goat]
Mus musculus Linnaeus, 1758, cells [mouse]
Homo sapiens Linnaeus, 1758, commercial cell lines [human]

Below we briefly discuss the relevant risks, costs and benefits, as required under the Hazardous Substances and New Organisms Act 1996 (HSNO). Key excerpts from the HSNO legislation can be found in Attachment 4.

Risks
The 2010 committee hearing the application was of the view that risks of a novel human disease were 'negligible' (ERMA, 2010b, p. 24). However, as recently evidenced, there was a very low probability that COVID-19 would emerge yet the magnitude was and continues to be significant. It is important to appreciate how novel these experiments are in terms of the global stage. GM animals are rare; largely because they are expensive to create, risks are acknowledged but unknown (e.g. the passing of the HSNO legislation) and the demand, at best, is minimal (e.g. FDA GM salmon, see Attachment 3). Of particular concern is that the majority of emerging infectious diseases that affect humans originate from animal reservoirs (Villabruna, 2019). Mammals (e.g. cows, goats or pigs) can act as reservoirs, enabling viruses to cross from animals to humans. A recent example (June 2020) is the new influenza virus that has emerged in China (NZ Herald, 2020). The virus is carried by pigs and can infect humans; 'researchers are worried the new virus could mutate so that it can spread easily between people' (NZ Herald, 2020).

Aggregation and comparison of risks, costs, and benefits
The Institute also has concerns about the weighing of benefits against the costs and risks. For example, how will the benefits of this experiment benefit the New Zealand public if the medical drugs are already able to be manufactured in a laboratory (see Attachment 4)? Furthermore, AgResearch has developed collaborations with overseas companies, which in effect muddies the water in terms of net benefits to New Zealand. In terms of costs, approximately $100 million of public funds has been used to progress this research. This means the sunk cost of each existing asset (GM livestock) is approximately $1.3 million per animal (see costs in Attachment 3). In a situation where risks and benefits are both negligible, and the public costs are significant, we believe the HSNO Act 1996 requires the precautionary approach to prevail and the application revoked. Attachment 3 contains a comprehensive OIA request to the EPA in order to provide more clarity.

Our request for Government to withdraw ERMA 200223
We believe it is timely for Government to withdraw approval of all GM animals in the outdoors on the basis that the risks exceed the benefits and costs. It has been ten years since the application was first approved (meaning the science upon which the decision was based is now ten years old) and the application has another ten years to run (expiring in 2030) (ERMA, 2010b, p. 44). COVID-19 has only amplified the risks of a novel human disease originating from an animal reservoir. ERMA 200223 has the potential to impact New Zealand in ways that are beyond what was initially considered in 2010. For example, recent responses to the current pandemic foretell a scenario where countries might choose to close their borders to New Zealand as a means of preventing the spread of a human disease originating here.

In light of the current global context, New Zealand has an opportunity to reconsider whether the risks, benefits and costs of outdoor GM experiments are in New Zealand's best interest. This letter asks you, as Minister, to make the most of this opportunity. If you have any questions, please do not hesitate to contact me.

Kind regards,

Wendy McGuinness
Chief Executive

Attachment 1: The 15 Controls Specified in ERMA 200223 Decision

Source: (ERMA, 2010b, pp. 42–44)

Appendix 2: Controls on approval

Organisms and activities approved:

1. The approval holder (AgResearch Limited) must ensure compliance with the following controls.

2. This approval is limited to the development of the organisms described in **Appendix 1,** for the purposes of producing human therapeutic proteins, or with altered levels of endogenous proteins for the study of gene function, milk composition and disease resistance.

3. Unless otherwise specified by the following controls, the approval holder must ensure that the location and nature of the development, and the disposal of animals and animal products, are in accordance with the activities and proposed controls described in the application.

Containment:

4. Subject to the other controls in this appendix, the approval holder must ensure that containment facilities that hold:
   a) *E. coli,* mammalian cell lines, embryos, sperm and ova are compliant with the requirements of the MAF/ERMA New Zealand Standard *Facilities for Microorganisms and Cell Cultures: 2007a* (the Microorganism Standard);
   b) laboratory animals are compliant with the requirements of the MAF/ERMA New Zealand Standard *Containment Facilities for Vertebrate Laboratory Animals* (the Vertebrate Standard);
   c) *E. coli,* mammalian cell lines, embryos, sperm, ova and laboratory animals are compliant with the Australian/New Zealand Standard *2243.3:2002 Safety in laboratories Part 3: Microbiological aspects and containment facilities* (AS/NZ 2243.3:2002); and
   d) sheep, goats, and cattle are compliant with the requirements of the MAF/ERMA New Zealand Standard *Containment Standard for Field Testing of Farm Animals* (the Field Test Standard). [18]

5. The approval holder must ensure that any animals used to control grass in the space between the double perimeter fences are not of the same species as the animals being held within paddocks which are adjacent to the inner fence.

Breach of containment:

6. The approval holder must ensure that a MAF Inspector is notified of any breach of containment,[19] including the details of any action taken to restore containment, within 24 hours of the discovery of the breach of containment.

Register:

7. In addition to the requirements of the Containment Standards, the approval holder must maintain a written (either hard copy or electronic) record of:

[18] A reference to any of these four Containment Standards in these controls also refers to any subsequent version approved or endorsed by ERMA New Zealand.
[19] Breach of containment includes: escape of organism(s), unauthorised entry to the facility, and/or the structural integrity of the facility being compromised. For the avoidance of doubt, this control does not permit breaches of containment.

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a) the HSNO Act approval under which each animal has been imported or developed;
b) any *in vitro* fertilisation (IVF), artificial insemination (AI) or other breeding procedures each animal has undergone and the outcomes of these procedures;
c) the date of transfer of animal(s), sperm, ova or embryos between indoor containment facilities and outdoor containment facilities (for GM only);
d) the identity of the authorised person responsible for the animal(s).

Production and use of replication-deficient viral particles:

8. All open container use and production of viral particles must occur within a Class II Biological Safety Cabinet.

Identification of animals within outdoor containment:

9. In addition to the requirement in the Containment Standards that all new organisms must be tagged, any conventional animals held within the outdoor containment facility must also be tagged in line with the methods specified in the Field Testing Standard.

Movement of conventional animals:

10. Conventional animals may only leave the facility if:
    a) the animal has not been successfully used as a surrogate or recipient animal; and
    b) the approval holder has confirmed twice, using scientifically verified methods, that the animal is not pregnant.

Annual reporting:

11. The approval holder must provide an annual report to ERMA New Zealand by 31 August of each year while this approval is in use. Each annual report will be made available to the public and must include a description of:
    a) any outdoor development activities;
    b) any unforeseen adverse effects resulting from the genetic modifications; and
    c) any relationship development and management initiatives undertaken with any iwi liaison group.

Ten year report:

12. In addition to the annual reporting requirements, and for the purposes of providing the Authority with information relating to whether there are grounds for reassessment of the approval, the tenth annual report must include additional information about:
    a) any progress that the approval holder has achieved towards completion of the proof-of-concept research;
    b) any adverse effects of the organisms that have occurred, including any effects which relate to the matters described in section 6(d) and the principles of the Treaty of Waitangi (Te Tiriti o Waitangi); and
    c) any beneficial effects of the organisms that have occurred in the first ten years, or that are forecast to occur over the next ten years.

Māori cultural effects:

13. The approval holder must establish an iwi liaison group as a forum for ensuring that iwi/Māori cultural matters relating to the approval are addressed. The approval holder

a) must invite mandated representatives of Ngāti Wairere and Waikato-Tainui to participate in the group;
b) may invite any other interested iwi/Māori groups to participate in the group; and
c) must establish a Terms of Reference (including regularity of meetings) by agreement with the mandated representatives of Ngāti Wairere and Waikato-Tainui.

Duration of the approval

14. This approval expires on 15 April 2030.

Completion of the development:

15. The approval holder must have completed destruction (i.e. killing and disposal) of all heritable material and organisms held under this approval by:
    a) the date of expiry of this approval; or
    b) 12 months from the date which work under this approval ceases (whichever is the earliest).

Attachment 2: A Review of Controls Specified in the ERMA 200223 Decision

Source: (EPA, 2018)

Issues of concern identified in the latest annual report, being the ninth annual report for the 12 months ending 30 June 2018, are as follows:

1. **Poor reporting and verification processes**

   The annual report is prepared by AgResearch. The latest annual report found on the EPA's website contains two MPI Verification Services Audit reports (audit reports) dated 22 August 2017 and 21 February 2018. Good process would suggest MPI should produce the report and attach AgResearch's report (not the other way around).

   The Institute considers Control 4 only reports on the containment facilities, whereas the committee were expecting something quite different in terms of the application of Control 11. We consider the original intent of the ERMA committee has been considerably weakened by AgResearch's poor annual reporting practices (see 2. below), MPI's style of audit report (see 3. below) and EPA's failure to monitor/manage/penalise AgResearch for their poor reporting and verification processes and their inability to implement controls (see 4. below).

2. **AgResearch's failure to deliver the 'ten year report' on time**

   As noted in page 1 of this letter, even if the 'ten year report' was not the 'reassessment annual report', it is now July 2020 and the latest annual report on the EPA website relates to June 2018 (just over 2 years ago). The 'ten year report' was due on the 31 August 2019, meaning it is now over 10 months late (see 4. below). This is not what the ERMA committee hearing the decision would have expected, nor what submitters and other interested parties were promised in terms of transparency and accountability. See Controls 10 and 11 in Attachment 1.

3. **Inadequate MPI audit reports (22 August 2017 and 21 February 2018)**

   a. Lack of timeliness. It is surprising that no other MPI inspection report is available on the EPA website given that the last inspection report was published on 21 February 2018 (i.e. two years and four months ago).

   b. The inspections were undertaken by one person (prepared by an MPI Containment Verifier) for both years. It is better to have more people involved in each inspection or at least alternative inspectors over different years.

   c. The time between inspection and the audit reports implies a lack of due diligence and care. The first audit report notes that an inspection took place on the 17 and the 22 August 2017 with the report dated 24 August 2017 (7 days max). The second audit report took only two days from inspection to completion (inspection dated 20 February 2018 and the inspection report date was 21 February 2018 (2 days max). It is difficult to accept that such a short timeframe can produce a comprehensive verification report on the outdoor GM animals, let alone the whole containment facility.

   d. The brief nature of the audit report and the fact that some controls (such as Control 8, see below) were not audited should also be a concern.

   e. Previous recommendations are not being implemented. This should be treated urgently (particularly given the risks). See excerpt from the executive summary of the 21 February audit report, particularly with regard to biological products tracking being an area that could be improved and the need to strengthen the compliance role:

      > No progress have been made the replace the Operating Manager, additional support has not been provided. The recommendation made in several previous reports in regards to reviewing the Delegated Operator roles and utilising a part time compliance role is still valid and MPI would strongly recommend this be give careful consideration.
      >
      > Biological products tracking was identified as an area that could be improved. AgResearch does not have a way to accurately stocktake risk material on site or identify if any items not in high use are missing.

One AgResearch tenant was assessed for compliance with the controls of their HSNO Approval during this visit. Selected laboratories in the Dairy Science, Animal Physiology and Plant Protection buildings were visited.

Overall the audit outcome was satisfactory, with some areas of concern. One recommendation was made and one non-compliance issued; both were for the laboratories.

f. This audit report indicates that outdoor GM animals may not be required to be inspected every year. The audit report indicates that only 'selected laboratories' are assessed for compliance (see Executive Summary). This point requires further clarification.

4. Failure to manage specific controls

It is important to keep mind there was very strong interest in this application; there were over 1500 written submissions and many experts provided evidence. The controls were put in place to manage the risks and together they were designed, as a package, to enable the application to proceed.

a. Controls 7 and 9

Control 7, stock records, are concerning. As noted in Attachment 1, Control 7 requires the approval holder to maintain a written record of stock (either hard copy or electronic) and Control 9 (requires outdoor GM animals to be tagged). Given the small number of GM animals in the outdoors (76 in total) (EPA, 2018, pp. 6–7) and the high cost (McGuinness Institute, 2013b, pp. 57–62), risks and benefits of each animal, one would expect that each animal's tag would be checked by an independent person/s against the records – at least annually. This is normal practice for prized livestock, so it is surprising that such a low standard of care and due diligence is not being practiced by MPI.

The audit report content is unnecessary confusing and conflicting.

The excerpt below is from a previous audit report (August 2017)

Control 7
Animal records are maintained electronically. Selected records for cow and sheep were viewed. Full stock counts were unable to be printed for this visit.

Control 9
Visible identification was seen on cows in the upper paddocks. Parentage records were able to be tracked back from the calf

It indicates that the inspectors did not view the tags of 'all' stock, in fact it is difficult to know what they mean by visible identification or what was inspected. For example:

- What does 'selected records' mean in practice?
- What does 'visible identification' mean in practice? For example, did they view the cows tags or just see them in a paddock?
- Why were selected records of sheep reviewed when there were no GM sheep as at 1 July 2017?
- Why are the goats not mentioned when there were 46 GM goats as at 1 July 2017?
- Why was full stock counts unable to be printed for the Inspector?
- Why was the Inspector not frustrated by AgResearch's lack of preparation – both in terms of preparing the GM animals for inspection and not providing a printed copy of their GM livestock? We would have expected the inspector to revisit the site another time when AgResearch had the GM livestock (with tags) in a yard and a printed copy available in order for a proper inspection to take place.
- Why are conventional animals being placed in paddocks with GM animals?
- Are there any cloned animals (or is this what is meant by conventional animals)?

The excerpt below is from the latest audit report (August 2018)

> Control 7
> Animal records are maintained electronically. Selected records for cow and sheep were viewed.
>
> Control 9
> Visible identification was seen on goats and cows. Sheep were unable to be checked without being yarded. Identification for surrogates and future labs was described.

The audit report actually acknowledges that the sheep could not be checked because they were not placed in a yard. This is surprising given placing sheep in a yard and checking tags is normal farming practice. It is also relevant that there was no GM sheep (only conventional sheep) but there were 39 GM goats yet no goat records were viewed (see Control 7). This provides further evidence of the inability by AgResearch, MPI and EPA to require and ensure the controls are being applied.

When comparing these audit reports, we believe it is not possible to have any confidence that the full stock count was printed out in 2018, nor whether the tags of any goats were checked against the print out. As a chartered accountant, this inability to undertake simple processes or provide clarity over what verification processes/method were applied is at best, perplexing. For scientists and inspectors not to write down their method of verification is quite shocking and is grounds for a serious breach of trust. For the EPA to read these audit reports and not be alarmed is beyond belief.

b. Control 8
Controls were excluded from the inspection; namely Controls 8, 11, 12, 14 and 15. Although most of these are understandable, Control 8 should in our view be included in the MPI inspection. Control 8 is to ensure 'All open container use and production of viral particles must occur within a Class II Biological Safety Cabinet'. If MPI does not inspect this control, we wonder whether anyone else is responsible for checking that this control is being implemented correctly.

c. Control 11
The Institute had expectations that the EPA would review the annual report in detail to ensure that it met the standard required by the committee. However, as evidenced in this attachment, we believe a higher standard of reporting was expected.

d. Control 12
An in-depth ten year annual report is required to be prepared by AgResearch by 31 August 2019 (see Attachment 1), with the purpose of providing the EPA with information relating to whether there are grounds for reassessment of the approval. This crucial report (the reassessment annual report) is overdue by more than ten months.

- The first ERMA200223 annual report was published for the period 13 April to 30 June 2010.
- The latest (ninth) annual report covers the period from 1 July 2017 to 30 June 2018.
- The next (tenth) annual report would be for the period 1 July 2018 to 30 June 2019 (and was due 31 August 2019).

In our view, AgResearch has failed to meet this control. Even if COVID-19 is taken into consideration, listed companies were only given a two-month extension to produce detailed and complex financial reports, begging the question as to why AgResearch should be given longer. Further, the fact that the report was due on 30 August 2019 makes an extension based on COVID-19, in our view, invalid. It is disappointing that the reassessment annual report is yet to materialise, particularly given its critical importance in terms of the reassessment process.

e. Control 13
The approval holder is required to establish an ERMA 200223 Iwi Liaison Group as a forum for ensuring that Iwi/Māori cultural matters relating to the approval are addressed. We expect this control was designed to manage the risks of placing human DNA into animals, which was a major risk discussed by submitters at the hearing – both in terms of cultural ethics/values/beliefs and pandemic risks.

The audit report notes that contact is being 'maintained':

> Control 13
> Contact is being maintained with Iwi.

This text contrasts with the ninth annual report, which states that the ERMA 200223 Iwi Liaison Group has not officially met since 2011. In our view, the MPI text above appears overly optimistic when compared with the reality, as explained in AgResearch's annual report (see text below).

> Iwi liaison group relationship development and management activities
>
> The ERMA200223 Liaison Group has still not officially met since December 2011.
>
> As advised in previous annual reports, at the request of a group of Ngati - Wairere elders the Liaison meetings were put on hold, while representation and membership of the Liaison group was discussed within the Hapu.
>
> Following some correspondence and individual contact, this group of Ngati - Wairere elders was invited and did visit Ruakura in October 2012 and a process to progress representation was discussed. Unfortunately due to circumstances outside of AgResearch influence, despite numerous attempts, no progress has been made in resolving this directly to date.
>
> There has been some informal contact with original monitoring group members and regular contact with Tainui Group Holdings on their development activities for Ruakura.
>
> AgResearch's Portfolio Leader - Māori Agribusiness who has local affiliations, is still working to build a relationship with Ngati - Wairere for Liaison Group and other Ruakura initiatives of interest to Ngati - Wairere and Tainui purposes.

Government should be concerned that there has been no meeting of the ERMA 200223 Iwi Liaison Group since 2011. Importantly, we believe this control was added due to the concerns raised at the hearing in relation to the use of human cell lines.

We also note that under s 5 of the Crown Research Institutes Act 1992, AgResearch is required to not only operate 'in a financially responsible manner' but to ensure that research is 'undertaken for the benefit of New Zealand' and that they must have regard of community interests ('that a Crown Research Institute should be an organisation that exhibits a sense of social responsibility by having regard to the interests of the community in which it operates and by endeavouring to accommodate or encourage those interests when able to do so').

What is clear is that AgResearch is not managing an important area of risk identified by ERMA in 2010 and that the EPA knowingly accepts that this control is not being managed yet continues to allow this experiment to proceed in 2020.

Going forward, this illustrates that the EPA should not delegate the management of risks to a third party after the fact without giving them some ability to influence the outcome (particularly in cases where they themselves are unable to manage that risk during a hearing). In the Institute's view this control placed an unfair obligation (arguably a burden) on iwi, making them complicit in the outcome but giving them no ability to influence the outcome. The response by iwi to put meetings 'on hold' is understandable.

Attachment 3: OIA Request to the EPA

Background

The Institute's work programme tends to focus on low probability/high magnitude events. In terms of public policy, we believe it is difficult to give attention to and make decisions based on events that are unlikely to happen. This is one of the reasons why, since 2005, our work programme has included a focus on pandemics. Concern over the possibility of GM experiments accidentally creating an epidemic (or pandemic) has been ongoing, both from an individual's perspective (founder W McGuinness), and as McGuinness Institute (previously Sustainable Future Institute). This led to the lodging of a number of submissions to ERMA (now the EPA) and the founder joining a legal case against ERMA and AgResearch (i.e. *Bleakley v Environmental Risk Management Authority [2001] 3 NZLR 213*). The Institute has since published a number of reports on this topic since 2008. Learn more about our research on our genetic modification page found under the PublicScienceNZ research project on the McGuinness Institute website. The risk of a GM experiment creating a human epidemic or pandemic has been an ongoing concern.

Questions

To help the Institute form a view of the next steps and to update our records, we have listed a number of questions for the EPA to answer (this can be treated as an OIA):

1. **Outdoor developments and field trials of GM animals**

    a. Can you provide a comprehensive list of outdoor developments and field trials in New Zealand that involve GM animals?

    Note: We have found a list on your website but it is not complete. The approvals only mention 'cattle' and although the following is referenced twice – 'All research is now conducted under the approval for ERMA200223 (below)' – but ERMA200223 is not mentioned below. By going through the register we found the link to ERMA 200223.

    You may also like to refer to Appendix 10 (page 50) of the Institute's *Report 16*, which contains a comprehensive list between 1998 to 2013. We would like to update this list.

2. **ERMA 200223 approval**

    b. Can you advise that in addition to the review of grounds for reassessment in 2019/2020, whether there is any other mechanism that would give the EPA or indeed the Government, grounds to withdraw the approval? Please refer to specific legislation.

    c. Please provide the policy for a review of the grounds for reassessment. We believe this is the first time that this has been made a control, could you please clarify this? Further, could you outline the process the EPA will undertake in completing this review and ideally make it public?

    d. Has the EPA received the tenth annual report from AgResearch – for the period 1 July 2018 to 30 June 2019 (and was due 31 August 2019)? If yes, can you please forward this report to the Institute and ideally make it public on your website. If no, can you confirm whether you have requested this copy from AgResearch? Can you also confirm the current status and the plans to action given this failure to report on time? We would appreciate copies of any correspondence that has taken place between the EPA and AgResearch discussing the ten year assessment and the tenth annual report during the last three years.

    e. Under what legislation could (i) the Minister, (ii) the EPA or (iii) a member of the public decide to call in (or go to court over in regard to (iii)) an approved development (such as ERMA 200223)? If yes, please list the section and identify grounds that could apply for each of these scenarios above (e.g. poor governance by AgResearch, new evidence on risks or new information on benefits being less than initially envisaged).

    f. Can you clarify to what extent the EPA completes a case-by-case assessment of each experiment under ERMA200223 (rather than approving the applicant or the containment facility)?

    g. What level of assurance do you have that this approval has been implemented correctly? Please clarify what processes you have put in place to ensure this is the case. In Attachment 2 we outline a number of concerns with the latest ERMA 200223 annual report (which also includes two MPI

inspection reports). Given that the EPA has accepted these reports and placed them on their website; the implication is that these issues, particularly in terms of a failure to apply controls, were satisfactory and did not require action by the EPA. Can you confirm if any action was taken by the EPA in the last 24 months based on the annual reports? If yes, please specify what actions were taken and where appropriate, please write your response to the specific control failures/general concerns outlined in Attachment 2 (point 4 (a)-(e)).

3. Risks

We are concerned about the associated risks: whether they have been identified and managed, whether AgResearch is operating under the purpose it was licensed to action, and what checks and balances the EPA have undertaken to ensure those risks are being identified and managed. We could not find any reference to the GM animal experiments in AgResearch's Rīpoata ā-tau 2019 Annual Report.

h. Has the EPA (or their agent, consultant or service provider) reviewed the science since the approval ten years ago? If yes, please expand.

i. Are there any plans to review the science in the future (this is particularly relevant given the experiment has another ten years to run)? If yes, please explain.

j. We are particularly concerned about the risks of DNA or RNA viruses crossing the species barrier, have these specific risks been reviewed in the last ten years, and whether the EPA is planning a review in the near future (particularly given the current pandemic). If so, please advise how those risks were identified, measured and mitigated and to what extent has the probability and magnitude of that risk been identified and reduced by the EPA? If this information is in a report, please direct us to the report/s.

k. Can you advise why MPI is not inspecting Control 8: 'All open container use and production of viral particles must occur within a Class II Biological Safety Cabinet'? Please give the name of the organisation completing this check and/or the reasons why it is not being inspected/checked.

4. Benefits

In terms of benefits, it is important that the EPA accesses benefits to the degree those benefits accrue to New Zealand and to New Zealanders. From previous research into AgResearch's experiments, we found that New Zealand was not always the sole financial beneficiary. For example, if AgResearch has sold shares/ benefits to overseas companies/entities, then those benefits may be much lower than initially envisaged, leading to risks much higher than what was understood to be the benefits. In the same way risks need to be identified, described, and made transparent, so do benefits.

An article in the latest *New Scientist*, 20 June 2020 (see Attachment 5) refers to AgResearch creating GM milk from GM goats in order to attempt to manufacture pre-existing cancer drugs (as opposed to exploring or developing new cancer drugs). Additionally, the production process being pursued by AgResearch (GM milk from GM goats) would require a long delivery time with many known obstacles. For example:

- There is no evidence that animal milk will be able to create medicine of the same standard or purity as those made in a laboratory (this is also noted at the end of the *New Scientis*t article below); and
- FDA approval would be required. Our understanding is that GM milk from GM animals has yet to be approved for medical purposes. FDA notes on its website that 'data requirements are proportionate to the risks of the product' (FDA, n.d.). Given the lack of approvals for GM product by the FDA, GM milk for human consumption would be treated as high risk and therefore the data requirements for such a product would be significant. There is no evidence to establish why the FDA would prioritise approving a drug derived from GM animals when a proven laboratory product (Erbitux) is currently available.

Given this:

l. Has the EPA identified who gains the benefits of the application? If yes, please advise or indicate where those benefits are listed and quantified.

m. Has the EPA undertaken a recent review of those benefits? If yes, please advise or indicate where those benefits are listed.

n. What health care/medical scientist has been engaged to advise on the benefits of this science pathway? This was a weakness of the original AgResearch application. Please advise if the EPA has done any further research/inquiry into the benefits claimed by the applicant.

o. We note that the latest audit report mentions collaborators (EPA, 2018, p. 3). Can you advise if they have a benefit in this experiment and if yes, whether this benefit dilutes the so called benefit to New Zealand identified by the applicant. Our understanding is that at the time of the application there were no other entities that had a shareholding or reagreed benefit from the experiment. Please can you provide an update as this would dilute the benefits to New Zealand, as assessed under the legislation.

p. The article in Attachment 5 notes 'the need to be sure that drugs derived from animal milk has the same standard and purity as normal'. In earlier research we found that the purity and quality control issues regarding drugs derived from animal milk would be a major obstacle and exceed manufacturing costs made in a laboratory. Has the EPA undertaken any recent secondary research to try and assess the likelihood that these obstacles could be overcome? If yes, we would like to review this research.

5. Costs

Total costs to New Zealanders for GM animals will include AgResearch's core funding, contestable funding and grants, which is likely to be in the vicinity of $100 million. This means the sunk cost of existing stock is approx. $1.3 million (McGuinness Institute, 2008; 2013a; 2013b).

The Institute has some general concerns about the use of public funds in the context of GM. For example, is it equitable that patients in New Zealand cannot obtain cheap access to the latest cancer treatments whilst a CRI can use public funds to explore ways of replicating medicine 'via animals' that already exist on the market 'via laboratory testing.' These GM experiments will require a great deal of work, time and additional money with no certainty as to the outcomes?

q. Has the EPA identified costs in terms of the accumulated costs to AgResearch to implement the experiments since 2010? If not, can you ask AgResearch to provide detailed costs?

r. Has the EPA identified the costs (for the EPA) to monitor and manage the risks of those experiments since 2010? If yes, what is the actual cost to the EPA? If not, can you estimate this? Lastly, if you are unable to estimate these costs, can you advise the estimated cost of all monitoring of outdoor GMDs?

s. Can you advise the costs of monitoring all AgResearch experiments by year for the last twelve years? (Note: This will provide an estimate of additional costs to the EPA).

t. The 2018 annual report notes that there were 76 GM animals (37 cows, 39 goats and no sheep) as at 30 June 2018. Given the experiments originally started in 1999 (these earlier applications were rolled into the 2010 application) and the EPA is required to consider costs; what is the EPAs calculation of the actual costs of each of these 76 GM animals to be?

6. Methodology

u. The risk management methodology that ERMA (and now the EPA) is required to apply is contained within the Hazardous Substances and New Organisms (Methodology) Order 1998. Can you advise where we can find any supporting documentation on how the EPA implements the methodology? Previously there has been a guide for this.

v. What is the process for the grounds for the reassessment and if found, that reassessment?

w. Will the public be invited to contribute regarding the 'grounds for the assessment' and the 'reassessment' proper? Please advise.

7. Interested Parties Register

x. If it is GMD02032 (see below), please clarify if there have been amendments to GMD02032 that the Institute is not aware of. It was our understanding that the Institute would be kept informed of all changes and had the ability to discuss any significant changes with ERMA (and the EPA). Can you clarify if a register of interested parties still exists and if so, whether the Institute's name or Wendy McGuinness's name remains on it? If there is such a register and we are not on it, can you please add us?

8. Other parties interested in creating GM animals

y. Has the EPA received applications or enquiries to create GM animals in New Zealand (i) from New Zealand companies or (ii) overseas companies in the last ten years? If yes, please elaborate.

Attachment 4: Excerpts from the Hazardous Substances and New Organisms Legislation

The bold showcases key parts of the legislation that relate to this request.

Section 4: Purpose of Act
The purpose of this Act is to protect the environment, and the health and safety of people and communities, by preventing or managing the adverse effects of hazardous substances and new organisms.

Section 5: Principles relevant to purpose of Act
All persons exercising functions, powers, and duties under this Act shall, to achieve the purpose of this Act, recognise and provide for the following principles:

(a) the safeguarding of the life-supporting capacity of air, water, soil, and ecosystems:

(b) the maintenance and enhancement of the capacity of people and communities to provide for their own economic, social, and cultural well-being and for the reasonably foreseeable needs of future generations.

Section 6: Matters relevant to purpose of Act
All persons exercising functions, powers, and duties under this Act shall, to achieve the purpose of this Act, take into account the following matters:

(a) the sustainability of all native and valued introduced flora and fauna:

(b) the intrinsic value of ecosystems:

(c) public health:

(d) the relationship of Maori and their culture and traditions with their ancestral lands, water, sites, waahi tapu, valued flora and fauna, and other taonga:

(e) the economic and related benefits and costs of using a particular hazardous substance or new organism:

(f) New Zealand's international obligations.

Section 7: Precautionary approach
All persons exercising functions, powers, and duties under this Act including, but not limited to, functions, powers, and duties under sections 28A, 29, 32, 38, 45, and 48, shall take into account **the need for caution in managing adverse effects where there is scientific and technical uncertainty about those effects.**

The Hazardous Substances and New Organisms (Methodology) Order 1998 states:

Approach to risk

Clause 33 When considering applications, the Authority must have regard to the extent to which the following risk characteristics exist:

(a) exposure to the risk is involuntary:

(b) the risk will persist over time:

(c) the risk is subject to uncontrollable spread and is likely to extend its effects beyond the immediate location of incidence:

(d) the potential adverse effects are irreversible:

(e) the risk is not known or understood by the general public and there is little experience or understanding of possible measures for managing the potential adverse effects.

Aggregation and comparison of risks, costs, and benefits

Clause 34 When evaluating the combined impact of risks, costs, and benefits, the Authority must, as far as possible,—

(a) combine groups of risks, costs, and benefits using common units of measurement, including where applicable, monetary valuations; and

(b) use other techniques where common units are not possible, including the identification of dominant risks (being risks that may have a deciding influence), and the ranking of risks in order of significance.

Attachment 5: Article: 'Goat milk could make cheaper cancer drugs'

Source: (Klein, A. (20 June 2020), New Scientist [paywalled], retrieved from https://www.newscientist.com/article/2245887-genetically-modified-goats-can-produce-cancer-drugs-in-their-milk)

Biotechnology

Goat milk could make cheaper cancer drugs

Alice Klein

GOATS can be genetically modified to produce a common cancer drug in their milk, which could slash its production costs.

A team led by Goetz Laible at AgResearch, a government-owned research institute in New Zealand, wanted to find out if it could make the bowel cancer drug cetuximab cheaply and at high volumes by genetically engineering goats to produce the protein in their milk.

The drug, which is sold under the name Erbitux, is a complex protein called a monoclonal antibody that is expensive to make. It costs around £3000 a month for a single patient in the UK.

First, the researchers inserted genes into goat embryos that carried instructions on how to make cetuximab in the mammary glands.

Female goats were then impregnated with the embryos and their genetically modified offspring were born five months later. The offspring were all female and once they began lactating, they were able to produce about 10 grams of cetuximab in each litre of their milk.

Since goats produce about 800 litres of milk every year, this means that each could manufacture multiple kilograms of cetuximab in a year (bioRxiv, doi.org/dzhp).

"The goats were able to produce about 10 grams of a cancer drug in each litre of their milk"

The genetic modification didn't appear to affect the goats' health, says Laible.

Goats producing this amount of cetuximab in a year would be "excellent productivity", says Stephen Mahler at the University of Queensland, Australia.

But we need to be sure that drugs derived from animal milk have the same standard and purity as normal, he says.

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