OFFICE OF THE PRIME MINISTER'S SCIENCE ADVISORY COMMITTEE

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Chief Science Advisor

Hon Dr Wayne Mapp
Minister of Research, Science and Technology

6 October 2010

Dear Minister

With the Prime Minister's consent, you requested me to conduct an inquiry into matters related to the death of transgenic cows at AgResearch's Ruakura facility. The agreed terms of reference are appended.

Because there might have been a perception of a potential conflict of interest given that I have had academic associations with components of AgResearch, albeit not those associated with the matters of this inquiry, I delegated this matter to Dr Alan Beedle, my Chief of Staff, and to Dr Jim Watson FRSNZ, both of whom have expertise pertinent to the issues at hand. Their report is attached.

The report finds no flaws in AgResearch's compliance with the consents and concludes that the experiment had unexpected results in that systemic hormone levels were elevated which led to ovarian hyperstimulation in the animals. The very nature of all research is that unexpected results can occur. And in this experiment, despite the use of a transgenic system that AgResearch had sound scientific reasons to believe would restrict the release of the hormone to milk, the genetic construct behaved differently than expected. This type of unexpected outcome is normative in all forms of research no matter the level of preliminary investigation undertaken. The report notes that animal care was of the highest standard and the animals were under constant veterinary supervision.

The report does, however, point out two matters which in retrospect merit consideration.

1. The research plan was devised to produce a biopharmaceutical for use in human reproductive medicine. Although AgResearch performed a market analysis to test the value proposition, there seems to have been no external scientific review by human reproductive biologists which might have provided a different perspective on the likely clinical value of the product or on the experimental protocol. In my view this is a matter worthy of reflection. Such lack of consultation is now less likely to occur given the CRI reforms you have implemented.

    a. First, the incentives to do this research were largely driven by the performance requirements on CRIs then in place. The restructured objectives of CRIs might place such research in a different context, although the idea of 'biopharming' was at that time and is still of interest to the market.

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b. Secondly, your requirements that CRIs have external Scientific Advisory Boards would likely have meant that the questions that have been raised in this report would have been raised at an earlier stage, possibly leading to a somewhat different protocol design.

c. Thirdly, the devolved authority now given to CRI Boards would mean that such a profile of experimentation would now be subject to Board approval, and a prudent Board may well have sought more information on the case for this protein being expressed.

I should point out that none of these caveats are reflections on the conduct of the experiment, but rather on the rationale for AgResearch doing work focused on human therapeutics without appropriate strategic input.

2. Although blood samples were taken that would, if measured, have alerted the scientists to the 'leaky' nature of the construct, the necessary assay, which is complex, was not available in-house for rapid turnaround. Outsourcing this assay was slow, at least in part because of restrictions imposed by ERMA containment regulations on distribution of samples taken from these transgenic animals. Given that there is no risk of horizontal gene transfer from such samples, the restrictions reflect an emotive rather than scientific approach to controlling molecular experimentation.

The wider New Zealand community has mixed views about research involving genetic modification and this has led New Zealand to have some of the tightest rules around such research. Nothing in my comments or in the attached report should be taken as any implication that transgenic animal research should be more restricted in New Zealand. Indeed, the level of restriction imposed was a factor in the limitations discussed above.

It is obviously important that all research is to the highest ethical and scientific standards, and there is nothing in this series of events to suggest that this was not the case here.

Yours sincerely

Peter

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APPENDIX

TERMS OF REFERENCE FOR CHIEF SCIENCE ADVISOR'S REVIEW OF THE DEATHS OF FSH TRANSGENIC COWS

With the consent of the Prime Minister, the Minister of Research, Science and Technology has asked the CSA to undertake a review consequent on the deaths of three transgenic cows at AgResearch.

I propose to operate the review under the following terms of reference.

1. Did the AgResearch submission to the ethics committee cover all reasonably anticipated scientific issues in inserting human FSH genes into cattle?
2. Was there an appropriate scientific rationale for the experiment?
3. Were the experiments carried out in accord with the required and received animal ethical approvals?
4. Were the complications leading to the deaths anticipatable and, if so, appropriately monitored?
5. What were the causes of death and would have any additional monitoring or interventions reduced the risk complications/death?
6. Were there any further actions that AgResearch should have considered taking after the death of the first calf?
7. Do these events have implications for future large animal transgenic research in New Zealand?
8. Are there any other scientific matters which you would wish to advise me on that arise from this review?

In conducting this review, I am mindful that I have had past research associations with AgResearch. Accordingly I have asked Dr Jim Watson FRSNZ, a distinguished molecular biologist and former President of the Royal Society of New Zealand, and my Chief of Staff, Dr Alan Beedle, a biochemist by background, who has not had any past association with AgResearch, to assist me in this review.

The draft report will be sent to AgResearch for correction of matters of fact before finalisation and forwarding to the Minister.

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