# Annual Report to Environmental Protection Authority

**for**

# Activities under ERMA 200223

# AgResearch Ltd

For the 12 months ending

**30th June 2020**

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**AgResearch Ruakura**
**Animal Containment Facility**

## Contents

## Summary of Activities for the period 1st July 2019 to 30th June 2020

This summary provides the information required by control 11 (Annual reporting) of the HSNO Act approval ERMA200223.

### Outdoor Development Activities

All outdoor development activities being carried out within the Animal Containment Facility at Ruakura comply with the requirements of the ERMA200223 approval.

Cattle, still alive at the end of the reporting period have now only been developed and maintained under the ERMA200223 approval.

Goat development and maintenance activities now only involve animals developed under the ERMA200223 approval.

Cattle, Goat and Sheep activities, other than the maintenance or growing of animals, have been flushing eggs from fertile animals, kidding of goats, lambing of recipient ewes and the transfer of embryos to recipient animals. Semen has been collected from Bucks and Rams for analysis or storage for future use.

Embryo Transfer activities this year have only been in goats or sheep.

These transferred embryos fall within the approved organism description for the ERMA200223 approval and are for either the production of human therapeutic proteins, or for the study of gene function.

All activities have been undertaken with the approval of the Ruakura Animal Ethics Committee.

Further details on development activities are provided within the following Science, Management and Ethics reports.

### Unforeseen adverse effects resulting from the genetic modifications

There have been no unforeseen adverse effects identified during this period.

### 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 and despite further attempts, no progress has been made in resolving this directly to date.

There has again been some informal contact with original monitoring group members and regular contact with Tainui Group Holdings on their development activities for Ruakura.

AgResearch's Manager Māori - Strategy and Engagement who has local affiliations and his team are still working to build a relationship with Ngati - Wairere for Liaison Group and other Ruakura initiatives of interest to Ngati -Wairere and Tainui.

Members of the AgResearch Maori and Animal Science teams did meet in November 2019 with representatives from Waikato Tainui and Maniapoto, principally to discuss a new area of GM animal science. These discussions did include a brief summary of current and previous research projects and consultation history, along with the goal of development of a long-term relationship for constructive consultation. A second meeting was planned for March 2020, but postponed due to Covid -19.

**Additional Supporting Information**

The following reports are supporting information provided to expand on the previous summary and provide evidence of wider compliance with ERMA200223 Controls and MAF/ERMA New Zealand Standard '*Containment Standard for Field Testing of Farm Animals'*.
This additional supporting information is also provided to enable equivalence to the previous annual reporting for the inactive GMF98009 approvals.

## Science Report

### Cattle modified for milk composition

- Cattle were maintained to investigate longevity and potential long-term effects
- The genetic engineered cattle show the same age-related health issues known from conventional cattle with increasing age
- Milk from different transgenic lines is functionally analysed as part of international collaborations

### Generating cattle with lighter coat colour

- The genotype of calves, edited with a naturally occurring sequence variant, were characterised in detail vs non-edited control calves
- The edited calves were fully converted to the intended genotype and no evidence was found for the presence of unintended mutations resulting from the genome editing process
- The genome editing process was optimised to allow the direct introduction of the coat colour dilution variant into in vitro produced embryos at high efficiency
- The genotype of edited embryos was characterised by analysing a biopsy. The biopsied embryos were cryopreserved enabling the exclusive transfer of fully validated embryos to generate live calves.

### Goats producing therapeutic proteins

- The first buck was born for a transgenic goat line that was previously only represented by female goats
- Semen was collected, processed and cryopreserved to capture the unique genetics and facilitate future breeding activities
- The number of integrated transgene copies were accurately determined by digital droplet PCR for two therapeutic antibody producing goat lines

### Goats producing female-only offspring

- We isolated sequence-verified knockin (KI) clonal strains, carrying a proprietary Y-chromosome inserted transgene for sex ratio-distortion, as donors for cloning by somatic cell transfer (SCT). Following SCT and embryo transfer, we slaughter-recovered 2 fetuses from one doe. Rejuvenated KI strains from each fetus were used for Cre recombinase-mediated excision of the loxP-flanked reporter sequences.

### Generating germline-complemented sheep and fertile founders for breeding sterile hosts

- Primary male Texel adult ear fibroblasts (TAEFs) were derived from genetically elite animals and used as donor cells for SCT (Group 1). As TAEF elite donors are genetically wild-type with respect to *NANOS2*, they can rescue the germline of sterile *NANOS2-/-* host rams through embryo complementation. Accordingly, TAEF donor embryos were combined with *NANOS2*$^{-/-}$ OFF3

hosts to generate chimaeric embryos (Group 2). To provide a long-term steady supply of sterile host embryos, we produced *NANOS2*-edited male heterozygous (Group 3) and female homozygous cell lines (Group 4) from composite OFF3 and Poll-Dorset fetal fibroblasts (PDFF3), respectively. Two heterozygous edited male strains and one homozygous female cell strain, as well as non-edited parental control PDFF3 cells (Group 5), were used for SCT. Resulting embryos were transferred into recipients. Pregnancies were established with exceptionally high efficiencies (32-50%) across all five groups. Viable lambs were obtained from all five genotypes, which are presently being phenotyped.

- Female *NANOS2*$^{-/-}$ and male *NANOS2*$^{+/-}$ cloned lambs were analysed for their testis phenotype, compared to OFF3 and TAEF wild-type controls. Ovaries of *NANOS2*$^{-/-}$ females appeared histologically normal and contained similar numbers of follicles at comparable developmental stages. In males, testis cords contained histologically normal somatic support cells and similar numbers of spermatogonia, indicating that heterozygote males are likely to be suitable for breeding.

**Generating immune-compatible sheep for xenotransplantation**

- *GGTA* and *CMAH* genes were knocked out by genome editing in male and female ovine fetal fibroblasts (OFFs) and used for SCT.
- OFF double knockout-derived cloned blastocysts were obtained from *GGTA*/*CMAH* null donor cells.
- Following SCT into abattoir-derived oocytes, blastocysts were transferred and at day 35 of development, ultrasonography scanning confirmed viable pregnancies.
- 5 female lambs were born and are currently being confirmed for loss of α-Gal and Neu5Gc. None of the male lambs survived.

**Generating anephrogenic sheep fetuses for xenotransplantation**

- *SALL1* was knocked out in *GGTA* and *CMAH* male cell lines to disrupt kidney development in sheep fetuses. Fetuses were recovered at D48 and showed variable phenotypes with renal hypoplasia.
- *SALL1* wild-type donor fibroblasts with an RFP reporter gene were generated and used for embryo complementation with *SALL1* knockout hosts. Recovered fetuses on D48 showed variable RFP chimaerism and partial kidney rescue.
- Overall, this suggests that the kidney niche in *SALL*$^{-/-}$ males is vacant but intact and can be partially rescued by embryo complementation

**Overexpression of the histone demethylase KDM4B in transgenic cattle**

- One female animal that overexpresses the histone demethylase KDM4B was sampled and confirmed to inducibly overexpress the GFP reporter transgene. This animal (#1801) has premature mammary development but is otherwise showing no abnormalities.
- To reduce potential damage of the udder through lactation, she was not put in calf but will be used for ovum pick-up based breeding at a later stage.

# On Farm Management Summary for year ending 30/06/2020

**Animal Numbers 01/07/2019– 30/06/2020** (Births exclude still born or animals which die soon after birth reported in Animal Ethics Reports, Aged In and Out records changes in animal age[1])

| Stock Class | Open (1/07/19) | Births | Transfer In | Transfer Out | Aged In | Aged Out | Killed | Deaths | Closing (30/06/20) |
|---|---|---|---|---|---|---|---|---|---|
| **Casein (ERMA200223)** | | | | | | | | | |
| MA Cows | **2** | | | | | | 2 | | **0** |
| **Total Casein** | **2** | **0** | **0** | **0** | **0** | **0** | **2** | **0** | **0** |
| | | | | | | | | | |
| **MBP (ERMA200223)** | | | | | | | | | |
| **Total MPB** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | | | | | | | | | |
| **rhLF (ERMA200223)** | | | | | | | | | |
| **Total rhLF** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | | | | | | | | | |
| **BLg - (ERMA200223)** | | | | | | | | | |
| MA Cows | **16** | | | | 3 | | 3 | | **16** |
| R2yr Heifers | **3** | | | | | 3 | | | **0** |
| **Total BLg -** | **19** | **0** | **0** | **0** | **3** | **3** | **3** | **0** | **16** |
| | | | | | | | | | |
| **Erbitux (ERMA200223)** | | | | | | | | | |
| **Total Erbitux** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | | | | | | | | | |
| **Coat Colour (ERMA200223)** | | | | | | | | | |
| **Total Coat Colour** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | | | | | | | | | |
| **KDM4B (ERMA200223)** | | | | | | | | | |
| R2yr Heifer | **0** | | | | 1 | | | | **1** |
| R1yr Heifer | **1** | | | | | 1 | | | **0** |
| **Total KDM4B** | **1** | **0** | **0** | **0** | **1** | **1** | **0** | **0** | **1** |
| | | | | | | | | | |
| **Conventional Cattle** | | | | | | | | | |
| MA Cows | **36** | | | | 0 | | 8 | | **28** |
| R2yr Heifers | **0** | | | | | | | | **0** |
| Other classes | **64** | | 0 | 5 | | | 1 | 1 | **57** |
| Total Conventional | **100** | **0** | **0** | **5** | **0** | **0** | **9** | **1** | **85** |
| | | | | | | | | | |
| **Cattle Total** | **122** | **0** | **0** | **5** | **4** | **4** | **14** | **1** | **102** |
| | | | | | | | | | |
| **Cattle developed under ERMA approvals (Tg and non Tg progeny)** | | | | | | | | | **17** |
| | | | | | | | | | |

[1] Aligns with normal livestock reconciliation aging practice.

| Stock Class | Open (1/07/19) | Births | Transfer In | Transfer Out | Aged In | Aged Out | Killed | Deaths | Closing (30/06/20) |
|---|---|---|---|---|---|---|---|---|---|
| **Goats** | | | | | | | | | |
| | | | | | | | | | |
| **Erbitux & Enbrel (ERMA200223)** | | | | | | | | | |
| Ma Doe | **23** | | | | 5 | | 2 | | **26** |
| R2yr Doe | **5** | | | | 1 | 5 | | | **1** |
| R1yr Doe | **1** | | | | | 1 | | | **0** |
| Doe Kid | **0** | | | | | | | | **0** |
| Buck Kid | **0** | 1 | | | | 1 | | | **0** |
| R1yr Male + | **4** | | | | 1 | | 5 | | **0** |
| Total Erbitux & Enbrel | **33** | **1** | **0** | **0** | **7** | **7** | **7** | **0** | **27** |
| | | | | | | | | | |
| **non Med inherit (ERMA200223)** | | | | | | | | | |
| Total TCR | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | | | | | | | | | |
| **Conventional Goats** | | | | | | | | | |
| MA Doe | **30** | | | | | | 7 | | **23** |
| R2yr Doe | **0** | | | | | | | | **0** |
| R1yr Doe | **0** | | | | | | | | **0** |
| Male R1yr + | **0** | | | | | | | | **0** |
| Kids | **0** | | | | | | | | **0** |
| Total Conventional | **30** | **0** | **0** | **0** | **0** | **0** | **7** | **0** | **23** |
| | | | | | | | | | |
| **Goat Total** | **63** | **1** | **0** | **0** | **7** | **7** | **14** | **0** | **50** |
| | | | | | | | | | |
| **Goats developed under ERMA approvals (Tg and non Tg progeny)** | | | | | | | | | **27** |

| Stock Class | Open (1/07/19) | Births | Transfer In | Transfer Out | Aged In | Aged Out | Killed | Deaths | Closing (30/06/20) |
|---|---|---|---|---|---|---|---|---|---|
| **Sheep** | | | | | | | | | |
| | | | | | | | | | |
| **AI on Hooves** | | | | | | | | | |
| R1yr Ewe | **0** | | | | 12 | | | | **12** |
| Ewe Lamb | **0** | 15 | | | | 12 | 2 | 1 | **0** |
| R2yr Ram | **0** | | | | 2 | | | | **2** |
| R1yr Ram | **2** | | | | 3 | 2 | 1 | | **2** |
| Ram Lamb | **0** | 4 | | | | 3 | 1 | | **0** |
| Total | **2** | **19** | **0** | **0** | **17** | **17** | **4** | **1** | **16** |
| | | | | | | | | | |
| **Conventional Sheep** | | | | | | | | | |
| MA Ewes | **40** | | | | 60 | | 12 | 4 | **84** |
| 2th Ewes | **119** | | | 3 | | 60 | 54 | 2 | **0** |
| Ewe Hgts | **0** | | | | 4 | | | | **4** |
| Ewe Lamb | **0** | 5 | | | | 4 | | 1 | **0** |
| R1yr Ram | **0** | | | | 7 | | | | **7** |
| Ram Lamb | **0** | 7 | | | | 7 | | | **0** |
| Total Conventional | **159** | **12** | **0** | **3** | **71** | **71** | **66** | **7** | **95** |
| | | | | | | | | | |
| **Sheep Total** | **161** | **31** | **0** | **3** | **88** | **88** | **70** | **8** | **111** |
| | | | | | | | | | |
| **Sheep developed under ERMA approvals (Tg and non Tg progeny)** | | | | | | | | | **16** |

The preceding tables provide animal numbers by species over the reporting period in the development lines and are linked to the EPA approval. This includes transgenic and non-transgenic animals (progeny) and the conventional animals which are used to support the programmes.

For cattle there has been one movement of conventional animals out of the facility during the period. This was 5 steers of 64 conventional beef animals, under 2 years of age on the facility for grass control purposes. There have been no movements of cattle into the facility.

14 cattle of varying ages have been euthanased (killed) and 1 of the grazing, a heifer died; these animals have been disposed of in offal holes on-site, having been identified as surplus or now unsuitable animals, or following veterinary advice during this period.

For goats there has been no movement of animals onto or from the facility (apart from approved exit and returns for surgery purposes) during the period.

14 goats of varying ages have been euthanased (killed) and no goats died during the period; these animals have also been disposed of in offal holes on-site, as now surplus or unsuitable animals, or following veterinary advice.

For sheep there has been only one movement of 3 conventional animals out of the facility as unsuitable for use as a recipients and the approved exit and returns for surgery purposes during the period.

70 sheep of varying ages have been euthanased (killed) and 7 sheep died during the period; these animals have also been disposed of in offal holes on-site, as unsuitable animals, during slaughter recovery at lambing or following veterinary advice.

For management purposes, as previously identified, the facility is treated as a separate small farm within the main Ruakura Farm. It is fully self-contained apart for some machinery requirements and specialist staffing.

Covid 19 Level 4 and 3 restrictions only impacted staff or science activities, animal care and welfare requirements continued as normal, with supplementary feeding as dry conditions impacted grass growth during this period. Animals on the facility continue to be managed in a way which aligns with normal farming practice in New Zealand, grazing outdoors on pasture.

This consists of daily shifts and restricted intakes depending on the age of the animal and its feed requirements. Examples are stage of pregnancy, lactating or rearing calf or kid, empty, young growing animals, etc.

No cattle, 11 goat and 156 sheep recipients have been used for ET (embryo transfer), with some of the grazing Heifers being mated with artificial insemination during the period to calve later in 2020, to then be available as future recipients. All animals are regularly monitored for live weight and health status.

All animals graze mainly on pasture, with some crops, supplementary feeding of hay, balage or concentrates when required.

Goats can at times receive a higher proportion of their daily intake as supplementary feed, as concentrates, to reduce their impact on pasture availability for cattle and often have access to covered shelter in inclement weather.

Surplus pasture is conserved when possible for use in periods of low growth, as balage or hay and there was only minimal purchasing of extra supplement (meal) required this season, mainly due to lower animal numbers which enabled maintenance of an adequate annual feed supply.

Regular pasture renewal is carried out with at least 10% of the facility receiving some form of renovation annually. Mineral supplementation is carried out using a mineral dispensing system through the water troughs for assisting Facial Eczema control and other normal mineral deficiencies during identified periods of risk, as occurs on many farms.

Maintenance fertiliser applied this season contained no nitrogen and no selective additional Nitrogen (Urea) has been used on areas not used for milk/waste irrigation during the year.

**Milk Production 19/20 season**

No GM cows were calved at all or specifically for seasonal milk production again this year.

The GM goat which kidded feed her kid.

This has meant there was again no milk stored this year for surplus disposal by irrigation to pasture.

**Ruakura Animal Ethics Committee Reports**

## RAEC # 14510 - Maintenance of Cattle on the Animal Containment Facility

### Ruakura Animal Ethics Committee Report: Third Quarter 2019

### Transgenic Cattle

Summarised below are the animal numbers and animal health status of the various cattle groups for the reporting interval July to September 2019 according to the conditions for approval of Application 14510 Maintenance of cattle on the Animal Containment Facility.

**A) Casein Plus cattle**

**A.1 Animal numbers**
2, no change

**A.2 Health status**
No health issues during reporting period

**B) Beta-lactoglobulin (BLG) knockdown/knockout cattle**

**B.1 Animal numbers**
19, no change

**B.2 Health status**
No health issues during reporting period

**C) KDM4B cattle**

**C.1. Animal numbers**
1, no change

**C.2 Health status**
No health issues during reporting period

**D) Conventional recipient cattle**

**D.1. Animal numbers**
41, no change

**D.2. Health status**
No health issues during reporting period

All Cattle (GM + Conventional) received annual vaccinations (BVD, B12, Covexin, Lepto) and a drench during July.

**Ruakura Animal Ethics Committee Report: Fourth Quarter 2019**

**Genetically Engineered Cattle**

Summarised below are the animal numbers and animal health status of the various cattle groups for the reporting interval October to December 2019 according to the conditions for approval of Application 14510 Maintenance of cattle on the Animal Containment Facility.

**A) Casein Plus cattle**

**A.1 Animal numbers**
2, no change

**A.2 Health status**
No health issues during reporting period

**B) Beta-lactoglobulin (BLG) knockdown/knockout cattle**

**B.1 Animal numbers**
19, no change

**B.2 Health status**
No health issues during reporting period

**C) KDM4B cattle**

**D.1. Animal numbers**
1, no change

**D.2 Health status**
Premature udder development. The plan was to AI Wonky but due to the abnormal udder development it was decided to not have her undergo a lactation.

**D) Conventional recipient cattle**

**E.1. Animal numbers**
41, no change

**E.2. Health status**
No health issues during reporting period

**Ruakura Animal Ethics Committee Report: First Quarter 2020**

**Genetically Engineered Cattle**

Summarised below are the animal numbers and animal health status of the various cattle groups for the reporting interval January to March 2020 according to the conditions for approval of Application 14510 "Maintenance of cattle on the Animal Containment Facility".

**A)Casein Plus cattle**

**A.1 Animal numbers**

2, no change

**A.2 Health status**
1434 (6 y/o)- chronic intermittent lameness affecting all four limbs- suspected arthritis

**B)Beta-lactoglobulin (BLG) knockdown/knockout cattle**

**B.1 Animal numbers**
19, no change

**B.2 Health status**
1503 underweight relative to cohorts, otherwise bright. Bloods normal. Annual health checks due to be completed in April 2020.

**C) KDM4B cattle**

**C.1. Animal numbers**
1, no change

**C.2 Health status**
Enlarged udder noted, not lactating. Otherwise well.

**D) Conventional recipient cattle**

**D.1. Animal numbers**
41, no change

**D.2. Health status**
No health issues during reporting period. Annual health checks due.

**Ruakura Animal Ethics Committee Report: Second Quarter 2020**

**Genetically Engineered Cattle**

Summarised below are the animal numbers and animal health status of the various cattle groups for the reporting interval April to June 2020 according to the conditions for approval of Application 14510 "Maintenance of cattle on the Animal Containment Facility".

**A) Casein Plus cattle**

**A.1 Animal numbers**
Initially 2, 2 euthanised due to age related health issues

**A.2 Health status**
Health issues of euthanised cows:
1434 - Chronic intermittent lameness
1656 - early cancer eye

**B) Beta-lactoglobulin (BLG) knockdown/knockout cattle**

**B.1 Animal numbers**
Initially 19, 2 euthanised due to health issues, 1 euthanised due to being nervous and hard to work with

**B.2 Health status**
Health issues of euthanised cows:
1503- lost weight relative to other cattle, ran bloods which were normal. Unsure for the loss of weight, perhaps struggled with the drought.
1510- early cancer eye (ocular squamous cell carcinoma left eye only at this stage).
1704- Nervous disposition leading to temperament problems and handling difficulties**.**

**C) KDM4B cattle**

**C.1. Animal numbers**
1, no change

**C.2 Health status**
Enlarged udder still present, though now has 'deflated' slightly- doesn't appear to be causing her any concern.

**D) Conventional recipient cattle**

**D.1. Animal numbers**
Initially 41, 13 euthanised due to age related health issues - early cancer eye (small lesions) and a hip injury.

**D.2. Health status**
No health issues during reporting period

## **RAEC #14834 -** Maintenance, Breeding, Production and Characterisation of Transgenic Goats

**Ruakura Animal Ethics Committee Report: Third Quarter 2019**

**Genetically Engineered Goats**

Summarised below is the status of the various goat groups and their offspring and any losses that have occurred during the reporting interval July to September 2019, in relation to the conditions for approval of Application 14834 " Maintenance, Breeding, Production and Characterisation of Transgenic Goats ".

**Biosimilars**

**A) Erbitux Goats**

**A.1 Animal numbers**
Initially 29 (25 females, 4 males)

**A.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period. Three goats were treated for scald/footroot.

**B) Enbrel Goats**

**B.1 Animal numbers**
Initially (4 females, 0 males)

1 male kid born 2/7/19

**B.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period

**C. Recipients**

**C.1. Animal numbers**
Initially (30 females, 0 males)

**C.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period. Three goats were treated for scald/footrot.

**Ruakura Animal Ethics Committee Report: Fourth Quarter 2019**

**Genetically Engineered Goats**

Summarised below is the status of the various goat groups and their offspring and any losses that have occurred during the reporting interval October to December 2019, in relation to the conditions for approval of Application 14834 " Maintenance, Breeding, Production and Characterisation of Transgenic Goats ".

**Biosimilars**

**A) Erbitux Goats**

**A.1 Animal numbers**
Initially 29 (25 females, 4 males)

**A.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period. Three goats were treated for scald/footrot- recovered.

**B) Enbrel Goats**

**B.1 Animal numbers**
Initially 5 (4 females, 1 male)

**B.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period

**2. Recipients**

**C.1. Animal numbers**
Initially (30 females, 0 males)

3 goats were euthanased for health issues: contracted fetlock, mastitis and skinny/poor feet.

1 goat died under GA for ET procedure- covered in adverse event 146 on application 14642.

Two goats were slaughtered to recover fetuses for 14642

**C.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period. Three goats were treated for scald/footrot- recovered. 16 goats were synchronised and 15 underwent ET surgery- covered by 14642

**Ruakura Animal Ethics Committee Report: First Quarter 2020**

**Genetically Engineered Goats**

Summarised below is the status of the various goat groups and their offspring and any losses that have occurred during the reporting interval January to March 2020, in relation to the conditions for approval of Application 14834 " Maintenance, Breeding, Production and Characterisation of Transgenic Goats ".

**Biosimilars**

**A) Erbitux Goats**

**A.1 Animal numbers**
29 (25 females, 4 males)

**A.2 Treatments and activities during reporting interval**
Attempts to collect semen by AV for three 2018 bucks failed as they showed no interest. Bucks were run next to does to raise their interest prior to a repeat collection. This had to be postponed due to COVID-19 lockdown.
All have had routine animal health treatments and hoof care during the period

**B) Enbrel Goats**

**B.1 Animal numbers**
Initially 5 (4 females, 1 male)

**B.2 Treatments and activities during reporting interval**
Semen collection by AV from the single buck was attempted but quality of semen sample was not sufficient for freezing. However, there was confidence to receive a good sample in a repeat collection. The repeat was planned but had to be postponed due to COVID-19 lockdown.
All have had routine animal health treatments and hoof care during the period

**2. Recipients**

**C.1. Animal numbers**
Initially (24 females, 0 males)

**C.2 Treatments and activities during reporting interval**
1 doe was euthanased on humane grounds due to an enlarged udder and poor foot health/conformation
All have had routine animal health treatments and hoof care during the period

**Ruakura Animal Ethics Committee Report: Second Quarter 2020**

**Genetically Engineered Goats**

Summarised below is the status of the various goat groups and their offspring and any losses that have occurred during the reporting interval April to June 2020, in relation to the conditions for approval of Application 14834 " Maintenance, Breeding, Production and Characterisation of Transgenic Goats ".

**Biosimilars**

**A) Erbitux Goats**

**A.1 Animal numbers**
Initially 29 (25 females, 4 males)
4 bucks euthanised as no longer required after collection and storage of semen

**A.2 Treatments and activities during reporting interval**
Collection of semen by AV for three 2018 bucks was repeated. The two additional attempts resulted in successful collection of sperm with suitable quality for freezing from two bucks.
All bucks were euthanised as sufficient semen straws could be frozen to capture the unique genetics of the two Erbitux lines.
All have had routine animal health treatments and hoof care during the period

**B) Enbrel Goats**

**B.1 Animal numbers**
Initially 5 (4 females, 1 male)
1 buck euthanised as no longer required after collection and storage of semen
2 Does euthanised on veterinary advice for health reasons

**B.2 Treatments and activities during reporting interval**
Semen collection by AV from the single buck was attempted two more times. Small numbers of semen straws, meeting quality requirements, could be frozen and stored. As the frozen straws now secure the genetics for any future breeding requirements, the buck was euthanised.

All have had routine animal health treatments and hoof care during the period

**C) Recipients**

**C.1. Animal numbers**
Initially (23 females, 0 males)

**C.2 Treatments and activities during reporting interval**
All have had routine animal health treatments and hoof care during the period

# RAEC #14696 – AI-on-hooves: generating healthy NANOS2-deficient sheep for breeding sterile host embryos.

### Ruakura Animal Ethics Committee Report: 3rd Quarter 2019

### Genetically Modified Sheep

Summarised below is the status of the various sheep groups during the reporting interval July 2019 to 30 September 2019 in relation to the conditions for approval of Application 14696.

We report D35 scan for the following 5 groups:
1) NANOS2-/- female (for sterile host embryo breeding), representing cell strains 6, 8, 22 and 62
55 embryos into 19 recipients (including 23 vitrified into 7 recipients), 1 ewe died due to unknown causes. Pregnant: 17/55=31%
2) NANOS2+/- male (for sterile host embryo breeding), representing cell strains 72 and 127
43 embryos into 15 recipients (including 25 vitrified into 9 recipients). Pregnant: 15/43=35%
3) PDFF wild-type (for commercial proof-of-principle), one pregnancy was aborted to study wild-type fetal kidney development.
45 embryos into 14 recipients (including 37 vitrified into 11 recipients). Pregnant: 18/45=40%
4) TAEF wild-type (for commercial proof-of-principle),
22 embryos into 8 recipients (all vitrified), 1 ewe died due to unknown causes. Pregnant: 11/22=50%
5) OFF3 (#12)<>TAEF chimaeras (for commercial proof-of-principle)
74 embryos into 24 recipients (including 46 vitrified into 15 recipients). Pregnant: 24/74=32%

### Ruakura Animal Ethics Committee Report: 4th Quarter 2019

### Genetically Modified Sheep

Summarised below is the status of the various sheep groups during the reporting interval September 2019 to 30 December 2019 in relation to the conditions for approval of Application 14696.

We have reviewed our current lambing procedures and found a limited response to hormonally induced parturition in recipient ewes. This frequent lack of observing stage 2 labour in recipient ewes makes natural delivery an increasingly unlikely option. Instead, we had better success with recovering lambs by C-section recovery, following euthanasia of the ewe. This recovery was successful at different time points following hormonal induction (24, 48 and 72h) but recent preliminary evidence suggests that it might be beneficial to shorten the time between induction and recovery to minimise fetal distress resulting from in utero meconium inhalation. Based on these observations, we proposed to move from default natural delivery to default C-section recovery, preferably recovering within 12-24 hours after the strongest hormonal DEX dose for induction.
Since modifying our recovery procedure, we have observed improved cloned lamb survival. We have been recovering 10 lambs from 3 different genotypes, including two GGTA/CMAH, as well as two NANOS2 double knockout edited female lambs and three non-edited wild-type animals. The latter two groups were derived from the Poll-Dorset genotype that had not been previously tested for somatic cell cloning. Overall, the revised protocol has resulted in 8 surviving lambs (80% survival at birth), with the remaining 2 lambs showing hydrops symptoms resulting in their demise. From the 8 viable lambs, 2 had to be euthanized for possibly cloning-unrelated reasons, one was naturally delivered in the early morning without being noticed and subsequently trampled on by another ewe housed in the same enclosure. This resulted in a fractured jaw, which could not be remedied. Another lamb had a broken rib that punctured the left lung, which again could not be remedied. Both lambs were euthanized.

**Ruakura Animal Ethics Committee Report: 1st Quarter 2020**

**Genetically Modified Sheep**

Summarised below is the status of the various sheep groups during the reporting interval January 2020 to 30 March 2020 in relation to the conditions for approval of Application 14696.

We have been monitoring survival of the different lamb genotypes so far produced, namely 1) homozygote NANOS2-/- female cell clones, 2) TAEF and PDFF wild-type controls. We also produced viable heterozygote NANOS2+/- males and aggregation TAEFxOFF3 NANOS2-/- chimaera lambs. Overall, we have produced viable lambs from all targeted genotypes. The results are tabulated below:

Cell line gene Term Born alive Alive 24 h Alive 1 wk Alive 1 mo % survival (of born)
AI control WT 4 4 4 4 4 100%
OFF3 NANOS+/-6 6 2 2 1 17%
OFF3<>TAEF2 KO<>WT 8 11 1 1 1 9%
PDFF3 NANOS-/-6 7 6 4 4 57%
PDFF3 WT 10 11 7 7 5 45%
TAEF WT 3 3 1 1 1 33%

The viability of lambs appeared to depend on the donor cell genotype, in line with previous observations, but insufficient to be statistically significant. We are now closely monitoring the surviving lambs, especially the precious single heterozygote NANOS2 male (Howie) and single putative chimaera lamb (Hoss), managing any potential problems as close as possible.

COVID-19
Phenotyping of absolute transmitters and other genotypes has been delayed by the time of the lockdown due to lack of lab and animal access. With respect to the two OFF3-derived NANOS2 rams, Bunter (*17/09/2018) and Hammer (*18/10/2018), both are alive and well. Their weight and scrotal circumference have been in regular intervals and there was one attempt to collect semen from them via artificial vagina (via ABS), which is to be repeated next breeding season to confirm their sterility and absence of viable sperm.

**Ruakura Animal Ethics Committee Report: 2nd Quarter 2020**

**Genetically Modified Sheep**

*No report submitted to the Ruakura Animal Ethics Committee*

**MPI Verification Services Audit reports**

Ministry for Primary Industries
Manatū Ahu Matua

# Verification Report[1]

| | |
|---|---|
| **Report ID:** | PBV/2501/2019/02 |
| **Outcome:** | **Unacceptable** |
| **Issued to:** | AgResearch - Ruakura Campus |
| **Operator ID(s):** | 2501 |
| **Issued by:** | Crystal Lange<br>**Phone:** 079578319<br>**Email:** crystal.lange@mpi.govt.nz |
| **Verification Period:** | 2019-02-14 to 2019-09-09 |
| **Verification Date:** | 2019-08-28 |
| **Published:** | 2019-08-28 10:10 |
| **Next Due Date:** | 2019-11-28 |
| **Level/Step:** | **5.1** (started on 6.2 , and ceiling is 6 ) |
| **Report Type:** | Scheduled |
| **Peer Reviewed By:** | Craig Mason |

1 A Verification Report is a formal report issued when sufficient evidence has been assessed to arrive at an outcome for a verification period. This report may contain Technical Reviews and external audit findings completed during the period. Inadequate and/or untimely responses to deficiencies identified in this report, poor/unacceptable performance, or failure to pass subsequent audits may result in the escalating imposition of sanctions and/or interventions provided by law.

## 1. Premises Profile

AgResearch - Ruakura Campus is, under section 39 of the Biosecurity Act 1993, approved as a Transitional and Containment Facility in accordance with the requirements of the MPI/EPA standard(s) identified. Under section 40 of the Biosecurity Act, Tom Richardson is approved as an operator of that facility and is primarily responsible for the facility, compliance with facility approvals and all activities involving risk goods.

The standards that the facility is approved to specify the structural and operating requirements for containment and/or transitional facilities holding regulated organisms and risk goods that are, or may contain:

- Agricultural Compounds
- Animals
- Animal Products
- Biologicals
- Miscellaneous
- Non-risk Goods
- Plant Products

**Physical Address :**
10 Ruakura Campus Bisley Road, Ruakura, Hamilton

## 2. Executive Summary

This was a scheduled and announced inspection of the AgResearch transitional and containment facility at Ruakura in Hamilton. The objective of this visit was to verify compliance with the facility manual, the standards identified in the "Biosecurity" section of this report, and the facility and operator approvals as held under the Biosecurity Act 1993.

The inspection undertaken July 30 and August 20 2019 had an UNACCEPTABLE outcome with one critical area of non-compliance being reported (unapproved transfer). A separate Non Compliance Report (NCR) was generated as a result of the critical non-compliance and a Root Cause Analysis (RCA) completed. 2501/2019/01 has been sent as an attachment to this report. This non-compliance has been closed, however due to the unacceptable outcome the external audit frequency has been increased (Step Drop) to three monthly. I believe this will be beneficial to the training of the new Facility Manager as closer monitoring of transfers, registers and structural compliance will catch rising issues early.

In addition to the above, one major (traceability) and two minor non compliances (hygiene and repairs and maintenance) with the MPI standards were noted during the audit. Corrective Action Requests (CAR) were issued and the major non-compliance has since been closed. The non compliance from the previous inspection was confirmed as closed during the inspection of Dairy Science.

If non-compliance is not addressed in a timely manner or is ongoing, MPI interventions could include infringement notices, compliance orders, increased inspection frequency, facility suspension or cancellation of the Operator approval.

## 3. Operator Summary

The entry and exit meeting along with the reality check of the Small Animal Containment (SAC), (July 30 2019) was conducted by Crystal Lange (MPI) with Genevieve (Gen) Sheriff (incoming site Facility Manager) and Ric Broadhurst (exiting SAC Manager), the Animal Containment Farm (ACF); August 20 with Tim Hale (Farm Manager) and Planthouse and laboratories (August 20); with Gen Sheriff. Containment areas (animal, plant and laboratory) were inspected, records for inventory, movement authorities and autoclave efficacy validation were reviewed. One significant change to health and Safety is the additional hazard of the access road to the ACF is now shared with the construction zone for the new water reservoir. Hi-viz is required when accessing this area by foot.

Crystal's authority of appointment (warrants) under the Biosecurity and Hazardous Substances and New Organisms (HSNO) Act were presented and displayed.

During this audit period the site Operating Facility Manger resigned and Gen Sherriff was appointed (Delegated Authority) as the Containment Facility Manager for Ruakura. Gen has attended audits in Hamilton and Palmerston North as part of her knowledge based training for this role.

## 4. Verification Completed (this period)

### Biosecurity

Good compliance was noted for animal containment (small and large). Structural and hygiene issues were noted for Plants and laboratory based (Biological Products and Microorganisms) standards. A critical issue was reported for the Microorganism and Cell Culture standard.

The following elements were verified in this PBV period:

| | |
|---|---|
| Biosecurity:Containment Facilities for Plants: 2007 | Acceptable |
| Biosecurity:Containment Facilities for Vertebrate Laboratory Animals | Acceptable |
| Biosecurity:Containment Standard for Field Testing of Farm Animals | Acceptable |
| Biosecurity:Facilities for Microorganisms and Cell Cultures: 2007a | Acceptable |
| Biosecurity:Transitional Facilities for Biological Products | Acceptable |
| Biosecurity:Transitional and Containment Facilities for Invertebrates | Acceptable |

### Quality Assurance

Genevieve has established a support network with staff at Grasslands. The facility manual needs to be updated following the departures of facility managers and authorised signatories: Marty Donnison and Ric Broadhurst, so that staff can identify the relevant contact persons.

Internal audits were reviewed for Small Animal Containment ((SAC) 16/7/19), Animal Containment Farm ((ACF) 22/06/2019), Glasshouse and research laboratories (May 2019). The SAC and ACF audits were thorough and included animal inventories and good supporting evidence. The Glasshouse and laboratories audits were superficial and solely focused on physical structures. Genevieve has attended internal audits at Grasslands as part of her training so it is expected that future audits will be appropriately robust. Presentations from the MPI Operator Workshop held March 2019 were also provided post inspection to provide additional guidance for internal audit improvement and as training material for Gen.

Site training for staff had been conducted across the site in group sessions; March to June 2019.

The following elements were verified in this PBV period:

| | |
|---|---|
| Quality Assurance:Biosecurity Contingency Plans | Acceptable |
| Quality Assurance:Chief Technical Officer (CTO) Permissions and Decisions | Acceptable |
| Quality Assurance:Operating Procedures | Acceptable |
| Quality Assurance:Operator Control | Acceptable |
| Quality Assurance:Operator Internal Verification | Acceptable |

The following elements were verified in this PBV period:

| | |
|---|---|
| Quality Assurance:Organizational Structure and Management | Acceptable |
| Quality Assurance:Risk Assessments | Acceptable |
| Quality Assurance:Training and Competency of Personnel | Acceptable |

## Documentation and Certification

Animal import, quarantine, breeding and health records were available in either hard or electronic copy. BACCs and copies of transfer forms were held. One copy held of a transfer, was not the MPI approved copy for CL11136. Several transfers while approved, had not been confirmed as completed. Genevieve has followed up and all transfers have been confirmed, the Receipt Checklists completed and the MPI approved from supplied by the recipient. Staff need to be aware that transfer events under a multiple transfer still need to be reported on each occasion for tracking purposes.

The following elements were verified in this PBV period:

| | |
|---|---|
| Documentation and Certification:Biosecurity Authority Clearance Certificates (BACCs) | Acceptable |
| Documentation and Certification:Documentation and Record Keeping | Acceptable |
| Documentation and Certification:Site Plans, Specification and Modifications | Acceptable |

**Subject:** Documentation and Record Keeping

Note List:

[Crystal Lange]

**This issue is now closed.**

A tenant had an approved single movement transfer (EM1216). Multiple transfers took place and more were planed after the noted completion date. There was no traceability for these transfers. This incident is a major non compliance.

A number of transfers in the register (single and multiple) had not been confirmed to the Facility Manager. AgResearch would be prudent to review the services provided to its tenants and its own accountability for the actions of these tenants.

NON COMPLIANCE
Failure to comply with the facility manual (4.2) and MPI Standard for Biological products (4.8). Transfer without current approval and failure to notify of transfer under a multiple transfer.

CORRECTIVE ACTION REQUEST

1. Ensure all transactions are covered by an appropriate transfer request
2. Ensure staff are aware of transfer limitations (e.g single / multiple)
3. Ensure all movements under a multiple transfer are recorded on the site database.

Transfer CM3578 obtained. CLOSED August 22 2019.

Ongoing non compliance will result in the cancellation of multiple transfers, all movements will then require approval prior to each transaction.

## Identification, Traceability & Management

Biological products registers are maintained centrally, cell culture collections are maintained by Agresearch staff or site tenants. The recently implemented receipt checksheet has assisted traceability of product when key users are absent.

Cage card checks and inventory reconciliation undertaken in the SAC and goat and sheep indentification techniques confirmed at the ACF.

The following elements were verified in this PBV period:

| | |
|---|---|
| Identification, Traceability & Management:Authorised Signatories | Acceptable |
| Identification, Traceability & Management:Inventory Control and Accuracy | Acceptable |
| Identification, Traceability & Management:Product and Organism Identification | Acceptable |
| Identification, Traceability & Management:Segregation | Acceptable |
| Identification, Traceability & Management:Transfer of Goods and Organisms | Unacceptable |
| Identification, Traceability & Management:Transport of Risk Goods and Organisms | Acceptable |

**Subject:** Transfer of Goods and Organisms

Note List:

[Crystal Lange]

**This issue is now closed.**

During the process of writing this report a planned transfer of Genetically Modified Organisms (GMO) took place at short notice. A transfer application had not been submitted and it wasn't until the samples were on the courier that the oversight was noted. An unapproved transfer is a critical non compliance.

The MPI supervisor was notified immediately of unapproved transfer. Samples were confirmed as received and held securely by recipient. Shipper also rang MPI to discuss the incident.

NON COMPLIANCE
Failure to comply with the requirements of section 52d of the Biosecurity Act, control 9 of the HSNO Act Approval (APP201857 and APP201858), section 4.4 of the EPA Standard: Facilities for Microorganism and Cell Cultures (section 8.8) and section 4.2 of the containment manual.

CORRECTIVE ACTION REQUIRED
7. Obtain retrospective Transfer Approval.
8. Complete Root Cause Analysis (CAR 2501/2019/01).
9. Ensure staff have been retrained in correct transfer procedure.

RCA supplied and training confirmed 23/08/2019. Transfer approved 26/08/2019 (DZ543). CLOSED August 26 2019.

Follow up audit to be conducted in three months time.

## Corrective Action Requests (CARs)

| | | | |
|---|---|---|---|
| **CAR ID:** | 2501/2019/01 | **Status:** | COMPLETE |
| **Date issued:** | 23 August 2019 | **Issued by:** | Crystal Lange |
| **Subject:** | Identification, Traceability & Management:Transfer of Goods and Organisms | | |
| **Date completed:** | 10 September 2019 | | |
| **Reason:** | Unapproved transfer of GMO material. | | |

## Hygiene & Sanitation

Autoclave records for the SAC ibutton runs were sighted with the shortest run over 121 degrees Celsius was 22 minutes.
Interwaste collections continue without issue. The ibutton results for Plant Protection showed a kill run of 121 degrees Celsius for 51 minutes.

The PC2 Glasshouse corridor was littered with dust and gib powder following the ceiling replacement, the ante room was littered with plant/straw fragments and surfaces were dusty. In Plant Protection cobwebs were noted under the sink (Synthase), hanging from ceiling panels and in corners (Main and Micro) and above lab coats hanging in the hall. A laboratory carry bucket was dirty and biological waste bins were overfill. Cardboard boxes were on the floor in Animal Physiology and cardboard had been used as a door stop, used tips were on a floor. Two small bags (empty) had been placed in a single waste bin, the in-use sharps bin did not have its lid on, the hands-free sanitiser was not working, a yellow damp or mould spot was identified on the ceiling and a multi-board and extension lead were on the floor and potentially an electrical hazard for cleaning or spills. A broom had accumulated dust hanging off the bristles.

The following elements were verified in this PBV period:

| | | |
|---|---|---|
| ◆ | Hygiene & Sanitation:Cleaning and Disinfection | Acceptable |

The following elements were verified in this PBV period:

| | |
|---|---|
| Hygiene & Sanitation:Personnel Hygiene and Personal Protective Equipment (PPE) | Acceptable |
| Hygiene & Sanitation:Pest, Vermin and Weed Control | Acceptable |
| Hygiene & Sanitation:Quarantine Isolation | Acceptable |
| Hygiene & Sanitation:Waste Management | Acceptable |

**Subject:** Cleaning and Disinfection

Note List:

[Crystal Lange]

A number of transitional and or containment spaces were not maintained at an acceptable standard.

NON COMPLIANCE Rating Minor

Good Laboratory practices not demonstrated to an acceptable standard

CORRECTIVE ACTION REQUIRED
4. Address cleaning of surfaces with particular attention to corners and area where cobwebs were detected.
5. Clean up renovation debris in PC2 Glasshouse
6. Address other items and implement preventative measures in laboratories not inspected this visit.

To be completed by: September 13 2019

## Design and Construction

SAC - SPF , Suite 2A, 3A&B were inspected with no issues noted. Containment had been maintained at the ACF during the installation of water pipes outside of and through the perimeter fence.

The walls in Dairy Science (5) had been well finished. Wallpaper continues to peel in other rooms in the building and wooden strip panelling around and above sinks should be sealed. A number of benches need to be sealed to the rear panelling. Unsealed wood was noted in a range or used in Animal Physiology along with cracked paint in ceiling / scotia joins in a PC2 laboratory, a bench edge had not been sealed after is was sectioned, the wall was not stopped and large portion was not sealed.

The following elements were verified in this PBV period:

| | |
|---|---|
| Design and Construction:Access and Security | Acceptable |
| Design and Construction:Animal Enclosures and Facilities (inc. invertebrates) | Acceptable |
| Design and Construction:Laboratories | Acceptable |

The following elements were verified in this PBV period:

| | |
|---|---|
| Design and Construction:Location | Acceptable |
| Design and Construction:Open Field Testing Facilities | Acceptable |
| Design and Construction:Physical Containment Level 1 (PC1) | Acceptable |
| Design and Construction:Physical Containment Level 2 (PC2) | Acceptable |
| Design and Construction:Plant Houses and Glasshouses | Acceptable |
| Design and Construction:Signage | Acceptable |

**Subject:** Laboratories

Note List:

[Crystal Lange]

NON COMPLIANCE Rating minor

Laboratories at level 1 and 2 physical containment (ASNZS 2243.3) were not maintained at an acceptable level.

CORRECTIVE ACTION REQUEST
10. Seal wall and bench edge in Animal Physiology (Rm24)
11. Address wallpaper and sealing issues in Dairy Science

To be completed by: September 13 2019

## Hazardous Substances and New Organisms (HSNO) Act

GMC03001, GMD02006, GMC99010, GMD04112.
See unapproved transfer non-compliance in relation to HSNO Act Approval APP201858.

The following elements were verified in this PBV period:

| | |
|---|---|
| Hazardous Substances and New Organisms (HSNO) Act:HSNO Act Approvals for Development of New Organisms | Acceptable |
| Hazardous Substances and New Organisms (HSNO) Act:HSNO Act Approvals for New Organisms for Containment | Acceptable |

## Mandatory Tasks

### 5. Definitions

**Acceptable** Where the Animal Products Officer (or Biosecurity Inspector) is satisfied that the operator is substantially complying with requirements; and where there have been any departures from

regulatory requirements, that the operator's corrective actions have been, or are being, applied appropriately and effectively.

Departures from regulatory requirements, identified by the Animal Products Officer (or Biosecurity Inspector), are to be transferred to the operator's issue management system for resolution. (Key Topic / Non-compliance)

**Unacceptable** Where the Animal Products Officer (or Biosecurity Inspector) has determined that the operator is not in substantial compliance with regulatory requirements; evidenced by inadequate operator controls. (Key Issue / Non-compliance)

# Ministry for Primary Industries
Manatū Ahu Matua

# Verification Report[1]

| | |
|---|---|
| **Report ID:** | PBV/2501/2020/01 |
| **Outcome:** | **Acceptable** |
| **Issued to:** | AgResearch - Ruakura Campus |
| **Operator ID(s):** | 2501 |
| **Issued by:** | Crystal Lange<br>**Phone:** 079578319<br>**Email:** crystal.lange@mpi.govt.nz |
| **Verification Period:** | 2019-11-27 to 2020-02-28 |
| **Verification Date:** | 2020-02-28 |
| **Published:** | 2020-03-02 14:12 |
| **Next Due Date:** | 2020-08-28 |
| **Level/Step:** | **6.1** (started on 5.2 , and ceiling is 6 ) |
| **Report Type:** | Scheduled |
| **Peer Reviewed By:** | Davide Zazzaro |

1 A Verification Report is a formal report issued when sufficient evidence has been assessed to arrive at an outcome for a verification period. This report may contain Technical Reviews and external audit findings completed during the period. Inadequate and/or untimely responses to deficiencies identified in this report, poor/unacceptable performance, or failure to pass subsequent audits may result in the escalating imposition of sanctions and/or interventions provided by law.

## 1. Premises Profile

AgResearch - Ruakura Campus is, under section 39 of the Biosecurity Act 1993, approved as a Transitional and Containment Facility in accordance with the requirements of the MPI/EPA standard(s) identified. Under section 40 of the Biosecurity Act, Tom Richardson is approved as an operator of that facility and is primarily responsible for the facility, compliance with facility approvals and all activities involving risk goods.

The standards that the facility is approved to specify the structural and operating requirements for containment and/or transitional facilities holding regulated organisms and risk goods that are, or may contain:

- Agricultural Compounds
- Animals
- Animal Products
- Biologicals
- Miscellaneous
- Non-risk Goods
- Plant Products

**Physical Address :**
10 Ruakura Campus Bisley Road, Ruakura, Hamilton

## 2. Executive Summary

This was a scheduled and announced inspection of the AgResearch transitional and containment facility at Ruakura in Hamilton. The objective of this visit was to verify compliance with the facility manual, the standards identified in the "Biosecurity" section of this report, the HSNO Act Approval and the facility and operator approvals as held under the Biosecurity Act 1993.

The inspection undertaken 27 February 2020 was limited (snap-shot) as two inspections had occurred in the preceding 6 months. The inspection had been given a marginally acceptable outcome as one of the non-compliances (Access) was out of the Operators control, and potential containment risks were already well managed. Two non-compliances were issued; one, rated minor for hygiene and construction, and the other major for Access Control.

If non-compliance is not addressed in a timely manner or is ongoing, MPI interventions could include infringement notices, compliance orders, increased inspection frequency, facility suspension or cancellation of the Operator approval.

## 3. Operator Summary

One entry meeting was held with Tim Hale (Facility Operator, Containment Farm Manager) at the Animal Containment Farm (ACF), the other with Tim and Genevieve Sheriff (Facility Operator, Senior Animal Technician) for Small Animal Containment (SAC) and other standards. Tim provided transport to and from the ACF as the roadway crosses and active construction site, Tim was present for

part of the laboratory inspections. Gen accompanied Crystal Lange (MPI) for all laboratory inspections.

Uninducted visitors are accompanied by AgResearch staff (as demonstrated), no additional hazards were notified. Crystal's authority of appointment (warrants) under the Biosecurity and HSNO Acts was displayed during the visit.

The inspection process included a review of onsite records, which may include: staff training, internal audit, activity logs, and a physical inspection of laboratories, animal identification and physical counts.

Trevor Stuthridge (Research Director) has been appointed as the (Body Corporate) delegate, replacing Tom Richardson.
One event had occurred that MPi should have been notified of. This is detailed in the report.

## 4. Verification Completed (this period)

### Biosecurity

The following elements were verified in this PBV period:

| | |
|---|---|
| Biosecurity:Containment Facilities for Vertebrate Laboratory Animals | Acceptable |
| Biosecurity:Containment Standard for Field Testing of Farm Animals | Acceptable |
| Biosecurity:Transitional Facilities for Biological Products | Acceptable |

### Quality Assurance

Contingency planning for Covid19 is not know at all levels of staffing. Currently staff packs are being prepared containing face masks and hand sanitiser. Animal care would be managed using bulk feeding systems, staff on roster or utilising onsite accommodation facilities. The laboratory relocations are being managed through a reputable carrier. No liquid or opened chemicals are permitted for transport. A risk assessment for the decommissioning of South Wing ground floor laboratoires was reviewed and approved.

Version 3.1 of the facility manual was accepted December 2019, it covered minor changes to improve functionality and the name changes for key contacts. Internal audits were completed in a timely manner for the Field Test (ACF) and Vertebrate (SAC) standards. Micro and Planthouse audits were done in November, the audits due in May should have GMO registers as a key area of assessment.

Three new users had been trained for access to the SAC, site cleaning staff had been undertaken 20/02/2020. No other training had been given, the site training package is being reviewed ready for presentation in March/April.

The following elements were verified in this PBV period:

| | |
|---|---|
| Quality Assurance:Biosecurity Contingency Plans | Acceptable |
| Quality Assurance:Chief Technical Officer (CTO) Permissions and Decisions | Acceptable |
| Quality Assurance:Operating Procedures | Acceptable |
| Quality Assurance:Operator Control | Acceptable |
| Quality Assurance:Operator Internal Verification | Acceptable |
| Quality Assurance:Organizational Structure and Management | Acceptable |
| Quality Assurance:Risk Assessments | Acceptable |
| Quality Assurance:Training and Competency of Personnel | Acceptable |

**Subject:** Notifications to MPI/EPA

Note List:

[Crystal Lange]

At the inspection visit MPI was advised of an incident occurring 19 January 2020 where and AgResearch tennant was given unsupervised access to the SAC without the knowledge of the delegated Facility Operator. The tenant had not

undergone the site or SAC specific training, nor was the person training in the use of the equipment accessed (autoclave), instruction was given by a third party.

This has been reported as a Security and Access non-compliance under the heading Design and Construction

## Documentation and Certification

All BACC records were available, the retro request was actions and BACC C2020/77999 issued the day of the visit and supplied immediately.

The following elements were verified in this PBV period:

| | |
|---|---|
| Documentation and Certification:Biosecurity Authority Clearance Certificates (BACCs) | Acceptable |
| Documentation and Certification:Documentation and Record Keeping | Acceptable |
| Documentation and Certification:Site Plans, Specification and Modifications | Acceptable |

## Identification, Traceability & Management

Additional authorised signatories were discussed. Restricted products for retention, transfer or disposal have been identified and applied to the appropriate register. Imported and transferred items were recorded in the Operators site register.

The following elements were verified in this PBV period:

| | |
|---|---|
| Identification, Traceability & Management:Authorised Signatories | Acceptable |
| Identification, Traceability & Management:Inventory Control and Accuracy | Acceptable |
| Identification, Traceability & Management:Product and Organism Identification | Acceptable |
| Identification, Traceability & Management:Segregation | Acceptable |
| Identification, Traceability & Management:Transfer of Goods and Organisms | Acceptable |
| Identification, Traceability & Management:Transport of Risk Goods and Organisms | Acceptable |

## Hygiene & Sanitation

No unexpected pest incidents have been notified. Some accumulation of dust was noted in the South Wing (112), dirty high level cupboard doors (111) and grimy floors and oily bench staines (114). A lab coat draped over a chair (G23) was touching the floor. Floor cleaning in the endophyte laboratory should be revisited as cobwebs were noted on cabinet base boards as well as accumulated dust.

The corridor and anteroom of the PC2 Glasshouse was much improved.

Virkon and ethanol solutions were being used to decontaminate equipment and laboratory spaces as part of the laboratory decommissioning and relocation.

Sufficient room was available post entry quarantine and/or isolation of sick animals.

The following elements were verified in this PBV period:

| | |
|---|---|
| Hygiene & Sanitation:Cleaning and Disinfection | Acceptable |
| Hygiene & Sanitation:Personnel Hygiene and Personal Protective Equipment (PPE) | Acceptable |
| Hygiene & Sanitation:Pest, Vermin and Weed Control | Acceptable |
| Hygiene & Sanitation:Quarantine Isolation | Acceptable |
| Hygiene & Sanitation:Waste Management | Acceptable |

**Subject:** Cleaning and Disinfection

Note List:

[Crystal Lange]

MINOR NON-COMPLIANCE ( Joint with Design and Construction)

Hygiene not maintained at an acceptable level.

CORRECTIVE ACTION REQUEST:
Accumulation of dust, debris and grime needs to be addressed meet the requirements of section 4.7 of AS/NZS 2243.3:2002 as required by the Micro2007a and Biological Products standards.

To Be Completed By: 28 March 2020

## Design and Construction

The sealing of the floor in the Endophyte 2 laboratory is incomplete. Silicon still needs to be applied around the door frames to prevent seepage under cut surfaces. The bench seal has separated at one end and shrinkage or insufficient sealing along the length of the bench mean the silicon is hard to see and the gap difficult to clean. Flooring was damaged in (SW) 144, the coving sealing strip in G22 had become fully detached and an unsealed door stop was noted in G23.

Access was not available for 116, 117, 119 and 101. These doors had physical (key) locks where as the others were unlocked as part of the electronic locking regime. These rooms will be scheduled for the next visit.

The following elements were verified in this PBV period:

| | |
|---|---|
| Design and Construction:Access and Security | Acceptable |
| Design and Construction:Animal Enclosures and Facilities (inc. invertebrates) | Acceptable |

[Crystal Lange]

MINOR NON-COMPLIANCE ( Joint with Hygiene and Sanitation)

Surfaces not maintained to meet the requirements of section 4.7 of AS/NZS 2243.3:2002 as required by the Micro2007a and Biological Products standards.

CORRECTIVE ACTION REQUEST:

Complete appropriate repairs

To Be Completed By: 28 March 2020

Follow-up Note
South Wing laboratories G22 and G23 were removed from the facility footprint following confirmation of decontamination prior to equipment relocation. Confirmation was emailed 28/02/2020.

## Hazardous Substances and New Organisms (HSNO) Act

Compliance with the approval (ERMA200223) was verified with animal registers and reality check.

The following elements were verified in this PBV period:

| | |
|---|---|
| Hazardous Substances and New Organisms (HSNO) Act:HSNO Act Approvals for Development of New Organisms | Acceptable |
| Hazardous Substances and New Organisms (HSNO) Act:HSNO Act Approvals for New Organisms for Containment | Acceptable |

## Mandatory Tasks

### 5. Definitions

**Acceptable** Where the Animal Products Officer (or Biosecurity Inspector) is satisfied that the operator is substantially complying with requirements; and where there have been any departures from regulatory requirements, that the operator's corrective actions have been, or are being, applied appropriately and effectively.

Departures from regulatory requirements, identified by the Animal Products Officer (or Biosecurity Inspector), are to be transferred to the operator's issue management system for resolution. (Key Topic / Non-compliance)

**Unacceptable** Where the Animal Products Officer (or Biosecurity Inspector) has determined that the operator is not in substantial compliance with regulatory requirements; evidenced by inadequate operator controls. (Key Issue / Non-compliance)