

**Annual Report to
Environmental Protection Authority
for**

Activities under ERMA 200223

AgResearch Ltd

For the 12 months ending
30th June 2018

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Animal Containment Facility**

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Summary of Activities for the period 1st July 2017 to 30th June 2018

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, which were field tested or developed under the GMF98009 or GMD02028 approvals continue to be maintained under the ERMA200223 approval and all new cattle development activities are now only being undertaken under the ERMA200223 approval.

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

Cattle and Goat activities, other than the maintenance or growing of animals, have been the calving of recipient cows, flushing eggs from fertile animals, kidding of recipient goats, milking of transgenic animals and the transfer of embryos to recipient animals. Semen has been collected from Bucks and Bulls for storage for future use and one buck was collected to export standard for United States collaborators use.

Embryo Transfer work in sheep has seen some recipients carry to term but as yet no offspring have been healthy enough to survive.

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 and all activity approvals have been renewed during the year.

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, 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.

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 and milk analysed to characterise changes to the milk composition

Generating cattle with lighter coat colour

- Bovine foetal fibroblasts were edited for a naturally occurring coat colour mutation
- Embryos were reconstructed with edited and control cells and transferred for development to term
- Two mutant and three control calves were produced
- Mutant calves showed a striking coat colour phenotype validating the causative nature of the mutation

Goats producing therapeutic proteins

- Assisted reproductive technologies were used to expand the number of transgenic goats, produce transgenic males, provide access to milk and confirm stability of genotype and phenotype
- Goat-produced therapeutic antibody was purified from milk and functionally characterised

Generating germline-deficient sheep for embryo complementation

- *NANOS2* was knocked out by CRISPR-mediated genome editing in male ovine fetal fibroblasts (OFFs) and used for cloning.
- OFF knockout-derived cloned blastocysts were obtained from *NANOS2* null donor cells.
- For embryo complementation with a reporter cell line, wildtype OFFs were modified to constitutively overexpress a red fluorescent protein (RFP).
- One clonal RFP cell line was used for aggregation with cloned *NANOS*^{-/-} embryos for germline replacement.
- A total of 50, 19 and 28 blastocysts were produced from *NANOS2*, *RFP* and *NANOS2*^{<>*RFP*} aggregate embryos, respectively, and transferred into recipient ewes.
- By Day 50, 6/50 (=12%), 0/19 (=0%) and 2/28 (=7%) of recipients receiving a *NANOS2*^{-/-} embryo were still pregnant.
- Resulting lambs will be analysed to confirm loss of germline and evaluated for RFP expression.

Generating immune-compatible sheep for xenotransplantation

- *GGTA* and *CMAH* genes were knocked out by CRISPR-mediated genome editing in male ovine fetal fibroblasts (OFFs) and used for cloning.
- OFF double knockout-derived cloned blastocysts were obtained from *GGTA/CMAH* null donor cells.
- Following SCNT into abattoir-derived oocytes, development into blastocysts was 19±3% (89/476, n=12).
- At day 35 of development, ultrasonography scanning confirmed that 19±6% of in vitro derived embryos (11/57, n=10) established a viable pregnancy. From these, 5 (=9%) pregnancies are still holding.
- Resulting lambs will be analysed to confirm loss of α -Gal and Neu5Gc and evaluated as donors for xenotransplantation.

Overexpression of the histone demethylase KDM4B in transgenic (TG) cattle

- Fetal fibroblasts that overexpressed the histone demethylase KDM4B were used for cloning to rejuvenate a senescent donor cell clone.
- Cloned blastocysts were transferred into surrogate heifers and one foetus recovered on D42 of gestation.
- Rejuvenated cell clones were expanded and used in future studies.
One female animal was born and will be used for breeding to preserve and expand this TG line. The line will aid future studies into improving somatic cell reprogramming.

On Farm Management Summary for year ending 30/06/2018

Animal Numbers 01/07/2017– 30/06/2018 (Births exclude still born or animals which die soon after birth reported in Animal Ethics Reports, Aged In and Out records changes in animal age¹)

Stock Class	Open (1/07/17)	Births	Transfer In	Transfer Out	Aged In	Aged Out	Killed	Deaths	Closing (30/06/18)
Casein (ERMA200223)									
MA Cows	12				1		1		12
R1yr Heifers	1					1			0
Bull Calves	0	1					1		0
Total Casein	13	1	0	0	1	1	2	0	12
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	0				12		1		11
R2yr Heifers	12				5	12			5
R1yr Heifers	8				2	5	2		3
Heifer Calves	2	7				2	7		0
R1yr + Bulls	3				2		4		1
Bull Calves	2	6				2	6		0
Total BLg -	27	13	0	0	21	21	20	0	20
Erbitux (ERMA200223)									
MA Cows	1								1
Total Erbitux	1	0	0	0	0	0	0	0	1
Coat Colour (ERMA200223)									
Bull calves	0	4						1	3
Total Coat Colour	0	4	0	0	0	0	0	1	3
KDM4B (ERMA200223)									
Heifer Calves	0	1							1
Total KDM4B	0	1	0	0	0	0	0	0	1
Conventional Cattle									
MA Cows	58				12		10		36
R2yr Heifers	0				5				5
Other classes	5					5			0
Total Conventional	63	0	0	12	5	5	10	0	41
Cattle Total	104	19	0	12	27	27	32	1	78
Cattle developed under ERMA approvals (Tg and non Tg progeny)									37

¹ Aligns with normal livestock reconciliation aging practice.

Stock Class	Open (1/07/17)	Births	Transfer In	Transfer Out	Aged In	Aged Out	Killed	Deaths	Closing (30/06/18)
Goats									
Erbitux & Enbrel (ERMA200223)									
Ma Doe	21				4		9		16
R2yr Doe	4				14	4			14
R1yr Doe	15			1	5	14	0		5
Doe Kid	0	5				5			0
Buck Kid	0	4				3	1		0
R1yr Male +	6		1		3		6		4
Total Erbitux & Enbrel	46	9	1	1	26	26	16	0	39
non Med inherit (ERMA200223)									
Total TCR	0	0	0	0	0	0	0	0	0
Conventional Goats									
MA Doe	6				18		4		20
R2yr Doe	18				22	18	1		21
R1yr Doe	22					22			0
Male R1yr +	9						9		0
Kids	0								0
Total Conventional	55	0	0	0	40	40	14	0	41
Goat Total	101	9	1	1	66	66	30	0	80
Goats developed under ERMA approvals (Tg and non Tg progeny)									39
Sheep									
Conventional Sheep									
MA Ewes	5						2		3
2th Ewes					52				52
Ewe Hgts	57					52	5		0
Total Conventional	62	0	0	0	52	52	7	0	55
Sheep developed under ERMA approvals (Tg and non Tg progeny)									0

The preceding tables provides animal numbers 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.

The transfer out of R1yr Doe and into R1yr Buck in Erbitux & Enbrel goats is correcting to male a goat which had been wrongly identified as a female in initial records in 2016.

For cattle there has been no movement of conventional animals into the facility during the period. 12 conventional animals were moved out of the facility, these 12 had never been used to receive GM embryos and were the progeny of non Tg cows present on the facility in 2014 for science purposes which was not related to the GM cattle programme.

32 cattle of varying ages have been euthanased (killed) and one calf 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 the facility (apart from approved exit and returns for surgery purposes) during the period.

30 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 also been no movement of animals onto the facility (apart from approved exit and returns for surgery purposes) during the period.

7 sheep of varying ages have been euthanased (killed) and no sheep died during the period; these animals have also been disposed of in offal holes on-site, as unsuitable animals, 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.

With the Ministry for Primary Industries Mycoplasma Bovis eradication program the Ruakura Farm was issued with a 'Notice of direction' for animal tracing purposes in June 2018 which has included the Animal Containment Facility because of its location within the main farm so biosecurity measures have been increased.

Animals on the facility continue to be managed in a way which is the 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.

35 cattle, no goat and 53 sheep recipients have been used for ET (embryo transfer), with others being mated with artificial insemination or bucks, on a rotational basis during the period. All animals are regularly monitored for live weight and health status.

All animals have been grazed mainly on pasture, with 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 17/18 season

No GM cows were calved specifically for seasonal milk production.

Those that did calve, reared their own progeny and small sample volumes were collected for science analysis only over a short period.

The milk from the GM goats which were milked was either used to feed kids, for science analysis or frozen on the facility.

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

Ruakura Animal Ethics Committee Reports

RAEC # 14236 - Production and characterisation of transgenic cattle, generic application

Ruakura Animal Ethics Committee Report: Third Quarter 2017

Transgenic Cattle

Summarised below is the status of the various cattle groups and their offspring and any losses that have occurred during the reporting interval July to September 2017 in relation to the conditions for approval of Application 14236 "Production and characterisation of transgenic cattle, generic application". Approval passed on 30th June 2017, valid until 31st May 2018.

A) Casein Plus cattle

A.1 Status of transgenic casein cattle

Multiple generations (F0-F3) of the transgenic casein lines have been produced with the animal born on 31st July 2003 now the oldest (14 years).

1434, TG3, calved heifer calf 18.9.17. (calf not required so euthanased)

A.2 Treatments and activities during reporting interval

Routine anthelmintic treatment and annual vaccinations.

A.3 Culling and losses during reporting interval

13003, calved 16.9.17, euthanased 22.9.17, cow had calved and had extremely large udder, suffering with compromised locomotion. She and male calf not required for research, so euthanased.

B) Erbitux cattle

One founder animal, 11001 healthy and now rising 6 years old.

B.2 Treatments and activities during reporting interval

Routine anthelmintic treatment and annual vaccinations.

C) Beta-lactoglobulin (BLG) knockdown /knockdown cattle

C.1. Status of transgenic BLGkd cattle

25 BLG animals alive, oldest born August 2015, now 2 years old

10 x 2015 born F1 calved mid September 2017. 1603 calved 30.9.17 (calf born dead)

Live calves: 6 bull calves, 4 heifer calves.

C.2 Treatments and activities during reporting interval

Group 81 hLZ KI (BLG disruption lysozyme insertion embryos), 1703 induced into lactation, (start 15.7.18) commenced lactation 7.8.17.

1505 slow and stiff post calving, given non steroidal anti-inflammatories.

Routine anthelmintic treatment and annual vaccinations.

C.3 Culling and losses during reporting interval

Nil

Recipients:

Group 84: 30 recipients synchronised and embryos transferred into on 17th May. Day 37 scan: 5-6 pregnancies.

Health Treatments: Routine anthelmintic treatment and annual vaccinations.

Ruakura Animal Ethics Committee Report: Fourth Quarter 2017**Transgenic Cattle**

Summarised below is the status of the various cattle groups and their offspring and any losses that have occurred during the reporting interval October to December 2017 in relation to the conditions for approval of Application 14236 "Production and characterisation of transgenic cattle, generic application". Approval passed on 30th June 2017, valid until 31st May 2018.

A) Casein Plus cattle**A.1 Status of transgenic casein cattle**

Multiple generations (F0-F3) of the transgenic casein lines have been produced with the animal born on 31st July 2003 now the oldest (14 years).

A.2 Treatments and activities during reporting interval

Fly repellent application.

A.3 Culling and losses during reporting interval

2017 born calf euthanased early October as not required for research.

B) Erbitux cattle

One founder animal, 11001 healthy and now rising 6 years old.

B.2 Treatments and activities during reporting interval

Fly repellent application.

C) Beta-lactoglobulin (BLG) knockdown/knockout cattle**C.1. Status of transgenic BLGkd cattle**

25 BLG animals alive, oldest born August 2015, now over 2 years old

C.2 Treatments and activities during reporting interval

2017 early born animals wormed.

Fly repellent application.

C.3 Culling and losses during reporting interval

Calves from September not required for research and euthanased.

Recipients:

Group 84: 2 pregnancies remain.

Health Treatments: Fly repellent application.

Ruakura Animal Ethics Committee Report: First Quarter 2018

Transgenic Cattle

Summarised below is the status of the various cattle groups and their offspring and any losses that have occurred during the reporting interval January to March 2018 in relation to the conditions for approval of Application 14236 "Production and characterisation of transgenic cattle, generic application". Approval passed on 30th June 2017, valid until 31st May 2018.

A) Casein Plus cattle

A.1 Status of transgenic casein cattle

Multiple generations (F0-F3) of the transgenic casein lines have been produced with the animal born on 31st July 2003 now the oldest (rising 15 years).

A.2 Treatments and activities during reporting interval

Fly repellent application.

A.3 Culling and losses during reporting interval

Nil

B) Erbitux cattle

One founder animal, 11001 healthy and now rising 6 years old.

B.2 Treatments and activities during reporting interval

Fly repellent application.

C) Beta-lactoglobulin (BLG) knockdown/knockdown cattle

C.1. Status of transgenic BLGkd cattle

24 BLG animals alive, oldest born August 2015, now rising 3 years old

C.2 Treatments and activities during reporting interval

2017 early born animals wormed.

Fly repellent application.

C.3 Culling and losses during reporting interval

1512 Euthanased due to large udder

Recipients:

Group 84: 1 live heifer calf, 1801 born 7th February 2018 by C-section Recip Euth.

Group 85: 5 pregnancies due late May.

Health Treatments: Fly repellent application.

Ruakura Animal Ethics Committee Report: Second Quarter 2018

Transgenic Cattle

Summarised below is the status of the various cattle groups and their offspring and any losses that have occurred during the reporting interval April to June 2018 in relation to the conditions for approval of Application 14236 "Production and characterisation of transgenic cattle, generic application". Approval passed on 30th June 2017, valid until 31st May 2018. New follow on application is for maintenance of existing cattle: 14510.

A) Casein Plus cattle

A.1 Status of transgenic casein cattle

Multiple generations (F0-F3) of the transgenic casein lines have been produced with the animal born on 31st July 2003 now the oldest (rising 15 years). 12 animals in total.

A.2 Treatments and activities during reporting interval

Nil

A.3 Culling and losses during reporting interval

Nil

B) Erbitux cattle

One founder animal, 11001, born February 2011, now 7 years old.

B.2 Treatments and activities during reporting interval

Mild lameness on front right foot end of May, and end of June, examined, pared and treated with anti-inflammatories.

C) Beta-lactoglobulin (BLG) knockdown/knockdown cattle

C.1. Status of transgenic BLGkd cattle

20 BLG animals alive, oldest born August 2015, now rising 3 years old.

C.2 Treatments and activities during reporting interval

Nil

C.3 Culling and losses during reporting interval

4 Bulls culled after onsite semen collection during May.

D) Group 85 Coat Colour Calves

D.1. Status of cattle

5 male calves delivered by planned caesarian section on 24th May 2018 at day 274 of gestation. Two calves carried the coat colour gene variant, three were non-modified Friesian control calves. One coat colour calf was euthanased a few hours after birth due to both organ and metabolic complications resulting from a hydrops pregnancy.

D.2 Treatments and activities during reporting interval

All calves treated for large navels at birth with prophylactic antibiotics.

Calves disbudded 8/6/18 and given primary clostridial vaccination. Coat colour calf ear notched for DNA retrieval.

D.3 Culling and losses during reporting interval

Coat colour calf 1805 died on 23.6.18. A post mortem revealed septicaemia resulting from a retrograde infection of the bladder and kidneys, originating from an internal abscess in a persistent urachus.

Recipients: maintenance only of recipients in this quarter, no further use approved under this application following the birth of Group 85 calves.

RAEC #14238 - Development of transgenic goats in containment

Ruakura Animal Ethics Committee Report: Third Quarter 2017

Transgenic 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 2017, in relation to the conditions for approval of Application 14238 "Production and Characterization of Transgenic Goats, generic application" approved on 1st July 2017.

Biosimilars

A) Erbitux Goats

A.1 Status of transgenic Erbitux Goats

Two generations (F0-F1) of the transgenic Erbitux lines have been produced with the founder Erbitux animals (F0) as the oldest, rising 6 years old (born 2011).

As at 30th September 2017 there were 38 animals made up of 33 mixed age females and 5 males.

A.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred.

Monthly Ultra sound scans to monitor pregnancies following AI of 7 F1 animals.

A.3 Culling and losses during reporting interval

Nil

B) Enbrel Goats

B.1 Status of transgenic Enbrel Goats

Two generations (F0-F1) of the transgenic Enbrel line have been produced with one founder Enbrel animal (F0) as the oldest (born September 2012).

As at 30th September 2017 there were 8 animals made up of 7 mixed age females and 1 male.

B.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred.

B.3 Culling and losses during reporting interval

Nil

Recipients

As at 30th September 2017, there were 55 non transgenic animals, made up of 46 mixed age does and 9 rising one year old bucks.

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Monthly U/S scans to monitor pregnancies following embryo transfer for 11 recipients.

Culling and Losses during reporting interval

Nil

Ruakura Animal Ethics Committee Report: Fourth Quarter 2017

Transgenic 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 2017, in relation to the conditions for approval of Application 14238 "Production and Characterization of Transgenic Goats, generic application" approved on 1st July 2017.

Biosimilars

A) Erbitux Goats

A.1 Status of transgenic Erbitux Goats

Three generations (F0-F2) of the transgenic Erbitux lines have been produced with the founder Erbitux animals (F0) as the oldest, rising 6 years old (born 2011).

As at 31st December 2017 there were 35 animals made up of 29 mixed age females and 6 males.

A.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred. During the reporting period 5 female and 4 male kids were born and genotyped. All kids were disbudded. 4 F1 does were milked for 6 weeks. 2 F1 does spontaneously lactated and were milked for 3 weeks. Superovulation programme carried out on 3 F1 females. This was aborted after AI by treating does with PG due to CIDR being left in. Monthly U/S scans to monitor pregnancies following AI of 7 F1 animals.

A.3 Culling and losses during reporting interval

4 bucks and 8 females (bad feet, bad udders, no longer needed or usable).

B) Enbrel Goats

B.1 Status of transgenic Enbrel Goats

Two generations (F0-F1) of the transgenic Enbrel line have been produced with one founder Enbrel animal (F0) as the oldest (born September 2012).

As at 31st December 2017 there were 6 animals made up of 6 mixed age females and 0 males.

B.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred.

B.3 Culling and losses during reporting interval

1 buck and 1 female (bad feet, bad udder, and buck had a grossly swollen testicle).

Recipients

As at 31st December 2017, there were 42 non transgenic animals, made up of 42 mixed age does and 0 males.

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Monthly U/S scans to monitor pregnancies following embryo transfer for 11 recipients. 20 younger animals were synchronised as recipients for Erbitux superovulation programme.

Culling and Losses during reporting interval

9 bucks and 4 females (bad feet, bad udders, no longer needed or not usable).

Ruakura Animal Ethics Committee Report: First Quarter 2018

Transgenic 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 2018, in relation to the conditions for approval of Application 14238 "Production and Characterization of Transgenic Goats, generic application" approved on 1st July 2017.

Biosimilars

A) Erbitux Goats

A.1 Status of transgenic Erbitux Goats

Two generations (F0-F1) of the transgenic Erbitux lines have been produced with the founder Erbitux animals (F0) as the oldest, rising 6 years old (born 2011).

As at 31st March 2018 there were 35 animals made up of 29 mixed age females and 6 males.

A.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred. Horn regrowth removed from 1 buck.

Superovulation programme with subsequent AI carried out on 3 F1 Erbitux animals. Animals were scanned by U/S.

A.3 Culling and losses during reporting interval

Nil

B) Enbrel Goats

B.1 Status of transgenic Enbrel Goats

Two generations (F0-F1) of the transgenic Enbrel line have been produced with one founder Enbrel animal (F0) as the oldest (born September 2012).

As at 31st March 2018 there were 6 animals made up of 6 mixed age females and 0 males.

B.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred.

B.3 Culling and losses during reporting interval

Nil

Recipients

As at 31st March 2018, there were 41 non transgenic animals, made up of 41 mixed age does and 0 males.

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. 20 younger animals were synchronised as recipients for Erbitux superovulation programme (see A.2). 2 embryos transferred into 1 synchronised recipient and pregnancy status checked by U/S scan.

Culling and Losses during reporting interval

One doe with a persistent foot abscess

Ruakura Animal Ethics Committee Report: Second Quarter 2018

Transgenic 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 2018, in relation to the conditions for approval of Application 14238 "Production and Characterization of Transgenic Goats, generic application" approved on 1st July 2017.

Biosimilars

A) Erbitux Goats

A.1 Status of transgenic Erbitux Goats

Two generations (F0-F1) of the transgenic Erbitux lines have been produced with the founder Erbitux animals (F0) as the oldest, rising 6 years old (born 2011).

As at 30th June 2018 there were 33 animals made up of 29 mixed age females and 4 males.

A.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred.

AI programme carried out on 3 F1 and 6 F2 does.

A.3 Culling and losses during reporting interval

Two bucks following semen collection as no longer needed.

B) Enbrel Goats

B.1 Status of transgenic Enbrel Goats

Two generations (F0-F1) of the transgenic Enbrel line have been produced with one founder Enbrel animal (F0) as the oldest (born 2012).

As at 30th June 2018 there were 6 animals made up of 6 mixed age females and 0 males.

B.2 Treatments and activities during reporting interval

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Any individual lameness treated as occurred.

B.3 Culling and losses during reporting interval

Nil

Recipients

As at 30th June 2018, there were 41 non transgenic animals, made up of 41 mixed age does and 0 males.

All drenched at required intervals dependant on worm counts, and feet checked and trimmed every 6-8 weeks. Recipient of embryo transfer scanned twice to check for pregnancy.

Culling and Losses during reporting interval

Nil



Ministry for Primary Industries External Inspection Report:

Facility	AgResearch - Ruakura
Location	Ruakura Research Centre 10 Bisley Rd, Hamilton
Facility Codes	TF02501 (364)
Operator	Tom Richardson
MPI Contact	██████████ Tim Hale, ██████████
Primary Verifier	Crystal Lange
Inspection conducted By	Crystal Lange
Inspection Date	August 17 & 22 2017
Inspection report Date	August 24 2017



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Executive Summary

The external inspection of AgResearch's Ruakura campus transitional and containment facility in Hamilton was carried out by the Ministry for Primary Industries (MPI) August 17 & 22 2017 for the period April 2017 – September 2017

No issues were noted with records or structural compliance for either of the animal containment units.

There were minor structural issues noted in the Microbiological laboratories reflecting in some cases the age of the facilities, in others; ongoing poor laboratory hygiene. Plants were noted growing in the and along the drain in the glass house indicating poor implementation of containment of seed.

The non-compliance for Internal Monitoring was continued; this has been a reoccurring theme for the past three external inspection although improvements are being made. The Operating Manager is resigned to the fact that he is unable to relinquish his role as there has been no suitable replacement found after several months. With the resignation of the Compliance Advisor there is now a lack of support for the Operating Manager and no one currently accountable for providing containment support or resourcing a replacement for his role.

As identified in the previous audit report, succession planning is essential for this site. The recommendation made in regards to reviewing the Delegated Operator roles and utilising a part time compliance role is still valid.

One AgResearch tenant has obtained their own HSNO Approval and was assessed for compliance with the controls during this visit. Laboratories in the Dairy Science building used by non AgResearch staff were visited.

Overall the audit outcome was satisfactory, with some areas of concern. MPI will continue to monitor progress and in the meantime the facility and operator approvals will be continued.

Sincerely



Crystal Lange
Travelling Technical Supervisor
Verification Services



Inspection Scope

The AgResearch site at the Ruakura is a transitional and containment facility, approved as such under the Biosecurity Act 1993 because it holds or processes goods that are risk goods as defined by the Biosecurity Act 1993 or may contain new organisms as defined by Hazardous Substances and New Organisms (HSNO) Act 1996.

The facility is approved to Environmental Protection Authority (EPA) Standards 154.03.02: *Containment Facilities for Microorganisms 2007a*, 154.03.06: *Containment Standard for the Field Testing of Farm Animals*, Standard 154.03.03: *Containment Facilities for Vertebrate Laboratory Animals*, 155.04.09 *Containment Facilities for Plants 2007*, 154.02.08 *Transitional & Containment Facilities for Invertebrates* and MAFBNZ Standard 154.02.17 *Transitional Facilities for Biological Products*. These standards specify the structural and operational requirements for transitional and containment facilities receiving and holding risk goods or new organisms.

The purpose of this inspection was to determine if the facility and operator approvals held by AgResearch and the HSNO Act approvals are being complied with. Consequently, the scope of the inspection includes the standards and HSNO approvals.

This report is written so that each Facility Manager can extract the parts that are specifically relevant to their own area.

References:

MAFBNZ Standard: *Transitional Facilities for Biological Products*
EPA Standard: *Facilities for Microorganisms and Cell Cultures: 2007a*
EPA Standard: *Containment Standard for the Field Testing of Farm Animals*
EPA Standard: *Containment Facilities for Vertebrate Laboratory Animals*
EPA Standard: *Transitional and Containment Facilities for Invertebrates*
EPA Standard: *Containment Facilities for Plants 2007*
Australian Standard & New Zealand Standard (AS/NZS) 2243.3: 2002 - *Safety in Laboratories: Microbiological aspects and containment facilities*
Facility Manual: version 1.0 January 2016
Approvals granted under the HSNO Act
MPI permits to import and associated Import Health Standards (IHS's)

Inspection Process

This scheduled external inspection was conducted by Crystal Lange (MPI), with [REDACTED] [REDACTED] Tim Hale (delegated Facility Operators) and [REDACTED] (delegated Facility Operator and Operating Manager). The inspection process included a review of onsite records where applicable, including staff training and internal audit records, registers, and physical inspection of the containment areas.



Animal Containment Facility

ERMA200223

Compliance with the controls of ERMA200223 was assessed. No issues were noted.
N.B. Controls 8, 11, 12, 14 and 15 are not applicable to this review.

Operational Requirements

Overall good operator control was demonstrated. Sampled records were up to date for animal treatments, transfer approvals, animal counts and training.

Control 1

AgResearch is meeting the requirements of all applicable controls.

Control 2

Three of the permissible species are in use for research purposes with sheep being added this reporting period.

Control 3

Practices comply with EPA, Animal Ethics and MPI requirements.

Control 4

The Requirements of the Standard are being met:

Training Refresher training was up to date, no inductions have taken place.

Access There have been no untoward security issues.

Internal Audit Programme The internal audit conducted June 2017. There were no areas of concern arising from this review.

Records Registers were up to date.

Physical Requirements Perimeter fencing was secure, internal fencing, gates and races were well maintained. Entry gates are monitored during daily activities.

Control 5

Sheep continue to be used to graze the perimeter. Stock rotation is managed with the AgResearch general farm to ensure co-grazing does not occur.

Control 6

There have been no reported breaches of containment or any suspicious activity.

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.

Control 10

Practice complies with this control.

Control 13

Contact is being maintained with Iwi.

MPI contact details

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Ministry for Primary Industries External Inspection Report:

Facility	AgResearch - Ruakura
Location	Ruakura Research Centre 10 Bisley Rd, Hamilton
Facility Codes	TF02501 (364)
Operator	Tom Richardson
MPI Contact	[REDACTED], Tim Hale, [REDACTED]
Primary Verifier	Crystal Lange
Inspection conducted By	Crystal Lange
Inspection Date	February 20 2018
Inspection report Date	February 21 2018



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Executive Summary

The external inspection of AgResearch's Ruakura campus transitional and containment facility in Hamilton was carried out by the Ministry for Primary Industries (MPI) February 20 2018 for the period October 2017 – March 2018

No issues were noted with records or structural compliance for either of the animal containment units.

There were some minor structural issues noted in laboratories and the status of the PC1 Endophyte Laboratory should be reviewed. Service and calibration certificates were well out of date for all laminar flow and biosafety cabinets checked.

The depth of internal auditing has improved and sample tracking at a surface level has been implemented. Training records for cleaning staff following the removal of the mop notified to MPI September 2017 could not be located. The ongoing non-compliance for Internal Monitoring has been closed.

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.

Sincerely



Crystal Lange
Technical Supervisor
Verification Services



Inspection Scope

The AgResearch site at the Ruakura is a transitional and containment facility, approved as such under the Biosecurity Act 1993 because it holds or processes goods that are risk goods as defined by the Biosecurity Act 1993 or may contain new organisms as defined by Hazardous Substances and New Organisms (HSNO) Act 1996.

The facility is approved to Environmental Protection Authority (EPA) Standards 154.03.02: *Containment Facilities for Microorganisms 2007a*, 154.03.06: *Containment Standard for the Field Testing of Farm Animals*, Standard 154.03.03: *Containment Facilities for Vertebrate Laboratory Animals*, 155.04.09 *Containment Facilities for Plants 2007*, 154.02.08 *Transitional & Containment Facilities for Invertebrates* and MAFBNZ Standard 154.02.17 *Transitional Facilities for Biological Products*. These standards specify the structural and operational requirements for transitional and containment facilities receiving and holding risk goods or new organisms.

The purpose of this inspection was to determine if the facility and operator approvals held by AgResearch and the HSNO Act approvals are being complied with. Consequently, the scope of the inspection includes the standards and HSNO approvals.

The EPA Standard: *Containment Facilities for Plants 2007* and EPA Standard: *Transitional and Containment Facilities for Invertebrates* were not included in the scope of this inspection. This report is written so that each Facility Manager can extract the parts that are specifically relevant to their own area.

References:

MAFBNZ Standard: *Transitional Facilities for Biological Products*
EPA Standard: *Facilities for Microorganisms and Cell Cultures: 2007a*
EPA Standard: *Containment Standard for the Field Testing of Farm Animals*
EPA Standard: *Containment Facilities for Vertebrate Laboratory Animals*
EPA Standard: *Transitional and Containment Facilities for Invertebrates*
EPA Standard: *Containment Facilities for Plants 2007*
Australian Standard & New Zealand Standard (AS/NZS) 2243.3: 2002 - *Safety in Laboratories: Microbiological aspects and containment facilities*
Facility Manual: version 2 June 2017
Approvals granted under the HSNO Act
MPI permits to import and associated Import Health Standards (IHS's)



Animal Containment Facility

ERMA200223

Compliance with the controls of ERMA200223 was assessed. No issues were noted. N.B. Controls 8, 12, 14 and 15 are not applicable to this review.

Operational Requirements

Overall good operator control was demonstrated. Sampled records were up to date for animal treatments, transfer approvals, animal counts and training.

Control 1

AgResearch is meeting the requirements of all applicable controls.

Control 2

Three of the permissible species are in use for research purposes.

Control 3

Practices comply with EPA, Animal Ethics and MPI requirements.

Control 4

The Requirements of the Standard are being met:

Training	No induction or refresher training has been required.
Access	There have been no untoward security issues.
Internal Audit Programme	The internal audit conducted December 2017. There were no areas of concern arising from this review.
Records	Registers were up to date.
Physical Requirements	Perimeter fencing was secure, internal fencing, gates and races were well maintained. Perimeter checks are generally noted but do occur as part of normal practice. Entry gates are monitored during daily activities.

Control 5

Sheep continue to be used to graze the perimeter. Stock rotation is managed with the AgResearch general farm to ensure co-grazing does not occur.

Control 6

There have been no reported breaches of containment or any suspicious activity.

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.

Control 10

There had been no slaughter during this reporting period.

Control 13

Contact is being maintained with Iwi.



MPI contact details

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