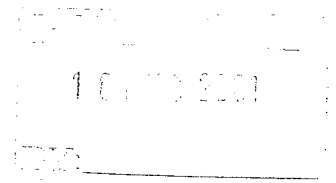




PPL Therapeutics (NZ) Ltd
Whakamaru
Main Road
R.D.1
Mangakino
New Zealand

Tel (07) 882 8543
Fax (07) 882 8056



14 December 2001

ERMA NZ
20 Customhouse Quay
PO Box 131
WELLINGTON

Attention: ~~_____~~ – Applications Officer

**ANNUAL REPORT TO THE ENVIRONMENTAL RISK MANAGEMENT
AUTHORITY (ERMA) ON COMPLIANCE WITH THE CONTROLS LAID DOWN
IN THE AUTHORITIES DECISION ON GMF98001 DATED 24TH MARCH 1999**

Statement:

"PPL Therapeutics (NZ) Ltd has at all times complied with the controls laid down in the ERMA Decision to approve the application "GMF98001 with Controls" on the field test (maintain a manufacturing ewe flock of) transgenic sheep for the purposes of producing a biopharmaceutical (human alpha-1-antitrypsin, hAAT)."

In support of this statement please find the following documents: -

- Appendix 1 – AgriQuality 6-monthly audit report on PPL Therapeutics (NZ) Ltd. This document addresses the specific areas identified in MAFR Standard 154.03.06 section 4.13 which you request comment on.
- Appendix 2 – Breakdown of numbers of transgenic animals on site.

The sentinel goats on PQF were euthanised as per MAFRA requirements and all tested negative.

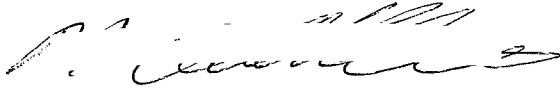
- Appendix 3 – MAF Histological report on goats.

We incorporated a neighbouring 20ha into the property.

- Appendix 4 – MAF approval for site extension.

One event to note is that during the year we changed the alarm system from a Trutest system to a Gallagher system. This change was necessitated because of electrical interference from the high-tension lines, which cross the property, affecting the settings.

Yours sincerely

A handwritten signature in black ink, appearing to be "M. J. [unclear]". The signature is written in a cursive style with a large initial letter.

FARM MANAGER

07 June 2001



MAF Biosecurity Authority
Box 2526
Wellington

Mr. M.
PPL Therapeutics
RD
Mangakino

Six Monthly Audit: PPL Therapeutics (NZ) Ltd Registered Sheep and Goat Transitional Facility, Whakamaru

The six monthly audit report of PPL Therapeutics (NZ) Ltd sheep and goat transitional facility was undertaken on 29 May 2001 as per MAFBA Standard 154.02.02. The report findings are summarised below.

1.0 Primary Facility

1.1 Livestock Tally

Livestock at 22/12/00	
Sheep	62
Plus Livestock Introduced (22/12/00 - 29/05/01)	
Sheep	0
	62
Less deaths (22/12/00 - 29/05/01)	
Sheep	3
Livestock on books	59
Physical count (29/05/01)	
Sheep	59
Discrepancy	0

1.2 Comments

Two exotic rams were euthanased during the 6 month period, one showing acute enteritis (PPL 97T4074 / Case No. R0109711) and the other as a result of severe head trauma from 'fighting' (PPL 97T4076) / Case No. 01097302). No evidence of scrapie was reported on tissues submitted for histological examination. A further ram (PPL

97T4043) was found in 'extremis' and laboratory examination indicated an acute bacterial septicaemia (Case R01095119). Ruakura Animal Health Laboratory however reported that no brainstem, midbrain or medulla was received from this animal for TSE examination. However, the Veterinary Practitioner who undertook the necropsy was adamant that the correct tissues as per the MAFBA Standard had been submitted. Procedures to be followed at necropsy are clearly displayed in the post mortem facility at PPL and as this was seen as an isolated event, no further action is envisaged.

1.3 Genetic Material

1.3.1 Imported Ram Semen

Nil

1.3.2 Lymph Node material

Nil

2.0 Secondary Facility

PPL's Secondary facility was approved on 23 March 1998 as a Transitional Facility under section 39 of the Biosecurity Act 1993.

2.1 Livestock Tally

Livestock at last audit (22/12/00)		
Sheep	3457	
Livestock Introduced (22/12/00 - 29/05/01)		
Sheep (purchased / transferred)	0	
Sheep (born)		0
Total Additions	0	
		3457
Less deaths and euthanasias (22/12/00 - 29/05/01)		131
Livestock on books		3326
Physical Count (29/05/01)		3326
Discrepancy		0

2.2 Genetic Material

Approximately 2400 straws of ovine semen collected from rams in the secondary facility are currently in storage on site.

2.3 General Comments

Post mortem reports on exotic and non exotic animals that died or were euthanased on management / welfare grounds indicated a range of conditions that are common in New Zealand. No evidence of scrapie was found in 10 brains submitted for histology from exotic animals as per the Standard.

Planning is underway to construct a milking facility on the secondary site with a view to commercial production following completion of containment towards the end of November 2002.

3 Supervision in relation to ERMA

ERMA approved on 17 March 1999 PPL's application to field test (maintain a manufacturing flock) of transgenic sheep for the purposes of producing a biopharmaceutical (hAAT) in the Waikato region, subject to certain controls (Application GMF98001). Examination of the facility and records indicated compliance with ERMA controls. However, PPL management has some concerns on the reliability of the perimeter fence alarm system and an alternative is being explored.

4 General Comments

The sentinel goats held in the primary facility were euthanased and necropsied on 12 April 2000 with no evidence of exotic disease including scrapie in tissues examined.

The last lamb was born in the primary facility on 30 November 1997 and thus containment is due to finish on 30 November 2002.

Management of both primary and secondary quarantine facilities including livestock, record keeping and structural maintenance continues to be of a high standard.

5 Acknowledgements

The assistance of _____ and his staff at PPL Therapeutics Whakamaru during this audit is acknowledged.



AgriQuality New Zealand Ltd
Rotorua

cc PPL Therapeutics NZ Ltd

26 June 2000



MAF Biosecurity Authority
Box 2526
Wellington

Six Monthly Audit: PPL Therapeutics (NZ) Ltd Registered Sheep Transitional Facility, Whakamaru

As per MAFRA Standard 154.02.02.01, attached is the six monthly audit report for the above facility undertaken on 20 June 2000.

1.0 Primary Facility

1.1 Livestock Tally

Livestock at 14/12/99		
Sheep	104	
Sentinel Goats	8	
Total Stock		112
Livestock Introduced (14/12/99 - 20/06/00)		
Sheep	0	
Sentinel goats	0	
Total additions		0
		112
Less deaths (14/12/99 - 20/06/00)		
Sheep	10	
Sentinel goats	8	
Total deaths		18
Livestock on books		94
Physical count (20/06/00)		
Sheep		94
Sentinel Goats		0
Total livestock		94
Discrepancy		0

1.2 Comments

- 8 sentinel goats euthanased at 3 years into quarantine period. No evidence of scrapie following histological examination of brain tissue (Ruakura AHL Case Numbers R00085024 to R00085031 inclusive).
- 9 'Original Imports' were euthanased as surplus to requirements. No evidence of scrapie on histological examination.
- 1 non exotic ewe died. Postmortem examination indicated septicaemia as probable cause of death.
- Some transgenic exotic ewes are being milked with the intent of sending frozen milk to UK for trial purposes.

1.3 Genetic Material

1.3.1 Imported Ram Semen

Physical count (05/05/99)

Ram 10122	106	
Ram 10141	146	
Total		252

Discrepancy 1

Physical count 02/02/00

Ram 10122	106 straws
Ram 10141	146 straws
Ram 10141	<u>1</u> straw (in bottom of tank)
	253

All imported semen straws destroyed by incineration 02/02/2000.

1.3.3 Lymph Node material

- The balance of imported lymph node material is still held frozen within the primary quarantine facility.

2.0 Secondary Facility

PPL's Secondary quarantine facility was approved on 23 March 1998 as a Transitional Facility under section 39 of the Biosecurity Act 1993.

2.1 Livestock Tally

Livestock at last audit (14/12/99)		
Sheep	1224	
Total		1224
Livestock Introduced (14/12/99 - 20/06/00)		
Sheep (purchased / transferred)	1697	
Sheep (born)	236	
Total Additions		1933
		3157
Less deaths (14/12/99 - 20/06/00)		
Exotic sheep euthanased	56	
Exotic sheep died	12	
Non exotic sheep euthanased	243	
Non exotic sheep died	18	
Total deaths		329
Livestock on books		2828
Physical Count (20/06/00)		2828
Discrepancy		0

2.2 Corrective Action Issued

An exotic 18 month ram (PPL 98T 4246) was euthanased in May 2000 because of severe respiratory distress and a post mortem carried out. However, during an AgriQuality NZ 2 weekly inspection, it was found that no tissues were submitted for exotic disease examination. This is contrary to MAFRA Standard 154.02.02 and as a result, a corrective action request was issued (attached). This appears to be an isolated case and was attributed to 'human error'.

2.3 General Comments

- Post mortem reports on exotic and non exotic animals that died or were euthanased on management / welfare grounds indicated a range of conditions which are common in New Zealand. No evidence of exotic disease was found.

3 Supervision in relation to ERMA

ERMA approved on 17 March 1999 PPL's application to field test (maintain a manufacturing flock) of transgenic sheep for the purposes of producing a biopharmaceutical (hAAT) in the Waikato region, subject to certain controls (Application GMF98001). Examination of the facility and records indicated compliance with ERMA controls.

4 General Comments

- Management of both primary and secondary quarantine facilities including livestock, record keeping and structural maintenance continues to be of a high standard. The non conformance detected appears to be an isolated instance.

5 Acknowledgements

The assistance of _____ and his staff at PPL Therapeutics Whakamaru during this audit is acknowledged.

A handwritten signature in black ink, appearing to be 'M. A.' followed by a long horizontal stroke.

AgriQuality New Zealand Ltd
Rotorua

cc PPL Therapeutics NZ Ltd

Appendix 2

NUMBER OF TRANSGENIC ANIMALS AT PPL NZ ON 09 DEC 01

SQF

BORN 1997	0
BORN 1998	55
BORN 1999	75
BORN 2000	912
BORN 2001	647
BORN 2001 Unconfirmed Transgenic	1001
<u>TOTAL</u>	<u>2690</u>

PQF

BORN 1997	58
<u>TOTAL</u>	<u>58</u>

Appendix 3

1046 Rangiora Street
PO Box 951, Rotorua
Telephone +64 7 349 9720
Facsimile + 64 7 349 9739

1 May 2000



PPL Therapeutics Ltd
Main Road
RD
Whakamaru

Dear ...

Sentinel Goats in Approved Transitional and Containment Facility

Following necropsy of the 8 sentinel goats on 12 April 2000 which had been inoculated with lymph node material from source rams in Scotland in April 1997, histological examination of brain tissues has indicated no evidence of spongiform encephalopathy.

Yours faithfully

K. ...
Supervising Veterinarian

cc: ... a, MAF Biosecurity Authority, Wellington

Appendix 4

1046 Rangiuru Street
PO Box 951, Rotorua
Telephone +64 7 349 9720
Facsimile + 64 7 349 9739

17 April 2000



PPL Therapeutics Ltd
RD
Mangakino

Dear

Approval of Extension to Transitional and Containment Facility

Following inspection, approval is now given to include the adjacent 19.5 ha originally owned by [redacted] to PPL's approved transitional and containment facility, Main Rd, Whakamaru.

Legal Descriptions of the whole facility are as follows:

Lots 2 & 3, DPS 42222 Secs 83, 96, Pt sec 81, BLK X Whakamaru SD
Lot 6, DPS 3925 Secs 71, 84 BLK X Whakamaru SD
Lot 2, DPS 28804, BLK X Whakamaru SD (150.7101 ha)
Lot 1, DPS 28804 Sec 85 BLK X Whakamaru SD (19.5910 ha)

Yours faithfully

A handwritten signature in black ink, appearing to be 'M.A.' followed by a horizontal line.

Supervising Veterinarian

cc [redacted], MAFBA