PPL Therapeutics (NZ) Ltd
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12 December 2002

Environmental Risk Management Authority
PO Box 131
WELLINGTON

Attention: – Applications Advisor

Dear Ms

PPL Therapeutics (NZ) Ltd Annual Report to ERMA

Please find enclosed our Annual Report.

Yours sincerely

Site Manager
PPL Therapeutics (NZ) Ltd

cc: (MAF)

Encl.

ANNUAL REPORT TO THE ENVIRONMENTAL RISK MANAGEMENT AUTHORITY (ERMA) ON COMPLIANCE WITH THE CONTROLS LAID DOWN IN THE AUTHORITIES DECISION ON GMF98001 DATED 24 MARCH 1999 AND AMENDED ON 24 APRIL 2002

1. **Statement:**

   "PPL Therapeutics (NZ) Ltd has at all times complied with the controls laid down by ERMA to maintain a manufacturing ewe flock of transgenic sheep for the purposes of producing a bio-pharmaceutical (human alpha-1-antitrypsin, hAAT)" (from *GMF98001 with Controls*).

   In support of this statement please find the following documents:

   - Appendix 1 – AgriQuality 6-monthly audit report on PPL Therapeutics (NZ) Ltd dated 4 July 2002. This document addresses the specific areas identified in MAFRA Standard 154.03.06 Section 4.13 upon which you request comment.

   - Appendix 2 – Breakdown of numbers of transgenic animals on site as at 2 December 2002.

   - Appendix 3 – MAF letter of clearance dated 29 November 2002 at the completion of quarantine.

2. PPL have met with members of ERMA on a frequent basis both to discuss issues of common interest and to keep ERMA advised of changes to the original development time-scale. PPL have indicated variations to the original time-scale as they have arisen and will continue to advise ERMA of these (this is now covered more fully under the new wording of PPL's Control 14).

   The development of the dairy and the first production milking are planned for later in 2003, as is the purchase and development of a second site.

   2.1 Current status of work being carried out and changes since the last report.

   - The completion and clearance of MAF Quarantine

   2.2 The interpretation and effectiveness of the controls and whether changes could be made that would achieve more cost-effective risk management and containment.

- We have in the past requested a change to PPL's Control 5, which requires that any material from transgenic animals no longer required, must be incinerated. This control is both inconsistent with the MAF view and Containment Standard 154.03.06, and different to the controls applied to the Ruakura decisions. I requested in December 2001 that you change PPL's Control 5 and apply section 4.6 of the Standard 154.03.06. You replied that you did not think such a change was minor or technical in nature.

2.3 The changes to the HSNO Act (Section 67A) allow ERMA to make changes to the controls that are minor or technical in nature without having to publicly notify the changes.

ERMA's corporate manual defines technical changes (Management of Risk) as:

"A change to a control for no other reason other than to reduce compliance costs for the applicant, everything else being equal (i.e. no change to the desired level of risk management), could be considered minor in nature."

And

"Therefore any changes to controls that are technical in nature and are made for reasons of consistency with other like decisions should be considered minor in effect."

Again I request that the authority change PPL's Control 5 to be the same as Section 4.6 of Standard 154.03.06 and to maintain consistency with other like decisions.

3. Other events of note during the year were:

- Export of a shipping container containing milk from the production flock to the UK for pharmaceutical processing
- Continuing export of tissue samples to the UK for DNA analysis
- The amending of some of the ERMA controls.

AgriQuality New Zealand Limited
Huarangi Aotearoa

Appendix 1

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04 July 2002

MAF Biosecurity Authority
Box 2526
Wellington

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 26 June 2002 as per MAFBA Standard 154.02.02. The report findings are summarised below.

1.0 Primary Facility

1.1 Livestock Tally

Livestock at audit on 29/01/02		
Sheep	57	
Plus Livestock Introduced (29/01/02 - 26/06/02)		
Sheep	0	
		57
Less deaths (29/01/02 - 26/06/02)		
Sheep		4
Livestock on books		**53**
Physical count (26/06/02)		
Sheep		53
Discrepancy		**0**

1.2 Comments

One ram was found dead on 22 February 2002 with a laboratory finding of possible zinc toxicosis. A further ram and two ewes were also euthanased during the period with PM findings of head injury, Johnes Disease and a squamous cell carcinoma

respectively. All four brains were examined with no evidence of scrapie.

53 sheep remain in the primary facility which should allow for at least 50 brains to be examined histologically towards the end of containment in 30 November 2002.

A request to reduce the size of the primary facility and incorporate this area into the secondary facility was approved by MAFBA.

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 (26/01/02)			
Sheep	4612		
Plus livestock Introduced (26/01/02 - 26/06/02)			
Sheep (purchased / transferred)	0		
Sheep (born)	23		
Total Additions		**23**	
			4635
Less deaths and euthanasias			744
Livestock on books		**3891**	
Physical Count (26/06/02)		**3891**	
Discrepancy		**0**	

2.2 Genetic Material

2381 straws of ovine semen collected from rams in the secondary facility are currently in frozen storage on site.

2.3 Comments

No evidence of scrapie was found in 37 brains submitted for histology from exotic animals in the secondary facility as per the Standard. 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.

Construction of the planned milking plant is on hold pending FDA approval for Phase 3 clinical trials. Because of this delay, PPL have advised MAFBA that they may exceed the maximum 5000 animals per site by 500 for a short period over the coming winter spring. This deviation was approved by MAFBA on 11 December 2001.

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.

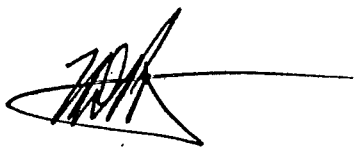
4 General Comments

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

No major or minor non compliances with the MAFBA standard were observed during the period and 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 [redacted] and his staff at PPL Therapeutics Whakamaru during this audit is acknowledged.



AgriQuality New Zealand Ltd
Rotorua

cc PPL Therapeutics NZ Ltd
cc Veterinary Co-ordinator, MQS, Box 53066, Auckland Airport

Appendix 2

PPL THERAPEUTICS (NZ) LTD

STOCK RECONCILIATION - DECEMBER 2002

Week ending 01 December 2002

SECONDARY QUARANTINE FACILITY

YEAR BORN	1995-7	1998			1999			2000			2001				2002				TOTAL
TYPE	Conv.	TG	N-TG	Conv.	TG	N-TG	Conv.	TG	N-TG	Conv.	Unconf	TG	N-TG	Conv.	Unconf	TG	N-TG	Conv.	
TOTAL	589	29	0	619	55	0	8	851	45	22	1	1454	0	15	524	388	0	23	**4623**

Conv. = conventional
TG = transgenic
N-TG = non-transgenic
Uncon = unconfirmed transgenic

Appendix 3

MA.

Ministry of Agriculture and Forestry, New Zealand
Te Manatu Ahuwhenua, Ngaherehere, Aotearoa

Ref: AF1-063

26 November 2002

Manager
PPL Therapeutics,
Whakamaru

Disease Risk Clearance for PPL sheep held at Whakamaru

On advice received from [redacted], the supervisor, of your transitional facility I can confirm the following:

1. All conditions of the import health permit (96/5/74) dated 02/07/96 and the import health standard 'Special import health standard for the importation of sheep semen into New Zealand from the United Kingdom' dated 05/06/96 have been met.

2. The quarantine facilities have operated according to MAF Biosecurity Standard 154.02.02: Standard for sheep and goat transitional facilities.

3. The flock of origin for imported ovine semen, PPL Therapeutics (Scotland) Ltd, East Mains Farm, Ormiston was certified on 31 October 2002 by Mr [redacted], Veterinary Inspector, Scottish Executive Environment and Rural Affairs Department as maintaining scrapie monitored negative status.

4. The two donor rams in Scotland were subjected to necropsy with no evidence of scrapie as per the Standard.

5. Sentinel goats inoculated intra-cerebrally with lymph node material from the original donor rams were subjected to necropsy after 3 years in primary quarantine with no evidence of scrapie as per the Standard

6. All original imports (progeny from imported semen) have been held in the primary quarantine facility since birth and have been subjected to necropsy with no evidence of scrapie as per the standard.

7. Original imports have been subjected to maedi-visna testing with negative results.

These sheep, being new organisms, do not qualify for a biosecurity clearance, but having met all of the quarantine requirements listed above, including the scrapie freedom assurance programme, qualify for a disease risk clearance on 29 November 2002. This date being 5 years after the last lamb was born in primary quarantine (30/11/1997).

A disease risk clearance does not change the legal status of the sheep as new organisms that must remain in containment, but provides confirmation from MAF that all requirements that were imposed for the management of disease risk have been met.

These sheep must remain on the property in containment according to the requirements of MAF Standard 154.03.06: Containment Standard for Field Testing of Farm Animals and the additional ERMA controls.

Chief Technical Officer
Biosecurity Authority