MEMORANDUM OF UNDERSTANDING

CONCERNING

LICENSING AND AUDITING OF AUSTRALIAN MANUFACTURERS OF VETERINARY MEDICINES

BETWEEN

THE AUSTRALIAN PESTICIDES AND VETERINARY MEDICINES AUTHORITY

AND

THE THERAPEUTIC GOODS ADMINSTRATION

MEMORANDUM OF UNDERSTANDING CONCERNING LICENSING AND AUDITING OF AUSTRALIAN MANUFACTURERS OF VETERINARY MEDICINES
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CONTENTS **PAGE**

THIS MEMORANDUM OF UNDERSTANDING

is made this day of , 2009

BETWEEN these Parties:

THE AUSTRALIAN PESTICIDES AND VETERINARY MEDICINES AUTHORITY (APVMA), a Statutory Authority established by the *Agricultural and Veterinary Chemicals (Administration) Act 1992,* of 18 Wormald Street, Symonston, ACT 2609.

and

THE THERAPEUTIC GOODS ADMINISTRATION (TGA), a Division of the Department of Health and Ageing of Narrabundah Lane, Symonston, ACT 2609.

This Memorandum of Understanding concerning the management of manufacturing facility audits replaces the Memorandum of Understanding entered into by the Parties on the 6th July 2001.

1. DEFINITIONS AND INTERPRETATION OF THIS MEMORANDUM OF UNDERSTANDING

1.1 In this Memorandum of Understanding (MoU), unless the contrary intention appears:

'**APVMA**' means the Australian Pesticides and Veterinary Medicines Authority;

'**APVMA Manufacturing Standards'** means the *Agricultural and Veterinary Chemicals Code Regulations 1995*, *Agricultural and Veterinary Chemicals Instrument No 1 (Manufacturing Principles) 2007*; the Australian Code of Good Manufacturing Practice for Veterinary Chemical Products and any other guidelines and standards applicable to the manufacture of Veterinary Medicines, which manufacturers of Veterinary Medicines must comply with in order to obtain or retain a manufacturing licence;

'**Audit**' means the inspection and assessment of documentation and Manufacturing Assets for the purposes of determining compliance with standards and guidelines for GMP;

'**CEO**' means the person from time to time holding, occupying or performing the duties of the office or position of Chief Executive Officer of the APVMA;

'**Code Act**' means the *Agricultural and Veterinary Chemicals Code Act 1994*;

GMP means Good Manufacturing Practice;

'**GMP Audit**' means an audit carried out by a TGA GMP Auditor/s of manufacturers of Veterinary Medicines and human therapeutic goods;

'**Information'** means information and documentation regarding the particulars of registration, manufacture, supply and possession of veterinary chemical products and active constituents pursuant to the disclosure provisions of Section 162 of the *Agricultural and Veterinary Chemicals Code Act 1994* and any other information that is reasonably necessary for compliance, audit or licensing purposes;

'**Manufacturing Assets'** means all the personnel and material assets, including facilities, equipment, systems, processes and procedures, employed in the manufacture of human therapeutic goods or veterinary medicines;

'**MRA**' means either the Mutual Recognition Agreement on Conformity Assessment between Australia and the European Community or the Agreement on Mutual Recognition in Relation to Conformity Assessment, Certificates and Markings between Australia and the Republic of Iceland, The Principality of Liechtenstein and the Kingdom of Norway Agreement on Conformity Assessment, as both have similar operational requirements;

'**MoU'** means this Memorandum of Understanding;

National Manager means the person from time to time holding, occupying or performing the duties of the office or position of National Manager of the TGA;

`Parties' means the TGA and the APVMA;

TGA means the Therapeutic Goods Administration, a Division of the Department of Health and Ageing;

'**TGA GMP Auditors'** means staff employed by the TGA to perform GMP Audits;

'**Veterinary Medicines'** means veterinary chemical products as defined in the *Agricultural and Veterinary Chemicals Code Act 1994*.

1.2 Words in the singular include the plural and words in the plural include the singular.

2. PURPOSE

2.1 This MoU establishes a formal framework to facilitate the auditing of relevant manufacturers and the exchange of audit reports, licence details and product information between the Parties. This cooperative framework underpins the licensing schemes managed by both Parties. It also supports both Parties' obligations under the MRA. This MoU does not create legally binding obligations between the Parties.

2.2 This MoU will also enhance the way in which the Parties work together in support of the operational aspects of licensing of manufacturers of mutual interest and will

not cover broader government regulatory policy.

3. UNDERSTANDING

3.1 This MoU is based on the mutual acceptance of differences in the legislative provisions and operating systems of the Parties.

3.2 The Parties understand that despite these differences, the APVMA may use the findings of a GMP Audit to determine whether manufacturers of Veterinary Medicines are complying with APVMA Manufacturing Standards for the purposes of licensing under the APVMA Manufacturers' Licensing Scheme, or certification under the MRA.

4. PRINCIPLES

4.1 Both Parties recognise that only licensed manufacturers are allowed to manufacture Veterinary Medicines that are registered for supply and use.

4.2 Both Parties licence manufacturers and apply risk management practices to assess continuing compliance with standards and guidelines for GMP, including periodic onsite auditing of Manufacturing Assets. TGA agrees to inform the APVMA if evidence other than, or in addition to, a GMP Audit of a manufacturer is used by it as a basis for any TGA licensing decision regarding that manufacturer.

4.3 Both Parties recognise that the exchange of information arising from GMP Audits is crucial for ongoing surveillance and the enforcement of compliance with standards and guidelines for GMP.

4.4 Both Parties recognise that the manufacture of Veterinary Medicines can pose a risk to the manufacture of human therapeutic goods and vice versa.

5. BACKGROUND

Australian Pesticides and Veterinary Medicines Authority (APVMA)

5.1 The APVMA is a statutory authority under the *Agricultural and Veterinary Chemicals (Administration) Act 1992*. One of its roles is to administer the Code Act, which includes the evaluation and registration of agricultural chemical products and Veterinary Medicines, control of the importation, manufacture and export of such products, compliance and enforcement, and quality assurance activities.

5.2 The Code Act requires manufacturers of Veterinary Medicines to be licensed. Licensees are required to comply with APVMA Manufacturing Standards. The

APVMA undertakes periodic audits and considers the outcomes of those audits in order to be satisfied that manufacturers of Veterinary Medicines are complying with APVMA Manufacturing Standards. The APVMA also considers the outcomes of those audits when making decisions to issue, amend, suspend or cancel APVMA licences.

5.3 The Code Act provides for a reduction in the cost of the APVMA licence fee for Veterinary Medicine manufacturers that also hold a licence from certain other authorities, including the TGA.

5.4 As a result of the framework outlined in this MoU, the APVMA may accept, for licensing purposes, a TGA GMP Audit report as evidence that a manufacturer of Veterinary Medicines at a particular site is complying with the APVMA Manufacturing Standards.

Therapeutic Goods Administration (TGA)

5.5 The TGA is responsible for administration of the *Therapeutic Goods Act 1989* which includes national controls over therapeutic goods standards, registration or listing of human therapeutic goods, and licensing of manufacturers of human therapeutic goods.

Both Parties

5.6 Australia entered into bilateral mutual recognition agreements with the European Community and three countries within the European Free Trade Association under a Sectoral Annex on Medicinal Products (including veterinary medicines) to the MRA ("Sectoral Annex"). The Sectoral Annex on Medicinal Products came into force on 1 July 2001. The TGA is the designated Official Inspection Service for both Veterinary Medicines and human pharmaceuticals in Australia.

6. SCOPE

6.1 This MoU is intended to cover those manufacturers who are of operational interest to both Parties and who have agreed to the bilateral exchange of Information between the Parties.

6.2 This MoU is also intended to include arrangements under the MRA, and therefore may also include manufacturers of Veterinary Medicines wishing to gain Certificates of Compliance under the current terms of the MRA.

6.3 The Code Act allows for certain exempt products and persons in relation to manufacture. This MoU is not intended to cover any assessments of manufacturers of exempt products unless requested by the other Party.

7. ACCESS TO AND EXCHANGE OF INFORMATION AND CONFIDENTIALITY

7.1 Subject to the other provisions of this clause:

7.1.1 the Parties intend that each will provide to the other copies of available Information required by the other Party to exercise its functions or make decisions regarding licensing as provided by this MoU;

7.1.2 the APVMA agrees to provide Information to the TGA on the expected, proposed or known manufacture of Veterinary Medicines for the purposes of this MoU;

7.1.3 the TGA agrees to provide Information to the APVMA about its GMP Audits including copies of any GMP Audit reports.

7.2 The Parties agree that the exchange of information between them under this MoU may be subject to the legislative provisions applicable to either Party. The sharing of information between the Parties will be subject to any relevant legislation and any other conditions, which the provider of information is or might lawfully be required to place on the use or disclosure of the information, such as claims of legal professional privilege.

7.3 The Parties also agree to protect the integrity and confidentiality of information exchanged between them. This MoU will not exclude the operation of any law intended to protect and preserve the confidentiality of any information that is subject to this MoU. In addition, to the extent that any applicable statutory provision allows it or requires it, any information exchanged between the Parties will be exchanged on a confidential basis. The parties also agree not to use or disclose any information that they receive under this MoU for any purpose unrelated to this MoU unless such use or disclosure is required or authorised by law.

7.4 Where a third party requests information from the APVMA that includes information relevant to this MoU, the APVMA will inform the TGA of that request and seek the views of the TGA in relation to the release of that material or seek the transfer of the request to the TGA where the information or request more closely relates to the TGA's functions.

8. NOTIFICATION OF LICENSING DECISIONS

8.1 Both Parties agree to notify each other of any suspensions, cancellations or withdrawals (total or partial) of manufacturing approvals or licences relevant to this MoU, where that licensing decision was based on non-compliance with GMP requirements as evidenced by a TGA GMP Audit. The procedures, timeframes and reporting formats for this notification will be consistent with current MRA procedures.

9. MANUFACTURERS' SELECTION OF AUDITORS

9.1 The Parties agree that the APVMA will allow relevant manufacturers to elect whether they wish the GMP Audit of their human therapeutic goods manufacture to also include their Veterinary Medicines manufacture in the scope of that audit. New Veterinary Medicines manufacturers will make the selection as part of their application for an APVMA manufacturing licence and their selection will stand until such time as it is changed by way of a notice in writing to the APVMA.

9.2 Neither the APVMA nor the TGA will require a manufacturer to have the audit of their human therapeutic goods and Veterinary Medicines manufacture combined.

9.3 Where a GMP Audit is delayed, or where some aspects of Veterinary Medicine manufacture are excluded from the scope of a GMP Audit, the APVMA may require an additional/separate audit by a non-TGA, APVMA-authorised auditor in order to make a licensing decision in respect of the Veterinary Medicines manufacturer.

10. DESIGNATION AND MONITORING OF TECHNICAL COMPETENCE OF TGA GMP AUDITORS

10.1 Section 122(2) of the Code Act requires that a person required to inspect manufacturing premises for the purposes of assessing an applicant for a licence, must either be an inspector or be authorised in writing by the APVMA. Therefore any TGA GMP Auditor carrying out a GMP Audit of a Veterinary Medicines manufacturer on the APVMA's behalf must also be authorised in writing by the APVMA.

10.2 Subject to clause 10.5, the APVMA accepts that TGA GMP Auditors possess the skills and necessary experience to conduct GMP Audits of Manufacturing Assets for the purposes of this MoU.

10.3 The TGA will from time to time provide the APVMA with a list of TGA GMP Auditors nominated to perform GMP Audits of Veterinary Medicines manufacturers, as well as their competencies and/or qualifications. The APVMA will authorise the individual TGA GMP Auditors as APVMA-authorised GMP Auditors unless it has cause to decline the authorisation. For the purposes of

authorising persons to conduct audits, the APVMA must be satisfied as to their competence to carry out these responsibilities.

10.4 Under the APVMA's ISO 9002 Quality Management System, the APVMA is required to satisfy itself that GMP Audits carried out on its behalf by the TGA are performed satisfactorily. The APVMA acknowledges that the TGA maintains a Quality Management System, and is a member of the international Pharmaceutical Inspection Cooperation Scheme (PIC/S).

10.5 Should the APVMA receive an adverse report of a conflict of interest or a complaint about a TGA GMP Auditor, the APVMA reserves the right to withdraw authorisation for that TGA GMP Auditor. However, before withdrawing the authorisation of any TGA GMP Auditor, the APVMA will discuss any concerns it may have about the performance of the TGA GMP Auditor with the TGA. The TGA may provide input as to the best means of resolving those concerns, before the authorisation is withdrawn.

10.6 Clause 10 applies unless varied through the *Maintenance Program* of the MRA, agreed to by the Parties, or upon receipt of advice from TGA that it has ceased to maintain its membership of the PIC/S.

10.7 TGA GMP Auditors duly authorised by the APVMA will continue to participate in ongoing training programs provided through the TGA and may from time to time be invited to participate in specific training and information sessions designated by the APVMA.

11. COSTS OF AUDIT

11.1 The Parties note that the TGA imposes fees in accordance with the *Therapeutic Goods Regulations 1990* and in the *Therapeutic Goods (Annual Charges) Regulations 1990* (the Regulations).

11.2 The fees charged by the TGA for a TGA Audit of a Veterinary Medicines manufacturer will be aligned with the fees in the Regulations.

11.3 The APVMA will advise Veterinary Medicine manufacturers to liaise directly with the TGA regarding the costs of any GMP Audits conducted by the TGA, including those conducted for MRA certification purposes.

12. PRE-AUDIT ARRANGEMENTS

12.1 The APVMA will provide the TGA with an up-to-date list of APVMA licensed manufacturers who have elected for the TGA to conduct a GMP Audit of their manufacture of human therapeutic goods and Veterinary Medicines. The list will be updated by the APVMA at least once every 12 months from the date of this MoU.

12.2 The TGA will provide the APVMA with the name and address of manufacturers for whom a GMP Audit is required, at least four weeks before the GMP Audit is to take place.

12.3 The APVMA will advise the TGA of what specific Veterinary Medicines need to be audited during a GMP Audit (if any), and any areas requiring particular attention during a GMP Audit at least two weeks before the scheduled date of the GMP Audit. The APVMA will nominate no more than two specific Veterinary Medicines for any one GMP Audit.

12.4 The APVMA will provide to the TGA at least two weeks before the scheduled date of a GMP Audit, all the information necessary for the performance of the GMP Audit and any other Information reasonably requested by the TGA for the purposes of its audit function under this MoU.

13. AUDIT ARRANGEMENTS AND RELEVANT STANDARDS AND GUIDANCE FOR GMP COMPLIANCE

13.1 The Parties agree that GMP Audits will be conducted at sufficient frequency to ensure continued compliance with standards and guidelines for GMP and will be conducted using risk-based methods. The Parties also agree that each manufacturer should be audited at least once every 36 months. The TGA will notify the APVMA if a GMP Audit of a Veterinary Medicines manufacturer will not be conducted within 36 months of the previous audit of that manufacturer (whether not the previous audit was undertaken by a TGA GMP Auditor).

13.2 The Parties agree that for manufacturing sites licensed by both authorities, each GMP Audit will include an audit of the Manufacturing Assets used in the manufacture of Veterinary Medicines, whether or not those particular Manufacturing Assets are also used in the manufacture of human therapeutic goods.

13.3 Subject to clause 13.4, where the same Manufacturing Assets are used to manufacture both Veterinary Medicines and human therapeutic goods, the Parties agree that manufacturers who elect for a GMP Audit will be audited against the relevant GMP Code for human therapeutic goods, namely the *Australian Code of*

Good Manufacturing Practice for Medicinal Products or other standards regarded as appropriate by the TGA.

13.4 Where Manufacturing Assets are employed solely for the manufacture of Veterinary Medicines, the Parties agree that manufacturers who elect for a GMP Audit for the purposes of the MRA will be audited against the requirements stated in the MRA.

13.5 The GMP Audit report should clearly describe where a manufacturer of Veterinary Medicines did not comply with any relevant requirements or standards as well as a brief outline of the observations that led to the reported non-compliances.

14. POST-AUDIT ARRANGEMENTS

14.1 The TGA will provide to the APVMA a copy of a GMP Audit report within 28 days of the GMP Audit being conducted. In order to simplify the finalisation of GMP Audits, it is anticipated that all non-compliances solely relevant to the manufacture of Veterinary Medicines will be clearly reported, preferably as an attachment to the GMP Audit report.

14.2 The TGA will notify the APVMA within 24 hours of the GMP Audit date, wherever possible, of a suspected deficiency that has produced, or may result in a significant risk of producing, a product that poses a risk to treated animals or human users (ie a “critical deficiency”).

14.3 The TGA will invite the APVMA to participate in a review panel formed to consider a potentially unacceptable GMP Audit outcome, or a critical deficiency, and to make recommendations for regulatory action by the TGA. If requested, the APVMA may provide input to a risk assessment prepared for consideration by the review panel.

14.4 The TGA will notify the APVMA within 14 days of the closure of each GMP Audit (that is, after acceptance of manufacturer’s corrective action, if any) together with details, where relevant, of licensing action being taken by the TGA, or any other changes to the scope and conditions of the TGA licence of that manufacturer.

14.5 The Parties agree that for all GMP Audits, responsibility for the implementation and verification of corrective actions will rest with the TGA. If the TGA has difficulty obtaining appropriate evidence from the manufacturer in order to assess correction of deficiencies related to Veterinary Medicines manufacture, the TGA should refer the matter to the APVMA for action.

14.6 Notwithstanding clause 14.5, the Parties also agree that responsibility for the resolution of disputes and the enforcement of compliance and licensing ultimately rests with the TGA for the manufacture of human therapeutic goods and with the APVMA for the manufacture of Veterinary Medicines. Neither authority is bound to take regulatory action identical to that taken by the other.

15. ADMINISTRATIVE ARRANGEMENTS

15.1 Routine operational information concerning the scheduling or outcomes of GMP Audits should be exchanged between the Designated Coordinators (see clause 18) or other staff nominated for this purpose by each of the Parties.

15.2 Each Party will write to the other Party to notify any significant changes to the legislation, operational policies, manufacturing principles, codes of GMP, practices or procedures of either Party, which relate to matters covered by the MOU, and which would impact on the operation of the MoU. Any consequential changes to the MoU will be subject to consultation between the Parties.

15.3 Either Party may propose a variation to the provisions of the MoU, but the CEO of the APVMA and the National Manager of the TGA must agree in writing to any variation.

15.4 The MoU will be maintained through quarterly discussions between the Parties on issues relating to this MoU or the licensing of manufacturers of Veterinary Medicines. These issues might include changes to the legislative provisions, manufacturing licensing programmes or GMP standards, collaboration on training of auditors, collaboration on issues relating to the MRA, and resolution of issues arising from GMP non-compliance which may be of interest to the other Party.

15.5 All formal communications in respect to reviewing, modifying or clarifying the MoU will be between the Designated Coordinators.

15.6 If either Party changes a Designated Coordinator, that Party will notify the other Party in writing of that change within 10 working days.

16. PERFORMANCE INDICATORS RELEVANT TO THIS MOU

16.1 The Parties agree that the following performance indicators will be used to monitor the effectiveness of the MoU

- Information supplied under 12.1, 12.2, 12.3, 12.4, 13.1, 14.1, 14.2
- Timeframes described under 12.1, 12.2, 12.3, 12.4, 13.1, 14.1, 14.2
- Feedback from manufacturers

16.2 The Parties agree to address any issues that may be raised as a result of such monitoring, within 7 business days of the issue being identified or as soon as possible thereafter.

17. PROBLEM RESOLUTION

In the first instance, Designated Coordinators will be responsible for investigating and resolving any disputes or differences between the parties in relation to the interpretation or performance of this MoU. If the dispute or difference cannot be settled in this way, it will be referred to the signatories to the MoU.

18. DESIGNATED CO-ORDINATORS

For TGA:

The person holding, occupying or performing the duties of the position of Head of Office, Office of Manufacturing Quality or such other persons as may be nominated by the National Manager of the TGA from time to time for this purpose.

For APVMA:

The person holding, occupying or performing the duties of the position of Manager, GMP or such other persons as may be nominated by the CEO of the APVMA from time to time for this purpose.

19. REVIEW OF THE MOU

19.1 On, or shortly after, the first anniversary of the date of this MoU, Designated Co-ordinators will review the flow of information between the Parties, and the scope of the MoU and consider, if appropriate, amendment of this MoU. Thereafter, periodic review of this MoU may take place on request from either Party, but not less than once every 36 months from the date of the first review.

19.2 Nothing in clause 19.1 precludes the Parties from mutually determining to amend this MoU at any time.

20. COMMENCEMENT DATE

20.1 This MoU will come into effect on the day that it is signed by both Parties and will continue in effect until it is terminated.

20.2 Either Party may terminate this MoU by written notice to the other Party. Unless otherwise agreed between the Parties, the MoU will terminate 30 days after the

date upon which the other Party received written notice of the intention to terminate.

21. SIGNATURE OF PARTIES

For TGA:	For APVMA:
National Manager	Chief Executive Officer
Date:	Date: