



Complementary Healthcare Council of Australia

Guideline for the Quality and Safety of Raw Materials used in Complementary Medicines

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Contents

- 1 Definitions**
- 2 Introduction**
- 3 Objectives**
- 4 Scope**
- 5 Principles of the Guidelines**
- 6 General Principles for the Quality and Safety of Raw Material**
- 7 Requirements for Specifications and Certificates of Analysis**
- 8 Compliance**
- 9 Complaints**
- 10 Publicising the Guidelines**
- 11 Review and Amendments**
- 12 Disclaimer**
- 13 Appendix 1 Requirements for Specifications and Certificates of Analysis**
- 14 Appendix 2 Other Information Which May be Provided by Manufacturers**
- 15 Appendix 3 Supplier Vendor Qualification Questionnaire**
- 16 Appendix 4 Raw Material Manufacturer Vendor Qualification Questionnaire**
- 17 Appendix 5 Packaging Material Manufacturer Vendor Qualification Questionnaire**
- 18 Appendix 6 Free From Information Questionnaire**
- 19 Appendix 7 TSE Questionnaire**
- 20 Appendix 8 References**

1 Definitions

- 1.1 **adulteration** - added substances in raw material(s) other than those that are supposed to be present.
- 1.2 **aflatoxin** - a naturally occurring toxin found in some raw materials of botanical origin and produced by various types of mould.
- 1.3 **batch** - a quantity of a product that is uniform in composition, method of manufacture and probability of chemical or microbial contamination, and made in one cycle of manufacture.
- 1.4 **batch number** - a number, or a combination of numerals, symbols or letters, which is given by a manufacturer to a batch of medicines to uniquely identify that batch and from which it is possible to trace that batch through all stages of manufacture and distribution.
- 1.5 **botanical reference standard** - an independently certified batch of botanical material shown by an extensive set of analytical and visual tests to be authentic.
- 1.6 **botanical name** - the Latin binomial used to uniquely define the plant species. It may sometimes include the classification system being employed such as Linneaus (L.) as a suffix.
- 1.7 **carrier** – see *excipient*.
- 1.8 **CAS registry number** - a unique identifying number assigned to a substance when it enters the Chemical Abstracts Service (CAS) Registry database.
- 1.9 **Certificate of Analysis** - a document certifying the test results for a particular batch of raw material.
- 1.10 **chemical identification** - a method that establishes the unique chemical composition of a substance.
- 1.11 **client identification number** a unique identification number allocated by the Therapeutic Goods Administration to identify sponsors.
- 1.12 **complementary medicines** – is defined as per *Therapeutic Goods Regulations 1990*.
- 1.13 **compositional guidelines** – is a summary of descriptions, tests and limits that define the composition and characteristics of a substance approved for use in

Listed medicines as either an active substance or an excipient. These guidelines are required when there is no standard for a substance in an approved Australian default standard.

- 1.14 **contamination** - refers to contamination by foreign material including bacteria, yeast, mould, heavy metals, pesticides, radionuclides, insects, faecal matter, fur and dirt.
- 1.15 **crude herbal starting material** - unprocessed herbal material used in the manufacture of a material of botanical origin.
- 1.16 **DNA fingerprinting** - a method of identifying materials of botanical origin by determining their unique genetic sequence.
- 1.17 **dry** - refers to materials of botanical origin that have been dried to reduce the moisture content to a specified level to allow storage and/or enable further processing.
- 1.18 **endangered species** - a plant or animal species that is in threat of extinction and is defined by the relevant Commonwealth and/or State and Territory legislation.
- 1.19 **enterprise identification number** - see *client identification number*.
- 1.20 **excipient** - an ingredient that is added to a raw material for a specific functional role. It can include antioxidants such as butylated hydroxytoluene (BHT), microbiological preservatives such as methyl hydroxybenzoate and diluents, flow agents and anti caking agents that help to alter/improve the physical characteristics of a raw material.
- 1.21 **expiry date** - the period of time during which the raw material is expected to remain within the established specifications if stored under defined conditions. It is determined from the raw material manufacturing date.
- 1.22 **fresh** - refers to materials of botanical origin that have not been dried to reduce the moisture content.
- 1.23 **genetic modification status** - a statement certifying whether the crude starting material that is used to manufacture a raw material has undergone genetic modification.
- 1.24 **harvesting period** - the time period or season during which harvesting is undertaken.
- 1.25 **heavy metals** - metals including arsenic, cadmium, lead and mercury that can be present in raw materials.

- 1.26 **lot** - see *batch*.
- 1.27 **lot number** - see *batch number*.
- 1.28 **macroscopic taxonomic identification** - a method used to establish the identity of a species of plant by visual examination.
- 1.29 **Material Safety Data Sheet** - a document containing health and safety information of a raw material.
- 1.30 **mechanical processing** - refers to processing of crude starting materials of botanical origin including sorting, sieving, cutting or chopping by machines.
- 1.31 **member** – a member of the Complementary Healthcare Council of Australia.
- 1.32 **microbiological contamination** - the undesired introduction of impurities of a microbiological nature into a raw material including bacteria, yeast and mould.
- 1.33 **microscopic taxonomic identification** - a method used to establish the identity of a species of plant by microscopy.
- 1.34 **native extract** – means the material consisting only of components present in the original plant or formed during the extraction process, excluding any excipients or other added substances.
- 1.35 **native extract ratio** – is the ratio of the mass of herbal material to the mass of the resulting native herbal preparation (=native extract).
- 1.36 **pesticide residues** - refers to residual levels of fungicides, herbicides, insecticides and rodenticides that may be found in raw material.
- 1.37 **proprietary ingredient number** - a unique number issued by the Therapeutic Goods Administration for formulated ingredients (usually commercially obtained) in which the formulation is to remain confidential.
- 1.38 **radionuclide** - a radioactive species of an atom.
- 1.39 **raw material** - an active ingredient or excipient used in the manufacturing of therapeutic goods.
- 1.40 **reference standard** – a certified batch of material shown, by an extensive set of analytical tests, to be authentic and of defined purity.
- 1.41 **residual solvents** - residues that can remain from the extraction solvent that was used in the manufacture of the raw material.

- 1.42 **retention sample** - a sample that is taken from a batch of raw material to enable testing at a later time, should it be necessary, for quality purposes.
- 1.43 **retest date** – refer to *expiry date*.
- 1.44 **sanitising treatment** - a process that is used to reduce levels of bacteria, yeast and mould that may be contained in a raw material. It includes processes such as chemical, dry heat, steam and gamma irradiation.
- 1.45 **shelf life** - refer to *expiry date*.
- 1.46 **solvent extraction** - a manufacturing process using solvents including, but not limited to, water, ethanol, glycerine, oils, and supercritical gases.
- 1.47 **specification** - the set of parameters and criteria that the raw material must conform to be considered acceptable for its intended use.
- 1.48 **sponsor** - as defined in the *Therapeutic Goods Act 1989*.
- 1.49 **standardised component** - a component that is present in a defined amount in a raw material.
- 1.50 **transmissible spongiform encephalopathy (TSE) status** - a statement certifying whether the crude starting material that is used to manufacture a raw material is of animal origin, and if so what methods have been employed to minimise the risk of TSE.
- 1.51 **validation** - proving there is a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined acceptance criteria.

2 Introduction

- 2.1 The Complementary Healthcare Council of Australia (CHC) is the peak body representing the complementary medicine industry in Australia. In consultation with key stakeholders, the CHC has undertaken the development of this Guideline.
- 2.2 Stakeholders involved in the development of this Guideline include:
 - 2.2.1 CHC Secretariat;
 - 2.2.2 Therapeutic Goods Administration (TGA);
 - 2.2.3 Raw material manufacturers and suppliers (members and non-members of the CHC);
 - 2.2.4 Complementary medicine sponsors and contract manufacturers (members and non-members of the CHC); and
 - 2.2.5 Australian Self Medication Industry Incorporated (ASMI)
- 2.3 This Guideline defines the principles for the quality and safety of raw materials in the Complementary Medicines Industry of Australia.
- 2.4 This Guideline may be referred to using the abbreviated title of the *CHC Guideline for Raw Materials*.
- 2.5 The source documents that were used in the development of this Guideline are listed in **Appendix 3 References**.

3 Objectives

- 3.1 To define the principles and minimum documentation requirements which need to be adhered to by industry, in their efforts to certify the quality and safety of raw materials being used in complementary medicines.
- 3.2 To define a guide to be followed by Industry to minimise their risk of breaching the *Therapeutic Goods Act 1989* and *Therapeutic Goods Regulations 1990* (both as amended from time to time), as well as all other relevant legislation, legislative instruments, government guidelines or standards (existing from time to time).
- 3.3 To enhance consumer confidence in the quality and safety of complementary medicines.
- 3.4 To maintain and enhance the credibility and the sustainability of the complementary medicines industry.

- 3.5 To minimise the risk of raw materials being used in illicit drug manufacture.

4 Scope

- 4.1 The provisions, requirements and principles described in this Guideline apply to all raw materials, raw material manufacturers and suppliers, brokers, distributors, re-packers, sponsors and contract manufacturers, and all other parties involved with the manufacture, supply or distribution of complementary medicines.
- 4.2 The provision of raw materials to healthcare professionals for the purpose of extemporaneous compounding is excluded from the scope of this Guideline.
- 4.3 Adherence to the requirements and principles described within this Guideline is encouraged for all of Industry.

5 Principles of the Guideline

- 5.1 Industry must not engage, directly or indirectly or be knowingly concerned in any unethical behaviour, misleading or deceptive conduct, unfair or unconscionable practices or conduct in normal commercial practice.
- 5.2 Members of CHC are permitted to use the CHC Logo as per the *CHC Policy and Procedures for the Use of the CHC Member Logo*.
- 5.3 As required by the *Therapeutic Goods Act 1989*, the ultimate responsibility for the quality and safety of raw materials used in therapeutic goods lies with the sponsor. However, the purpose of this document is for raw material suppliers to understand their role and obligations to the sponsor.
- 5.4 Industry shall ensure they are familiar and comply with the provisions of this Guideline and all Commonwealth, State or Territory legislation or instruments applicable to the **manufacture, supply and distribution** of raw materials for use in complementary medicines.
- 5.5 Industry shall ensure that all raw materials supplied by or through them or on their behalf comply with the relevant standards, quality and safeguards set out in the ***General Principles for the Quality and Safety of Raw Materials***.

- 5.6 Industry shall ensure that all Certificates of Analysis and specifications provided by or through them or on their behalf for raw materials comply with the requirements, procedures and methods set out in the Appendix 1 ***Requirements for Specifications and Certificates of Analysis***
- 5.7 Industry shall ensure that all other information referred to in **Appendix 2 *Other Information to be Provided by Manufacturers***, where requested is provided without delay and is provided on the original manufacturer letterhead.
- 5.8 Industry shall ensure they do everything reasonably possible to minimise the risk of raw material(s) being diverted into illicit drug manufacture by, amongst other things:
- 5.8.1 complying with the principles of the Plastics and Chemicals Industries Association (PACIA) and Science Industry Australia (SIA) *Code of Practice for Supply Diversion into Illicit Drug Manufacture*;
 - 5.8.2 complying with all policy and legislative requirements relating to the Government's National Drug Strategy in relation to supply diversion into illicit drug manufacture; and
 - 5.8.3 closely monitoring the sale of raw materials that could be used in illicit drug manufacture.

6 General Principles for the Quality and Safety of Raw Materials

- 6.1 The information provided has been summarised from various documents including the *Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PICS) 2010 Annex 7- Manufacture of Herbal Medicinal Products*, and the *Australian Regulatory Guidelines for Complementary Medicines (ARGCM)*. More detailed information can be found in these and other reference documents listed in **Appendix 3 References**.
- 6.2 Where applicable, raw materials shall comply with the requirements of the current editions of the approved Australian default standards, TGA Guidelines, TGA Standards and TGA final Compositional Guidelines.
- 6.3 Where applicable, raw materials shall comply with the requirements of the general monographs of the current editions of the approved Australian default standards relating to residual solvents and pesticide residues. In the case of raw materials of natural origin, testing for pesticide residues can be undertaken on the crude starting material as long as validation has been undertaken to show that these contaminants are not concentrated during subsequent processing.

- 6.4 Where applicable, raw materials shall be tested for adulteration, contamination, microbiological contamination, aflatoxins and radionuclides. In the case of raw materials of natural origin, testing can be undertaken on the crude starting material as long as validation has been undertaken to show these contaminants are not concentrated during subsequent processing.
- 6.5 Where applicable, raw materials shall be tested for physical properties such as, but not limited to; specific gravity, pH, total solids, bulk density, loss on drying, solubility, taste, smell, total ash and particle size distribution.
- 6.6 A Material Safety Data Sheet (MSDS) shall be provided prior to the supply of any raw material. A MSDS should be compliant with the National Occupational Health and Safety Commission (NOHSC) guidelines.
- 6.7 Analytical methods used to test raw materials should be scientifically valid.
- 6.8 Retention samples of both the crude starting material and the raw material should be held for a minimum of the expiry date plus one year.
- 6.9 Repackaging of already manufactured raw materials is considered a step in manufacture by the TGA, and must be undertaken in a facility that has been licensed to manufacture therapeutic goods (if located in Australia) or has been given overseas GMP preclearance (if located overseas).
- 6.9.1 Relabelling and sampling of raw material is not considered to be a step in manufacture and is therefore not required to be carried out in a TGA licensed facility. These activities should be assessed by the manufacturer as part of the qualification of the raw material supplier.
- 6.10 Translation of non English documents should:
- 6.10.1 include the name, date and signature of the person who has undertaken the translation from an authorised company; and
- 6.10.2 include the original language document.

7 Requirements for Specifications and Certificates of Analysis

- 7.1 The information provided in this Section has been summarised from various documents including the *Australian Code of Good Manufacturing Practice for Medicinal Products August 2002 Annex 7- Manufacture of Herbal Medicinal Products*, and the *Australian Regulatory Guidelines for Complementary Medicines (ARGCM)*. More detailed information can be found in these and other reference documents listed in **Appendix 3 References**.

- 7.2 Specifications requirements are listed below and in more detail in **Appendix 1 Requirements for Specifications and Certificates of Analysis**.
- 7.2.1 Specifications shall be provided with commercial supply of any raw material.
- 7.2.2 Specifications shall be provided on the original manufacturer letterhead and should not be transcribed or altered in any way. Raw material suppliers may provide additional information relating to their specification on their company letterhead, alongside the original document, if desired.
- 7.2.3 Copies of specifications should only be reproduced in full, and methods should be employed to reduce the ability of third parties to alter or tamper with the integrity of the specifications.
- 7.3 Certificates of Analysis requirements are listed below and in **Appendix 1 Requirements for Specifications and Certificates of Analysis**.
- 7.3.2 Certificates of Analysis shall be provided with each lot of the raw material.
- 7.3.3 Certificates of Analysis shall be provided on the original manufacturer letterhead and should not be transcribed or altered in any way. Raw material suppliers may provide additional information from their Certificates of Analysis on their company letterhead, alongside the original, if desired.
- 7.3.4 Copies of Certificates of Analysis should only be reproduced in full, and methods should be employed to reduce the ability of third parties to alter or tamper with the integrity of the document.

8 Compliance

- 8.1 Industry should take all measures reasonably required to ensure compliance with this Guideline by their employees and company representatives. Industry should adopt effective compliance programs by issuing written policies and procedures, conducting training programs and implementing clear procedures, controls and enforcement mechanisms.
- 8.2 Industry are encouraged to inform all customers, institutions, healthcare practitioners and other professionals with whom they deal, of the requirements of this Guideline.

9 Complaints

- 9.1 Industry members are in the position where they could become aware of companies that may be adulterating raw materials deliberately, or risking adulteration through poor business practices.
- 9.2 To safeguard consumers and protect the reputation of industry, there is an obligation for members to raise their concerns about these issues.
- 9.3 Before lodging a formal complaint with the relevant authorities, complainants should first seek to resolve the complaint directly with the company whose behaviour has given rise to the complaint.
- 9.4 If the complaint cannot be resolved directly with the company, the complaint should be forwarded to the TGA, state health authorities or the Australian Competition and Consumer Commission (ACCC), depending on the nature of the complaint.

10 Publicising the Guidelines

- 10.1 The CHC must ensure this Guideline is publicly available on its website and will encourage members to reference and provide links to this Guideline on their own websites, including using the CHC Member logo as appropriate (as per the policy provisions outlined in the *CHC's Policy and Procedures for the Use of CHC Member Logo*).
- 10.2 The CHC will encourage its members to otherwise promote this Guideline on a regular basis; this can be done through the use of the CHC Member logo as appropriate (as per the provisions outlined in the *Policy and Procedures for the Use of the CHC Member Logo*).

11 Review and Amendments

- 11.1 This Guideline shall be internally reviewed on a regular basis, and at a minimum of once every three years.
- 11.2 The internal review process will be managed by the CHC Secretariat. In conducting the internal review the CHC Secretariat may seek comment or submissions from industry and other relevant stakeholders.

11.3 The internal review process should consider as a minimum the following issues:

11.3.1 Is there a high level of Industry awareness of this Guideline?

11.3.2 Is there a high level of stakeholder awareness of this Guideline?

11.3.3 Is this Guideline meeting its stated objectives?

11.4 Amendments to this Guideline must be approved by the CHC Secretariat.

11.5 Amendments must be adequately publicised so that all stakeholders are made aware of changes/updates.

12 Disclaimer

12.1 This Guideline is not intended to provide nor shall it be construed as legal advice.

12.2 Where there is any conflict or inconsistency between the provisions of this Guideline and any Commonwealth, State or Territory legislation or instrument, that legislation or instrument will take precedence over this Guideline.

12.3 The rules of conduct and the standards of good practice encouraged by this Guideline, are both fair and reasonable and are otherwise necessary for the Guideline to achieve its objectives.

13 Appendix 1 Requirements for Specifications and Certificates of Analysis

13.1 Specifications and other document packages for raw material(s) should include the following information:

13.1.1 Unique product item/code.

13.1.2 Botanical/scientific species name (where applicable).

13.1.3 Plant part(s) used (where applicable).

13.1.4 Chemical structure including CAS registry number (where applicable).

13.1.5 Shelf life.

13.1.6 Pharmacopoeial reference (where applicable).

- 13.1.7 Reference to the specification for the crude starting material (where applicable).
- 13.1.8 Storage conditions.
- 13.1.9 Preparation type (where applicable).
- 13.1.10 Physical properties including reference to the analytical methods used (where applicable).
- 13.1.11 Whether the crude starting material was fresh or dry (where applicable).
- 13.1.12 Name and percentages of solvents used to extract the crude starting material including reference to the quality standard used (where applicable).
- 13.1.13 Final extraction ratio (where applicable).
- 13.1.14 Name and quantity of any excipients present, including reference to the quality standard used (where applicable).
- 13.1.15 Microbiology including reference to the analytical methods used.
- 13.1.16 Chemical identification, including reference to the analytical methods used.
- 13.1.17 Chemical analysis of any standardised components including reference to the analytical methods used (where applicable).
- 13.1.18 Heavy metals, residual solvents, pesticide residues, aflatoxins and radionuclides including reference to the analytical methods used (where applicable).
- 13.1.19 Other tests as required including reference to the analytical methods used (where applicable).
- 13.1.20 Source of the botanical reference standard used to perform the botanical identification (where applicable).
- 13.1.21 Source of the reference standard used to perform the chemical identification (where applicable).
- 13.1.22 Signature, name and position of the person authorising the specification, or an equivalent electronic signature.

- 13.2 Certificates of Analysis for raw materials should include the following information except where stated otherwise:
- 13.2.1 Unique product item/code.
 - 13.2.2 Lot number.
 - 13.2.3 Date of manufacture.
 - 13.2.4 Expiry date/ retest date/ shelf life.
 - 13.2.5 Physical properties including reference to the analytical methods used (where applicable).
 - 13.2.6 Microbiology.
 - 13.2.7 Chemical identification.
 - 13.2.8 Chemical analysis of any standardised components.
 - 13.2.9 Heavy metals, residual solvents, pesticide residues, aflatoxins and radionuclides including reference to the analytical methods used (where applicable).
 - 13.2.10 Other tests as required including reference to the analytical methods used (where applicable).
 - 13.2.11 Signature, name and position of the person authorising the Certificate of Analysis, or an equivalent electronic signature.

14 Appendix 2 Other Information to be Provided by Manufacturers

- 14.1 The genetic modification status of the crude starting material used to produce the raw material, including reference to the analytical methods used (where applicable).
- 14.2 The TSE status of the material used to produce the raw material, including reference to the analytical methods used. Where applicable, a TSE Questionnaire must be provided.
- 14.3 A Material Safety Data Sheet (MSDS) shall be provided prior to the supply of any raw material. A MSDS should be compliant with the National Occupational Health and Safety Commission (NOHSC) guidelines.

- 14.4 The endangered species status of the crude starting material (where applicable).
- 14.5 The raw material manufacturer's enterprise identification number and proprietary ingredient number (where applicable).
- 14.6 Details of any sanitising treatment the raw material or crude starting material is subjected to (where applicable).
- 14.7 The country of origin of the raw material and crude starting material (where applicable).
- 14.8 Whether the crude starting material was wild crafted or cultivated (where applicable).
- 14.9 The harvesting period and any specific harvesting requirements of the crude starting material (where applicable).
- 14.10 Free from and allergen information.
- 14.11 Kosher status (where applicable).
- 14.12 Halal status (where applicable).

15 Appendix 3 Supplier Vendor Qualification Questionnaire

<http://www.chc.org.au/CHC-Guidelines>

16 Appendix 4 Raw Material Manufacturer Vendor Qualification Questionnaire

<http://www.chc.org.au/CHC-Guidelines>

17 Appendix 5 Packaging Material Manufacturer Vendor Qualification Questionnaire

<http://www.chc.org.au/CHC-Guidelines>

18 Appendix 6 Free From Information Questionnaire

<http://www.chc.org.au/CHC-Guidelines>

19 Appendix 7 TSE Questionnaire

<http://www.chc.org.au/CHC-Guidelines>

20 Appendix 8 References

- 15.1 American Herbal Products Association Guidance Documents for the Manufacture and Sale of Botanical Extracts
www.ahpa.org/
- 15.2 *Australian Regulatory Guidelines for Complementary Medicines (ARGCM)*
<http://www.tga.gov.au/docs/html/argcm.htm>
- 15.3 Code of Practice for Supply Diversion into Illicit Drug Manufacture
<http://designer-drugs.com/pte/12.162.180.114/dcd/chemistry/law/illicitdrugcode.au.pdf>
- 15.4 Microbial Limits Reviewed: The Basis for Unique Australian Regulatory Requirements for Microbial Quality of Non-Sterile Pharmaceuticals. *PDA Journal of Pharmaceutical Science and Technology* Vol 52 No. 3 May/June 1998. <http://journal.pda.org/content/52/3/100.abstract>
- 15.5 *National Guideline for the Preparation of Material Safety Data Sheets, Second edition* [NOHSC:2011(2003)]
<http://www.safeworkaustralia.gov.au/NR/rdonlyres/6AA1E55D-D444-4909-B18B-812688B49A7F/0/MSDSCoNOHSC20112003.pdf>
- 15.6 Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PICs) 2010 Annex 7- Manufacture of Herbal Medicinal Products <http://www.tga.gov.au/manuf/mp2009requirements.htm>
- 15.7 *Questions & Answers for the Identification of Herbal Materials and Extracts*
<http://www.tga.gov.au/cm/idherbal.htm>
- 15.8 *Starting Material Analytical Procedure Validation for Complementary Medicines*
<http://www.tga.gov.au/cm/analyticalval.htm>
- 15.9 Supplementary Requirements for Therapeutic Goods for Minimising the Risk of Transmitting Transmissible Spongiform Encephalopathies (TSEs) November 2002 <http://www.tga.gov.au/docs/html/tsesupp.htm>
- 15.10 *Therapeutic Goods Act 1989*
<http://www.comlaw.gov.au/comlaw/management.nsf/lookupindexpagesbyid/IP200401372?OpenDocument>
- 15.11 Therapeutic Goods Administration Compositional Guidelines
<http://www.tga.gov.au/docs/html/compguid/compguid.htm>

- 15.12 Therapeutic Goods Administration Laboratories' Guidelines for Assessing the Results of Microbiological Tests on Non-Sterile Pharmaceuticals for Human Use
<http://www.tga.gov.au/docs/html/unsteril.htm>
- 15.13 Therapeutic Goods Order No. 77 – *Microbiological standards for medicines*
<http://www.tga.gov.au/legis/tgo/tgo77.htm>
- 15.14 *Therapeutic Goods Regulations 1990*
<http://www.comlaw.gov.au/comlaw/management.nsf/lookupindexpagesbyid/IP200400127?OpenDocument>
- 15.15 Transmissible Spongiform Encephalopathies (TSEs) information
<http://www.tga.gov.au/docs/html/tse.htm>