



Australian Government

Department of Health

Therapeutic Goods Administration

Transmissible Spongiform Encephalopathies (TSE)

TGA approach to minimising the risk of
exposure

Version 2.0, April 2014

TGA Health Safety
Regulation

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, and is responsible for regulating medicines and medical devices.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <<http://www.tga.gov.au>>.

Copyright

© Commonwealth of Australia 2014

This work is copyright. You may reproduce the whole or part of this work in unaltered form for your own personal use or, if you are part of an organisation, for internal use within your organisation, but only if you or your organisation do not use the reproduction for any commercial purpose and retain this copyright notice and all disclaimer notices as part of that reproduction. Apart from rights to use as permitted by the *Copyright Act 1968* or allowed by this copyright notice, all other rights are reserved and you are not allowed to reproduce the whole or any part of this work in any way (electronic or otherwise) without first being given specific written permission from the Commonwealth to do so. Requests and inquiries concerning reproduction and rights are to be sent to the TGA Copyright Officer, Therapeutic Goods Administration, PO Box 100, Woden ACT 2606 or emailed to <tga.copyright@tga.gov.au>.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Office of Scientific Evaluation	15/12/2004
V2.0	Revised policy	Office of Scientific Evaluation	02/04/2014

Contents

Purpose	5
Background	5
TGA approach	6
Products of human origin	6
Products of animal origin	6
Industry self-assessment of low risk materials	7
Eligibility for self-assessment	7
Demonstrating compliance	7
Information to be provided for all other materials	8

Purpose

This document describes the approach the TGA follows to assess the safety of materials derived from human and other animal species, naturally susceptible to Transmissible Spongiform Encephalopathy (TSE), used in the manufacture of therapeutic goods. This approach applies principles that aim to minimise the risk of exposure to TSEs posed by the use of medicines, medical devices and biologicals containing materials from TSE-relevant species in Australia.

This document replaces the 2004 *TGA approach to minimising the risk of exposure to TSEs through medicines and medical devices* and the *TGA Supplementary requirements for therapeutic goods for minimising the risk of transmitting Transmissible Spongiform Encephalopathies*. The document will be effective from the date of publication.

Background

Transmissible Spongiform Encephalopathies caused by agents known as prions include:

- Bovine Spongiform Encephalopathy (BSE) in cattle
- Scrapie in sheep and goats
- Chronic Wasting Disease (CWD) in deer
- Kuru, Creutzfeldt-Jakob Disease (CJD) and Variant CJD (vCJD) in humans

Scientific evidence supports a link between the agent responsible for BSE in cattle and vCJD in humans. Furthermore it is generally accepted that BSE may be transmitted from animals to humans by consumption of contaminated materials of ruminant origin. Therefore it is important to minimise the potential for this agent to be transmitted to humans.

Transmission of the classical form of CJD has been reported via human pituitary extracts and certain tissues such as dura mater (5 cases in Australia)¹ and corneas (3 cases worldwide). There is also good evidence that vCJD can be transmitted through blood transfusion in humans^{2,3}. While there have been no reported cases of vCJD in Australia, the TGA believes that in the interests of protecting public health and safety, the potential risks of exposure to these agents in the manufacture and use of medicines, biologicals and medical devices should be minimised.

Since the publication of the 2004 TGA approach documents, mentioned above, control measures have been introduced in many countries which have led to a reduction in incidence of BSE⁴. These controls, together with emerging scientific data, have led to changes in the acceptability of many materials of ruminant origin for use in the manufacture of therapeutic goods and the countries from which they are derived. These changes have been incorporated into documents

¹ Department of Health and Ageing (2004). *Creutzfeldt-Jakob disease information*. viewed January 2014. <http://www.health.gov.au/internet/main/publishing.nsf/Content/icg-guidelines-cjd_factsheet.htm>.

² World Health Organisation (2006). *WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies*. Geneva: WHO Press.

<<http://www.who.int/bloodproducts/TSEPUBLISHEDREPORT.pdf>>

Update table:

World Health Organisation (2010). *WHO Tables on on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies*. Geneva: WHO Press.

<<http://www.who.int/bloodproducts/tablestissueinfectivity.pdf>>

³ Mathews J. (Oct 2009). *Review of scientific evidence to inform Australian Policy on Transmissible Spongiform Encephalopathies (TSEs); 2009 Addendum*. Carlton North: Health Explanations Pty Ltd. <<http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-bse-review-2009-addendum>>

⁴ Budka H. Editorial: *The European response to BSE: A Success Story*. EFSA Journal 2011; 9(9):e991.

<<http://www.efsa.europa.eu/en/efsajournal/pub/e991.htm>>

listing the requirements for minimisation of TSE risk via therapeutic goods. In particular, the requirements included in the European Pharmacopoeia (*Ph. Eur*) were revised in 2012.

The TGA accepts the position taken by the *Ph. Eur* as reflecting the current status of scientific understanding in regard to minimisation of TSE risk in relation to the use of ruminant derived materials in the manufacture of therapeutic goods.

TGA approach

All therapeutic goods containing or manufactured using human or ruminant materials must be assessed for TSE safety before entry in the [Australian Register of Therapeutic Goods \(ARTG\)](#).

Products of human origin

The sourcing of human derived materials for use in therapeutic goods includes the following Australian-specific requirements:

- Human derived materials must not be procured from anyone with a risk of prion disease:
risk of prion disease⁵ means where a donor has been exposed to the putative causative agent(s) of any one of the family of pathogenic transmissible spongiform encephalopathies through one of the following:
 - a. genetic (familial);
 - b. environmental, which includes donors who have lived in or visited England, Scotland, Wales, Northern Ireland or the Isle of Man for a cumulative period of six months or more, between 1st January 1980 and 31st December 1996 inclusive; or
 - c. iatrogenic, which includes donors who have received a transfusion or injection of blood or blood components while in England, Scotland, Wales, Northern Ireland or the Isle of Man at any time since 1st January 1980 onwards.

Products of animal origin

Products of animal origin must comply with the *Ph. Eur* general monograph 1483: *Products with risk of transmitting agents of animal spongiform encephalopathies*, including General Text 5.2.8: Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products⁶ (the *Ph. Eur* monograph).

The assessment for animal (non-human) derived material must be against the principles and requirements detailed in the *Ph. Eur* monograph, and can be conducted:

- for low risk materials, by [self-assessment](#); and
- for all other materials, by TGA evaluation.

⁵ **Risk of prion disease** as defined in Therapeutic Goods Order 88 – Standards for donor selection, testing and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products, issued under Section 10 of the *Therapeutic Goods Act 1989*.

⁶Ph. Eur general text 5.2.8 is identical to the European Medicines Agency (EMA) [Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products](#) (EMA/410/01 Rev. 3, July 2011).

Industry self-assessment of low risk materials

Eligibility for self-assessment

Sponsors of therapeutic goods containing or manufactured using ruminant materials may self-assess for compliance against the *Ph. Eur* monograph. To be eligible for self-assessment, the following requirements must be met:

- the final therapeutic goods are for oral or topical applications only;
and
- contain ruminant derived materials that:
 - are cervid derived materials from infectivity category IB or IC tissues *and* sourced from CWD free countries;
or
 - are non-cervid derived materials from infectivity category IC tissues *and* are sourced from category A (negligible BSE risk) or category B (controlled BSE risk) countries as classified by the World Organisation for Animal Health (OIE);
or
 - are one of the following materials, and are compliant with the relevant sections of the *Ph. Eur* monograph:
 - gelatin
 - collagen
 - tallow derivatives
 - animal charcoal
 - bovine milk and milk derivatives
 - wool derivatives
 - amino acids
 - peptones.

Demonstrating compliance

If goods are eligible for self-assessment, the sponsor must hold all relevant information to demonstrate compliance with the *Ph. Eur* monograph.

The section [Information to be provided for all other materials](#) provides guidance on the relevant information that should be collected and held for any self-assessment.

Although these materials are considered low TSE risk, this information must be readily available to the TGA should a TSE concern emerge and further risk assessment is required.

Information to be provided for all other materials

Information must be provided to the TGA as part of submissions for marketing approval, or for variations to products already approved, which demonstrates compliance with the *Ph. Eur* monograph.

The following advice is provided with regard to the information to be provided to the TGA in order to demonstrate compliance with the *Ph. Eur* monograph:

- Where the EDQM has issued a TSE Certificate of Suitability, both the certificate and any supporting information are to be supplied to the TGA.
- Where a EDQM certificate is not available, information on the following is required:
 - Country(ies) of origin of animals, including all countries the animal resided in
 - Status of the country(ies) of origin in accordance with the OIE classification
 - Type of tissue used
 - Details of measures taken to prevent cross contamination with higher risk tissues (particularly category IA) and tissues from other animals
 - Evidence that ante-mortem and post-mortem (where applicable) inspections are carried out and an assurance that the materials are derived from healthy animals fit for human consumption
 - The age of animals
 - Any relevant certificates e.g. veterinary certificates
 - Evidence that materials sourced from slaughtered animals are procured from government approved slaughter houses, where applicable
 - Name and address of the raw material manufacturing facility and/or the name and address of the supplier or distributor
 - Details, such as a flow chart, of the manufacturing process.
- Additional information required in the relevant sections of the *Ph. Eur* monograph, including any specific considerations included in Part 6 of the *Ph. Eur* monograph must also be provided.
- *Ph. Eur* monograph - Part 2 Scope - Seed lots, cell banks and routine fermentation production
This Part refers to ‘approval’ of ‘market authorisation applications’ and ‘properly conducted risk assessments’. All seed lots or cell banks used in the manufacture of therapeutic goods for use in or export from Australia must be assessed and approved by the TGA.
- *Ph. Eur* monograph - Part 6 Specific Considerations - 6.1 Collagen
For collagen sourced from bones as the starting material, the conditions specified for gelatin are applicable. This section also notes that the inactivation capacity expected from the collagen manufacturing process is lower than that expected for the gelatin manufacturing process and thus starting material sourcing is more critical for collagen. While the *Ph. Eur* monograph does not restrict the source of bones used for gelatin production, the TGA prefers that bones used for collagen manufacture are sourced from countries with a negligible or a controlled BSE risk (Categories A or B, respectively) unless otherwise justified.

This section also states that: “hides represent safer raw material for human implants derived from collagen. However, cross-contamination with brain material released during the slaughtering process, which may have dried on the surface of hides, would be difficult to eliminate”. While the *Ph. Eur* monograph does not restrict the source of hides for collagen

production, the TGA prefers that hides are sourced from countries with a negligible or a controlled BSE risk (Categories A or B, respectively) unless otherwise justified.

- *Ph. Eur* monograph - Part 6 Specific Considerations - 6.3 Bovine blood and blood derivatives
As the production process for many vaccines has minimal inactivation capacity, foetal bovine serum used in vaccine production must be sourced from Category A countries unless otherwise justified.

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6232 8605
<http://www.tga.gov.au>

Reference/Publication #