



Australian Government

**Department of Agriculture,
Fisheries and Forestry**

Import risk review for dehydrated and pre-sterilised microbiological media

Final report

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Animal Biosecurity Branch



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Acknowledgement of Country

We acknowledge the Traditional Custodians of Australia and their continuing connection to land and sea, waters, environment and community. We pay our respects to the Traditional Custodians of the lands we live and work on, their culture, and their Elders past and present.

Accessibility

This document contains mathematical symbols. Screen reader users may need to adjust their settings to read all content in this document.

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Summary

The Department of Agriculture, Fisheries and Forestry has prepared this risk review to revise the current import conditions for dehydrated and pre-sterilised microbiological media.

This risk review takes into account new and relevant peer-reviewed scientific information, advice from international scientific experts, and relevant current industry practices and operational practicalities.

Australia permits the importation of dehydrated and pre-sterilised microbiological media, with most media types requiring case-by-case assessment.

This risk review proposes that the importation of dehydrated and pre-sterilised microbiological media to Australia from all countries be permitted, subject to a range of biosecurity measures.

[Baseline risk management measures](#) have been proposed to ensure the goods have undergone the expected level of processing prior to importation, and to manage the biosecurity risk of bulk disposal or environmental contamination of microbiological media. The proposed baseline risk management measures for dehydrated and pre-sterilised microbiological media are:

- 1) Assurance that the goods are dehydrated microbiological media or pre-sterilised microbiological media

AND

- 2) Dehydrated microbiological media is imported in quantities of ≤ 5 kg per individually packaged unit

This risk review identifies hazards that require biosecurity measures to manage risks to a very low level in order to achieve Australia's appropriate level of protection (ALOP). The hazards requiring specific measures are the protease-resistant prion protein responsible for bovine spongiform encephalopathy (PrP^{BSE}) and the protease-resistant prion protein responsible for scrapie (PrP^{Sc}).

Dehydrated and pre-sterilised microbiological media

In addition to the baseline risk management measures listed above, this risk review proposes the following risk management measures that will reduce the risk associated with the importation of dehydrated and pre-sterilised microbiological media from all countries into Australia to achieve Australia's ALOP, specifically:

3) For bovine-derived material:

- a) Material does not contain Category A (high infectivity) bovine tissue as listed on the department's list of [Transmissible Spongiform Encephalopathy \(TSE\) risk categories of tissues and fluids](#)

AND

Goods are manufactured in countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status, as listed on the [Bovine Spongiform Encephalopathy \(BSE\) Country List](#)

OR

- b) Material is collected in countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status, as listed on the [Bovine Spongiform Encephalopathy \(BSE\) Country List](#)

AND

Goods are manufactured in countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status, as listed on the [Bovine Spongiform Encephalopathy \(BSE\) Country List](#)

AND

4) For ovine/caprines-derived material:

Material is sourced from ovines/caprines born, raised and slaughtered/born, raised and residing in Australia/New Zealand only.

5) If 1 and 2 and 3 and 4 above cannot be met, assessment on a case-by-case basis is required.

This risk review contains details of the risk review for the identified hazards and the proposed biosecurity measures to allow interested parties to provide comments and submissions to the department within the consultation period.

Introduction

1.1 Australia's biosecurity policy framework

Australia's biosecurity policies aim to protect Australia against risks that may arise from exotic pests entering, establishing and spreading in Australia, thereby threatening Australia's unique flora and fauna, agricultural industries that are relatively free from serious pests and diseases, and human health.

Risk analysis is an important part of Australia's biosecurity policies. It enables the Australian Government to formally consider the level of biosecurity risk that may be associated with proposals to import goods into Australia. If the biosecurity risks do not achieve Australia's ALOP, risk management measures are proposed to reduce the risks to an acceptable level. If the risks cannot be reduced to an acceptable level, the goods will not be imported into Australia until suitable measures are identified.

Successive Australian Governments have maintained a conservative, but not a zero risk, approach to managing biosecurity risks. This approach is reflected in Australia's ALOP, which reflects community expectations through government policy and is currently described as providing a high level of protection aimed at reducing risk to a very low level, but not to zero.

Australia's risk analyses are undertaken by the department using technical and scientific experts from relevant fields, and involve consultation with stakeholders at various stages during the process.

Risk analyses conducted by the department are consistent with Australia's international biosecurity obligations including those under the World Trade Organization (WTO) Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) and the World Organisation for Animal Health (WOAH). Risk analyses aim to establish a balance between our international obligations and the various risks that goods may pose.

Risk analyses may take the form of a biosecurity import risk analysis (BIRA) or a non-regulated risk analysis (such as scientific review of existing policy and import conditions, or scientific advice).

More information about Australia's biosecurity framework is provided in the [Biosecurity import risk analysis guidelines 2016](#).

The department recognises that new scientific information and technologies, or other combinations of measures, may provide an equivalent level of biosecurity protection for the disease agents identified as requiring risk management. The department will consider technical submissions that objectively demonstrate alternative biosecurity measures.

1.2 Background

Microbiological media refers to a large subset of culture media products imported into Australia for a wide range of laboratory purposes including human and veterinary diagnostics, manufacturing, food safety testing, and scientific research and development. Microbiological media products can contain a broad range of highly processed animal-derived ingredients sourced from multiple animal species. Australia does not manufacture microbiological media or its key constituent ingredients in

sufficiently large quantities to provide the wide range of necessary laboratory services. Therefore, it is essential for Australia to import microbiological media.

Currently, imported microbiological media and raw supplements such as whole blood and serum are treated as a homogenous animal biosecurity risk group, and importation requires a case-by-case assessment. However, many microbiological media products are highly processed and require sterilisation prior to use which provides inherent biosecurity risk mitigation.

This review considers the risks of media for the specific culture of microorganisms.

For the purposes of this review the use of the term microorganism, and by association microbiological, includes all prokaryotes, as well as protists, fungi, and all unicellular organisms which do not require either animal, human or plant cells to replicate, reproduce or survive. This differs from the definition of microorganism used for the purposes of the [Biosecurity \(Conditionally Non-prohibited Goods\) Determination 2021](#) (the Goods Determination), which is listed in the [Glossary](#).

For the purposes of this review, microbiological media includes media designed for the culture of plasmids, which are defined as infectious agents for the purposes of the Goods Determination as listed in the [Glossary](#).

Viruses of prokaryotes, such as bacteriophages and mycoviruses, are important in research and development. These viruses are of key interest to many scientific communities particularly in the field of alternatives to antibiotics. As they pose a limited biosecurity risk they are not considered in this review. Reference to viruses throughout the remainder of this review solely refers to viruses of animals and humans.

The risks posed by the deliberate importation of any living or replication-competent organism, microorganism, or infectious agent on a microbiological media carrier are not considered in this review.

1.2.1 Types of media

Dehydrated microbiological media

Dehydrated microbiological media is a highly processed, composite product with a specific end use. The majority of microbiological media are nutrient-rich to facilitate growth of microorganisms, and include material derived from either plant or animal tissue. Animal-derived ingredients included in the media are highly processed, having received various thermal, chemical or physical processing treatments. Due to the inclusion of components in the form of extracts or hydrolysates of animal or plant material, the exact chemical composition of most types of microbiological media is unknown. These types of media are often referred to as complex microbiological media (Chauhan & Jindal 2020). This contrasts with 'synthetic' or 'chemically defined' media for which the exact chemical composition of the media is known.

Dehydrated microbiological media does not support the growth of animal or human cells and consequently does not support the replication of viruses of animals and humans. Due to the extensive processing, the requirement for sterilisation and the inability to support replication of viruses, dehydrated microbiological media poses a much lower biosecurity risk than other types of media/media supplements that contain raw supplements (e.g. blood or blood products). It also poses

a much lower animal biosecurity risk than media containing animal-derived ingredients that supports the growth of cells derived from animals, humans, or plants and the replication of viruses.

Pre-sterilised microbiological media

Pre-sterilised microbiological media consists of dehydrated microbiological media that has been reconstituted and sterilised prior to import. Pre-sterilised microbiological media most often takes the form of poured plates of reconstituted dehydrated microbiological media which has had agar added to enable it to solidify or semi-solidify, and has been autoclaved. Pre-sterilised media may also take the form of reconstituted dehydrated microbiological media without agar in the form of a broth, or combination products containing both dehydrated microbiological media and sterilised water for combination through break or smack packs.

Pre-sterilised media are ready to be used and do not require further sterilisation. The media must be sterile to prevent overgrowth of contaminating microorganisms in liquid media bags or on agar plates prior to receipt by the end user; lack of sterility will be visibly apparent as microbial growth on receipt of the media. As well as the risk mitigation measures inherent to dehydrated microbiological media, pre-sterilised microbiological media has the additional inherent risk management measures of dilution and sterilisation prior to import.

Media for the culture of cells derived from animals, humans, and plants

Microbiological media is distinct from the media used for the culture of animal, human, and plant cells, which is colloquially termed 'cell culture media'. This media is used to culture cells and other material derived from multicellular organisms, and these cells can be used to grow viruses, parasites, and intracellular microorganisms. The vast majority of these media are 'defined media' as the exact composition of the media is known, and these media may be supplemented with undefined components such as foetal bovine serum, albumin, and other proteins. Media used for the culture of cells derived from animals, humans, and plants are mostly synthetically produced with defined quantities of distinct amino acids, vitamins, inorganic salts, glucose, and other chemical substances. Media used for the culture of cells derived from animals, humans, or plants will not be considered further in this review.

Media supplements

Media supplements may be minimally processed heat labile components, such as blood or blood components. These are added to the media after thermal sterilisation of rehydrated media. When these supplements comprise blood or blood components they pose a greater animal biosecurity risk than dehydrated and pre-sterilised microbiological media. Blood for this purpose may be derived from sheep, horses, rabbits, cattle, or humans (Atlas 2010), and is not thermally sterilised or irradiated at 50 kGy prior to use. Microbiological media supplements will not be considered further in this risk review.

1.2.2 Components of microbiological media

There are over 7,000 distinct types of microbiological media to provide the diversity of conditions required to grow different types of microorganisms, and to support their diverse metabolic pathways (Atlas 2010). This number continues to grow as microorganisms with more specialised or extreme growth requirements continue to be identified and more specialised media are developed. Despite the vast number of microbiological media formulations available, the general composition of microbiological media is similar between formulations.

General composition of microbiological media

Microbiological media formulations typically contain the following (Atlas 2010; Chauhan & Jindal 2020):

- A source of carbon to be incorporated into biomass (e.g. in the form of bicarbonate to provide carbon dioxide, or as organic compounds).
- An energy source (e.g. carbon sources mentioned above, ammonium ions, nitrite ions, reduced iron, or elemental sulfur).
- A nitrogen source for microbial growth (e.g. inorganic nitrogen compounds, amino acids, proteins, or peptones).
- Buffers (e.g. phosphate, acetate or citrate buffers) to maintain the pH within the limits required by the microorganism/s being cultivated.
- Trace elements (e.g. boron, cobalt, copper, molybdenum, manganese, nickel, zinc, selenium, silicon, vanadium).
- Growth factors (e.g. amino acids, purines, pyrimidines, vitamins, serum, blood) may be added to assist in cultivation.
- Selective agents (e.g. antibiotics, inhibitory dyes) may be added to enable selection of a particular microorganism.
- Indicator dyes (e.g. bromocresol purple, phenol red) may be added to enable differentiation of different types of microorganisms.

Whilst there are similarities in the ingredient profile of the many different media types, the exact ingredient profile is unique for each type of media. Microbiological media formulations may contain ingredients that have been derived from multiple animal species. Typical animal species from which microbiological media ingredients are derived are cattle, pigs, sheep, goats, horses, birds, rabbits, and fish (Atlas 2010). Microbiological media can be divided into the following broad categories:

- **Nutritive media:** used to support the growth of a wide range of microorganisms.
- **Enrichment media:** designed to favour the growth of particular microorganisms over others, and used for culturing fastidious microorganisms that have particular culture requirements.
- **Selective media:** contains ingredients that inhibit the growth of non-target microorganisms, enabling selection for specific microorganisms.
- **Differential media:** contains ingredients that allow microorganisms to be differentiated from each other, usually by the appearance of the colony or the surrounding media.

Peptones

In many dehydrated microbiological media formulations, the animal-derived ingredients present in the fully finished, packaged product imported prior to reconstitution, sterilisation, and addition of any additional heat-labile supplements are present as peptones. Peptones are protein hydrolysates, which are water-soluble products derived from the partial hydrolysis of proteins derived from animal, plant, or microbial sources. Protein hydrolysates are often prepared using acid or enzymatic hydrolysis (Thermo Fisher Scientific 2019), and may occasionally be prepared using alkaline hydrolysis (Pasupuleti & Braun 2010).

Animal tissue extracts

The other major source of animal-derived ingredients in microbiological media are animal tissue extracts or infusions. Animal tissue extracts are aqueous extracts from a meat source and are commonly used in microbiological media as a source of nutrients, including amino acids, low molecular weight peptides, carbohydrates, vitamins, minerals, and trace metals (Atlas 2010).

Agar

Microbiological media may take the form of a gel medium which contains a solidification agent, or a broth medium which is a liquid. Agar, derived from marine algae (commonly *Gelidium* spp. or *Gracilaria* spp.), is the most common solidification agent added to create solid microbiological media (Atlas 2010). Agar can be added in low concentrations to produce a soft agar or semisolid medium. Agar added at a higher concentration will produce a solid medium. Medium with no agar added retains its liquid form, and is known as a liquid/broth medium (Atlas 2010; Chauhan & Jindal 2020). Agar melts at approximately 85°C and tends to solidify at temperatures below 45°C (Atlas 2010; Chauhan & Jindal 2020; Zimbro et al. 2009). As agar is not animal derived it does not pose an animal biosecurity risk.

1.2.3 Uses of microbiological media

Microbiological media has many laboratory applications, including use in diagnostic tests for significant diseases in both human and veterinary health systems; screening of food, water, pharmaceutical, cosmetic, and environmental samples for microbial contamination; sterility testing in manufacturing processes; teaching; and scientific research and development.

Microbiological media is an important resource in molecular and synthetic biology. The use of artificial chromosomes for cloning and mapping of DNA sequences involves microbial culture. Similarly, recombinant DNA technology requires microbial culture and is important for the production of recombinant proteins and the research of other bioactive molecules. These tools and other contemporary molecular biology tools often require microbiological media for replication and protein expression.

Although microbiological media is predominantly imported for laboratory use, it also has important applications in vaccine and therapeutic research, development and manufacture where the final end use is *in vivo* in non-laboratory animals. Dehydrated and pre-sterilised microbiological media specifically imported for direct *in vivo* use in non-laboratory animals is outside the scope of this review and requires assessment against the department's vaccine policies ([Section 1.4.1](#)).

A laboratory animal is defined for the purposes of the [Biosecurity Regulation 2016](#) as:

‘an animal that is, or is intended to be, brought into Australian territory to be used in a laboratory or research institution.’

For the purposes of this risk review, the definition of ‘laboratory animal’ has been extended to include animals already present in Australia. Therefore, for the remainder of this risk review, a laboratory animal is considered to be an animal that is used in a laboratory or research institution for scientific or research purposes, as defined in the [Glossary](#).

1.2.4 Disease outbreaks caused by contamination of microbiological media used in vaccine and therapeutic production

Human and veterinary vaccine and therapeutic products containing animal-derived material have been associated with disease outbreaks due to contamination of the constituents used in manufacture. Untreated media supplements and reagents have resulted in the introduction of significant disease agents into vaccines, cell lines, and therapeutics, with subsequent introduction of exotic diseases into naïve populations. Such contamination and associated disease outbreak events have been reported following the use of contaminated bovine serum (Pastoret 2010), trypsin (Victoria et al. 2010), improperly inactivated vaccine antigen (Caramelli et al. 2001; Furesz 2006), and virus-contaminated cell lines (Petriccioni et al. 2014).

The vast majority of vaccine/therapeutic contamination events have been reported in viral vaccines where embryonated chicken eggs or cells derived from animals, humans, or plants are used in vaccine antigen production. Embryonated chicken eggs or cells used to produce vaccine antigen provide an opportunity for contaminating viruses or intracellular microorganisms to survive and replicate. Contamination reports of bacterial vaccines or products derived from precision fermentation are rare. A *Mycoplasma agalactiae* vaccine administered to sheep in Italy from 1994 to 1996 resulted in iatrogenic scrapie in multiple flocks of sheep and goats (Agrimi et al. 1999; Caramelli et al. 2001). The contamination was due to inclusion of scrapie-contaminated sheep brain and mammary gland in the antigen preparation, not due to contamination of microbiological media used in vaccine antigen production (Agrimi et al. 1999; Caramelli et al. 2001; Zanusso et al. 2003).

There is no evidence to suggest contaminated microbiological media as a significant source of contamination of vaccine or therapeutic products. However, there have been numerous reports of 'pseudo-outbreaks' whereby the microbiological media used in diagnostics carries microbial contamination. In these cases the culture results have initially been attributed to the pathogen being present in patient samples, but have later been found to be due to contamination of the media used to test the samples. These pseudo-outbreaks have largely been attributed to contaminated supplements added to microbiological media (Ashford et al. 1997; Calfee, Kornblum & Jenkins 2007; Lee et al. 2017; Matanock et al. 2016; Perez et al. 2014).

1.3 Scope

The scope of this risk review is to consider the biosecurity risk associated with importing dehydrated and pre-sterilised microbiological media from all countries for laboratory use, including for *in vivo* use in laboratory organisms. A laboratory organism is a guinea pig, hamster, mouse, rabbit, rat or microorganism that is used in a laboratory, as defined for the purposes of the Goods Determination.

For the purpose of this risk review, the biosecurity risk will be considered through assessment of the 5 identified exposure pathways ([Section 2.4](#)). This risk review does not address the import of dehydrated and pre-sterilised microbiological media for *in vivo* in non-laboratory organisms end use; for use in the research and development of vaccines or therapeutic products with an intended end use in non-laboratory animals or humans; or commercial production of vaccines and therapeutics with an intended end use in animals or humans. However, these end uses are considered in the risk review as diversion pathways.

This risk review specifically excludes the following:

- media used for the culture of cells derived from animals, humans, and plants
- media used for the fermentation of food and beverages for human consumption
- microbiological media supplements that are not highly processed and dehydrated or pre-sterilised (e.g. raw serum or whole blood products)
- liquid culture media products that are not pre-sterilised
- dehydrated microbiological media imported in quantities of > 5 kg per individually packaged unit
- the risks posed by the deliberate importation of any living or replication-competent organism, microorganism, or infectious agent on a microbiological media carrier.

1.4 Existing policy

1.4.1 International policy

A valid import permit and an accompanying manufacturer's declaration or supplier's declaration is required for the import of:

- culture media containing no more than 20 mL or 20 g animal derived material for laboratory use only
- prepared media (including pre-poured plates, swabs, vials) in individually packaged units of up to 50 g or 50 mL for laboratory use only
- selective/differential media.

Culture media containing synthetic materials only may be imported with an accompanying manufacturer's declaration, supplier's declaration, product label, or invoice. An import permit is not required.

Other types of culture media may be imported with appropriate government certification in volumes no greater than 5 kg / 5 L following a case-by-case assessment of ingredients and sourcing. Volumes greater than 5 kg / 5 L may be imported into an Approved Arrangement.

The import conditions can be found on the [Australian Biosecurity Import Conditions database](#) (BICON).

Dehydrated and pre-sterilised microbiological media for use *in vivo* in non-laboratory organisms or for use in vaccines and therapeutics must meet the requirements outlined in the following policies:

- [Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines 1999](#)
- [Specific quarantine requirements for the importation of inactivated veterinary vaccines 1997](#)
- [Guidelines for managing the risk of transmitting transmissible spongiform encephalopathies \(TSEs\) via veterinary vaccines and other in vivo veterinary products 2012.](#)

1.4.2 Domestic arrangements

The Australian Government is responsible for regulating the movement of animal products into and out of Australia. However, the state and territory governments are responsible for animal health and environmental controls within their individual jurisdiction. Once animal products have been cleared

by Australian Government biosecurity officers, they may be subject to interstate movement conditions. The importer is responsible for ensuring compliance with all requirements.

1.5 Consultation

Stakeholders were notified of the release of the draft risk review through [Animal Biosecurity Advice 2023-A13](#) on 17 October 2023. Comments on the draft risk review were invited through [Have Your Say](#) during the 60-day consultation period, which closed on 15 December 2023. The department has considered comments received during the consultation period in finalisation of this risk review.

1.6 Next steps

Following release of the final report the import conditions will be developed and implemented during new non-standard permit application assessments (including re-applications). There will be a transition period for the implementation of the new biosecurity measures, the length for which is still to be determined.

2 Method

The World Organisation for Animal Health (WOAH), in its Terrestrial Animal Health Code (the Terrestrial Code), describes 'General obligations related to certification' in Chapter 5.1 (WOAH 2022d).

The Terrestrial Code states in Article 5.1.2. that:

'The import requirements included in the international veterinary certificate should assure that commodities introduced into the importing country comply with the standards of WOAH. Importing countries should align their requirements with the recommendations in the relevant standards of WOAH. If there are no such recommendations or if the country chooses a level of protection requiring measures more stringent than the standards of WOAH, these should be based on an import risk analysis conducted in accordance with Chapter 2.1.'

Article 5.1.2. further states that:

'The international veterinary certificate should not include measures against pathogenic agents or diseases which are not WOAH listed, unless the importing country has demonstrated through import risk analysis, carried out in accordance with Section 2, that the pathogenic agent or disease poses a significant risk to the importing country.'

The components of risk analysis as described in Chapter 2.1 of the Terrestrial Code are:

- hazard identification
- risk assessment (entry assessment, exposure assessment, consequence assessment and risk estimation)
- risk management
- risk communication.

Hazard identification, risk assessment and risk management are sequential steps within a risk analysis. Risk communication is conducted as an ongoing process and includes both formal and informal consultation with stakeholders.

2.1 Risk review

Although not defined or described in the Terrestrial Code, risk review is recognised by risk analysts as an essential component of the risk analysis process (Barry 2007; FSA 2006; Purdy 2010).

Australia applies a process of risk review to the biosecurity risks associated with the importation of an animal commodity (animal product or live animal) for which current biosecurity measures exist.

Risk review differs from the monitoring and review component of risk management, as described in the Terrestrial Code, in that each component of the risk analysis process (hazard identification, risk assessment and risk management) is reviewed under the risk review process. If a change (either an

increase or a decrease) in the biosecurity risk associated with a live animal or animal product that is currently imported into Australia is identified based on updated scientific information, risk management measures can be revised accordingly.

This risk review has drawn on these sources of information (this list is not exhaustive):

- the Terrestrial Code (WOAH 2022g)
- current requirements for importation of microbiological media into Australia
- a review of relevant scientific literature
- expert opinion.

Risk – defined by the Terrestrial Code as ‘the likelihood of the occurrence and the likely magnitude of the biological and economic consequences of an adverse event or effect to animal or human health’ – is dynamic in nature; it changes with time. Consequently, risk should be regularly reviewed.

2.2 Processes inherent to dehydrated and pre-sterilised microbiological media

There are a number of processes inherent to the production and use of dehydrated and pre-sterilised microbiological media that reduce the biosecurity risk of these products when imported for laboratory use. These include:

- the high degree of processing of raw animal-derived ingredients, and
- the requirement for the media to be sterilised prior to use.

In the case of pre-sterilised microbiological media, the latter has occurred prior to import.

2.2.1 Composition and processing

Dehydrated microbiological media is a highly processed, desiccated product. The processing of raw animal ingredients during manufacture will inactivate or cause a reduction in titre of many pathogens of biosecurity concern, and is considered to provide a significant level of biosecurity risk management for animal-derived materials used in manufacture. Processing methods that may be applied to the animal-derived ingredients during manufacture include acid and alkaline hydrolysis, enzymatic digestion, and thermal treatments.

Acid and alkaline hydrolysis

Acid and alkaline hydrolysis may be used in peptone production. Commercial acid hydrolysis is almost exclusively used in the biotechnology sector; alkaline hydrolysis is used rarely, if at all for biotechnology applications (Pasupuleti & Braun 2010). Acid hydrolysis procedures can be undertaken using various parameters. Typically, hydrolysis will be undertaken using hydrochloric acid or sulfuric acid, which are both strong acids. The procedure is undertaken at high temperatures (120°C to 137°C) and pressures (32 to 45 psi) and lasts from 2 to 8 hours (Pasupuleti & Braun 2010).

Alkaline hydrolysis procedures involve the use of strong bases such as calcium hydroxide, potassium hydroxide, or sodium hydroxide. The temperatures employed for alkaline hydrolysis are lower than those used for acid hydrolysis, typically ranging from 27°C to 55°C. Alkaline hydrolysis is undertaken for several hours prior to evaporation, pasteurisation (thermal treatment), and spray drying

(Pasupuleti & Braun 2010). It should be noted that pasteurisation in the context of peptone production typically far exceeds the temperatures used for pasteurisation of dairy products, and products are often pasteurised multiple times to reduce or eliminate contaminating microorganisms (Pasupuleti & Braun 2010).

The extremes of pH, high temperatures, and high pressures used in combination or individually for acid and alkaline hydrolysis will assist in inactivation or reduction in titre of contaminating microorganisms and viruses in the final product. For example, the low pH used for acid hydrolysis and the high pH used for alkaline hydrolysis will rapidly inactivate foot-and-mouth disease virus (Bachrach et al. 1957). The thermal treatment and duration used for acid hydrolysis is also sufficient to inactivate pathogens that may be resistant to other treatments, such as *Mycobacterium bovis* which can maintain infectivity following treatment at 80°C for 20 minutes (Bemer-Melchior & Drugeon 1999).

Enzymatic hydrolysis

Peptones can also be produced using animal-derived proteolytic enzymes such as trypsin, pepsin, or pancreatin, which are usually of porcine origin. Enzymatic hydrolysis may also be undertaken using enzymes of plant or microbial origin (Pasupuleti & Braun 2010). The animal-derived ingredients in the resulting peptones may comprise the substrate (raw material) being digested to produce the peptones, the enzymes used to digest the proteins, or both. The enzymes used for hydrolysis of proteins constitute only a very small proportion of the resulting hydrolysate (typically, 0.2 to 20 g of enzymes are added to 1 kg protein to be hydrolysed) (Lee, Hahn & Musser 2007). The process of digestion varies according to the substrate, the enzyme being used, and the enzyme's optimal pH. As an example, manufacturing using trypsin involves prolonged exposure to a low pH for 24 to ≥ 48 hours. Production of hydrolysed protein using these enzymes often involves use of high temperatures. These treatments can last anywhere from seconds to hours, depending on the enzyme, its substrate, and the final product requirements.

Enzymatic hydrolysis typically includes pre-treatment with heat (up to 93°C), acid, or alkali. The pH and temperature are adjusted for optimal enzyme activity and hydrolysis is undertaken until the desired hydrolysate is achieved; this may take from 1 to 100 hours. The protein digest is then pasteurised (often multiple times, as for acid/alkaline hydrolysis) and may undergo further purification processes prior to evaporation and spray-drying (Pasupuleti & Braun 2010). In addition, peptone manufacturing typically involves a heat treatment step or adjustment of pH immediately following enzymatic hydrolysis in order to inactivate the enzyme and end the hydrolytic process (Pasupuleti & Braun 2010).

The extremes of pH and high temperatures used during enzymatic hydrolysis and to terminate enzyme activity will assist in inactivation or reduction in titre of contaminating microorganisms and viruses in the final product. For example, the temperatures used for enzymatic hydrolysis greatly exceed the temperatures required for inactivation of *Brucella* spp., which demonstrates environmental stability and can survive in various substrates for months (Franke-Whittle & Insam 2013; Kaden et al. 2018; Worth Calfee & Wendling 2012).

Animal tissue extracts

Animal tissue extracts are prepared by boiling a known weight of animal tissue (e.g. 500 g beef heart). The resulting broth can be harvested as a liquid, but is more commonly dried and the solids

are harvested. Although the exact duration of boiling is not specified by manufacturers, the tissue needs to reach 100°C for long enough, and/or under sufficient pressure, to enable decomposition of the tissue and release of the nutrients into the water.

Boiling of animal tissues for prolonged duration or under high pressure will assist in inactivation or reduction in titre of contaminating microorganisms and viruses in the final product. For example, the temperature and duration of thermal treatment used for preparation of animal tissue extracts exceeds parameters demonstrated to inactivate the inherently stable infectious bursal disease virus, which has been demonstrated to be resistant to extremes of pH and to maintain very low levels of infectivity following thermal treatment at 100°C for 1 minute (Mandeville, Cook & Jackwood 2000; Rani & Kumar 2015).

Agar

Agar solubility is temperature dependent. It is insoluble in cold water and soluble in boiling water (Armisen & Galatas 1987). In order to dissolve agar, the powdered agar is added to the microbiological media and either boiled or autoclaved. The high temperatures required for solubilisation of agar will assist in inactivation or reduction in titre of contaminating microorganisms and viruses in the final product. For example, the temperatures used to dissolve agar exceed parameters demonstrated to inactivate porcine circovirus 2, which is a very thermally stable virus able to maintain infectivity following treatment at 90°C for 5 minutes (Emmoth et al. 2004; O’Dea et al. 2008). As well as providing a mandatory moist heat treatment and dilution factor for the animal-derived ingredients in dehydrated microbiological media, agar provides additional risk mitigation through solidification of the media following reconstitution. This reduces the animal biosecurity risk of the media by further limiting the end use and preventing disposal down the sink or in animal feed.

Dilution

Microbiological media is a composite product and usually contains a relatively small proportion of animal-derived ingredients. This provides a dilution factor for any contaminating microorganisms and infectious agents in the final composite product. The approximate > 1:20 dilution provided by reconstitution of dehydrated microbiological media (Atlas 2010) introduces an additional dilution factor, reducing the titre of contaminating microorganisms and viruses in the final product.

2.2.2 Sterilisation of microbiological media

In order to be useful for its intended purpose, dehydrated microbiological media needs to be reconstituted and thermally sterilised prior to use. Reconstitution is usually performed with laboratory grade sterile water or liquid buffers.

Sterilisation is a fundamental step in microbiological media preparation as microbiological media must be free from contaminating microorganisms before it is used to propagate and isolate microbial cultures. Microbiological media is specifically formulated to provide the required nutrients for the growth of microorganisms. Due to the ubiquitous nature of microorganisms it is inevitable that environmental or other laboratory microorganisms will grow and contaminate microbiological media that is not sterilised prior to use. Without being sterilised, any contaminating microorganisms introduced into the media through the manufacture, packaging, or reconstitution processes will contaminate the culture, rendering the results invalid. This leads to decreased productivity and wasted resources.

The method of sterilisation may vary depending on the type of media and whether the media contains heat labile ingredients.

Typically, liquid buffers and distilled water will be added to dehydrated microbiological media powder and the reconstituted media will be autoclaved at 121°C for 15 minutes. In some cases, precipitates will form during thermal sterilisation due to the interactions of various components. To avoid this, sterilisation of individual components can be undertaken prior to mixing. Antibiotics or thermally unstable supplements such as blood may be added as the reconstituted media cools (Atlas & Snyder 2013).

Due to the absolute requirement for microbiological media to be sterile prior to use, sterilisation of the microbiological media has been directly considered throughout the risk assessment process.

The vast majority of microbiological media formulations are distributed with manufacturer's instructions to sterilise by autoclaving. In the unusual cases where the media will not withstand autoclaving, other sterilisation techniques are available.

Some microorganisms and infectious agents may be protected from inactivation treatments by the composition of the substrate they are in. For example, foot-and-mouth disease virus can be protected from thermal inactivation by lipid micelles in milk (Spickler & Roth 2012; Tomasula & Konstance 2004). Due to the high degree of processing and homogenisation of microbiological media ingredients prior to incorporation into the media, the protective effects of specific biological components such as lipid micelles is not expected.

Autoclaving

Autoclaving of microbiological media usually involves exposure to steam under pressure. The standard autoclaving protocol is 15 minutes at 121°C at 15 psi; this exposure kills vegetative bacterial cells and spores (Atlas & Snyder 2013) and is a department-approved method for inactivation of microorganisms and viruses. There are other pressure/temperature combinations that will result in sterility for media containing substances that will not tolerate the standard protocol (Atlas & Snyder 2013).

Ionising radiation

Ionising radiation treatments include gamma, x-ray, and electron beam radiation. Ionising radiation is routinely used as a biosecurity treatment for many products of animal origin, including laboratory products. The standard dose of ionising radiation accepted by the department to address most animal biosecurity concerns is 50 kGy (Department of Agriculture 2014).

Tyndallisation

Tyndallisation is useful for media or components that do not tolerate autoclaving. It involves exposure to flowing steam at 100°C for 30 minutes using an Arnold steriliser. This treatment will kill vegetative bacteria, but not spores. Following heating, the media is allowed to cool and is kept under conditions that will allow germination of spores. The steam treatment at 100°C for 30 minutes is repeated on 3 successive days which enables spores to germinate and resulting vegetative bacteria to be killed (Atlas 2010). A moist heat treatment of 100°C for 30 minutes is considered by the department to be suitable for inactivation of contaminating microorganisms and viruses.

Inspissation

High protein materials that cannot tolerate high temperatures can be sterilised using inspissation. There are several protocols available for performing inspissation, and they result in the protein coagulating without causing significant changes to its chemical properties. Although not autoclaved or held at 100°C for 30 minutes, properly inspissated microbiological media is sterile following treatment.

2.3 Review of hazard identification

Hazard identification is described in the Terrestrial Code (Article 2.1.2) as a classification step that is undertaken to identify potential hazards that may be associated with the importation of a commodity.

In accordance with the Terrestrial Code, a disease agent was considered to be a potential hazard relevant to the importation of dehydrated and pre-sterilised microbiological media if it was assessed to be:

- a disease agent of the species from which microbiological media ingredients are derived: domestic cattle (*Bos taurus* and *Bos indicus*), sheep (*Ovis aries*), pigs (*Sus scrofa*), goats (*Capra hircus*), horses (*Equus caballus*), rabbits (*Oryctolagus cuniculus*), birds (Class Aves), crustaceans (Phylum Arthropoda, Subphylum Crustacea), and finfish (Classes Actinopterygii, Chondrichthyes, and Sarcopterygii)
- WOAH-listed, emerging and/or capable of producing adverse consequences in Australia
- a causative disease agent for a disease listed on the department's [National list of notifiable animal diseases](#) for the animal species mentioned above
- a relevant disease agent of the above-mentioned species identified in previous department import risk analyses or risk reviews including for chicken meat, turkey meat, sausage casings, dairy products, beef, ovine and caprine semen and embryos, horses, pig meat, marine finfish, ornamental finfish, prawns and prawn products, and salmon.

A hazard was retained for further review (hazard refinement) if:

- the disease or infection caused by the hazard is exotic to Australia (serotypes or strains considered exotic to Australia may meet this criterion), or if present, is nationally notifiable or subject to official control or eradication.

Hazards were excluded from further review if they met the following criteria:

- a significant reduction in titre of the hazard is expected following one of the processes outlined in [Section 2.2.1](#)
- there is scientific evidence demonstrating the disease agent is inactivated by one of the following sterilisation procedures as it is a necessity for microbiological media to be sterile prior to use (Department of Agriculture 2014; Goff, Hill & Ferrer n.d.; Myrseth 1985; Rutala & Weber 2008):
 - a moist heat treatment of 100°C for 30 minutes, or equivalent; or
 - autoclaving at 121°C for 15 minutes at 15 psi, or equivalent; or

- ionising radiation to achieve a minimum absorbed dose of 50 kGy or equivalent; or
- a combination of risk management measures that, when combined, are considered to provide an equivalent level of risk management to one of the above as described in [Section 2.2](#).

These specific treatments, or equivalent combinations of treatments, were considered attained by the offshore processing methods outlined in [Section 2.2.1](#), and the preparation and sterilisation of dehydrated microbiological media that occurs in Australia following importation.

A list of hazards excluded from further review based on these criteria is included in [Appendix A: Summary of disease agents excluded based on susceptibility to sterilisation with standard processes](#).

Where a particular disease agent was considered ubiquitous worldwide, a common commensal in Australia, opportunistic, or not reported to be pathogenic, a judgement was made based on the strength of the available evidence.

Where evidence for the inclusion or exclusion of a particular disease agent was equivocal, a judgement was made based on the strength of the available evidence for the disease agent to survive in dehydrated and pre-sterilised microbiological media.

2.4 Exposure pathways

In considering the animal biosecurity risk associated with the importation of dehydrated and pre-sterilised microbiological media, five pathways describing the possible routes of exposure of susceptible species to dehydrated and pre-sterilised microbiological media were identified. These were divided into two groups:

- 1) Pathways resulting in exposure through laboratory use of microbiological media:
 - a) Basic research, industrial use, teaching, and diagnostic services
 - b) Diversion into commercial vaccine/therapeutic production
 - c) Diversion into vaccine/therapeutic research and development.
- 2) Pathways resulting in environmental exposure of microbiological media:
 - a) Inappropriate handling and disposal
 - b) Environmental contamination.

Pre-sterilised microbiological media was not considered in these pathways as it has been reconstituted and sterilised prior to import. The exposure pathways consider dehydrated microbiological media only.

2.4.1 Pathways resulting in exposure through laboratory use of microbiological media

Pathway 1: Basic research, industrial use, teaching, and diagnostic services

This pathway covers the use of microbiological media in high school and university teaching facilities; university and government research facilities; manufacturing facilities for products such as industrial enzymes, biofuels, and organic chemical compounds; and private and government diagnostic

laboratories. It includes the use of microbiological media in quality assurance and quality control processes.

Once imported, bulk consignments of dehydrated microbiological media will be transported to distribution warehouses, from which smaller individually packaged quantities are distributed to recipient laboratories. Within these laboratories, dehydrated microbiological media is reconstituted and sterilised according to manufacturer's instructions. Any necessary heat labile ingredients are then added (e.g. locally-sourced sterile blood) prior to use.

Bulk consignments of dehydrated microbiological media may also be directly imported and manufactured into sterilised pre-prepared plates prior to distribution to the recipient laboratory.

Microbiological media in this pathway is intended for laboratory use. Following use of the media in this pathway, it is standard practice to sterilise (e.g. autoclave) the media prior to disposal to prevent further microbial growth. *In vivo* studies in this pathway are restricted to laboratory animals.

Considerations relevant to this pathway are:

- Personnel preparing and using microbiological media have varied levels of training and experience.
- Laboratories predominantly adhere to specific standards or guidelines. Laboratories may have oversight from the following:
 - animal ethics committees
 - institutional biosafety committees.
- Laboratories may also adhere to local standards such as the Australian/New Zealand Standard (AS/NZS) 2243.3-2022 Safety in laboratories Part 3: Microbiological safety and containment, or be certified or accredited to a relevant international standard:
 - ISO/IEC 15189 – Medical laboratories – Requirements for quality and competence (ISO 2022)
 - ISO/IEC 17025 – General requirements for the competence of testing and calibration laboratories (ISO 2017)
 - ISO/IEC 17043 – Conformity assessment - General requirements for proficiency testing (ISO 2023).

All of these factors can influence the biosecurity risk within the pathway.

- It is an absolute necessity for microbiological media in this pathway to be sterile prior to use. In the case of diagnostics, improperly sterilised media resulting in inconclusive results could cause significant delays in the diagnosis of life-threatening infections. In the case of industrial use, contaminated media could result in entire batches of product being discarded which would be considered prohibitively costly in a commercial manufacturing environment.
- Dehydrated microbiological media is expensive and can be time consuming to prepare. Improper sterilisation of dehydrated microbiological media would be considered an unnecessary waste of time and resources.

- A large proportion of the microbiological media imported for use in this pathway will not have a direct pathway into an animal.
- The *in vivo* work undertaken in this pathway is likely to involve laboratory animals in laboratory animal houses.
- Livestock and poultry research in Australia is heavily focused on improving animal welfare; improving productivity (e.g. through improved genetics or grazing management systems); improving sustainability of agricultural systems; and advancing reproductive technologies. There is very limited general research involving livestock or poultry that would require direct administration of microbiological media.
- The most commonly used mammalian livestock species for general research in Australia is sheep.

Risk mitigation measures intrinsic to this pathway:

- To ensure the microbiological media is fit for purpose and not subject to overgrowth with contaminating microorganisms, it must be sterilised prior to use.

Pathway 2: Diversion into commercial vaccine/therapeutic production

In this pathway the likelihood of diversion is not assessed; diversion is assumed to have happened.

This pathway considers microbiological media specifically imported under Pathway 1 which is subsequently diverted into use for production of a commercial vaccine or therapeutic product. This may occur through a deliberate breach of import conditions, through a misunderstanding of import conditions or a mix up of products. Once imported and used in commercial vaccine and therapeutic production, the resulting product will be administered to companion animals and/or commercial flocks/herds, or humans. Large-scale use is likely and entire flocks/herds spanning a wide geographical area could be administered the product within a short timeframe.

Considerations relevant to this pathway are:

- Microorganisms cultivated for incorporation into a vaccine/therapeutic product are likely to be purified prior to inclusion in the product. This is expected to leave very little, if any, microbiological media in the final product.
- The users of dehydrated microbiological media in this pathway are most likely private commercial entities within the biotechnology sector.
- Commercial laboratories are highly specialised for the products they are producing. The environment is highly controlled and companies are required to adhere to relevant guidelines, standards, certifications and government oversight depending on the final market for their products.
- Products imported into Australia for use in the production of commercial veterinary vaccines and therapeutic products are required to comply with the following department policies which outline stringent sourcing, extraneous agent testing, and sterilisation requirements for ingredients and finished products:
 - [Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines 1999](#)

- [Specific quarantine requirements for the importation of inactivated veterinary vaccines 1997](#)
- [Guidelines for managing the risk of transmitting spongiform encephalopathies \(TSEs\) via veterinary vaccines and other in vivo veterinary products 2012](#)
- In Australia, commercially available veterinary vaccines and therapeutic products are regulated through the Australian Pesticides and Veterinary Medicines Authority (APVMA). The APVMA conducts rigorous assessments for product registration to allow use in Australian animals.
- The manufacturing processes for commercial veterinary vaccines and therapeutics in Australia require adherence to the following which mandate traceability through stringent documentation, ingredient sourcing and testing requirements, quality assurance, and quality control:
 - [Agricultural and Veterinary Chemicals Code \(Manufacturing Principles\) Determination 2014](#)
 - [Australian Code of Good Manufacturing Practice for Veterinary Chemical Products 2007](#)

Risk mitigation measures intrinsic to this pathway:

- Sterility of the microbiological media prior to use in culturing/isolating microorganisms is required to ensure there are no contaminating microorganisms being cultivated alongside the target microorganism. This is a crucial aspect of quality control of the final product.
- Failure to sterilise the media is likely to result in product withdrawal due to iatrogenic infections in recipient animals that will be linked to product use through pharmacovigilance reporting.

Pathway 3: Diversion into vaccine/therapeutic research and development

In this pathway the likelihood of diversion is not assessed; diversion is assumed to have happened.

This pathway considers microbiological media specifically imported under Pathway 1 which is subsequently diverted into use in the production of an investigational vaccine or therapeutic product in its research and development stage. This may occur through a deliberate breach of import conditions, through a misunderstanding of import conditions or through a mix up of products. Once imported and used in an investigational vaccine or therapeutic product, the product will be administered to target animal species (e.g. companion animals or livestock) in the clinical phases of drug development. Pen studies and field studies involving target animal species may involve multiple research facilities and properties/households, respectively. Use of the investigational product may be geographically widespread and not confined to research facilities.

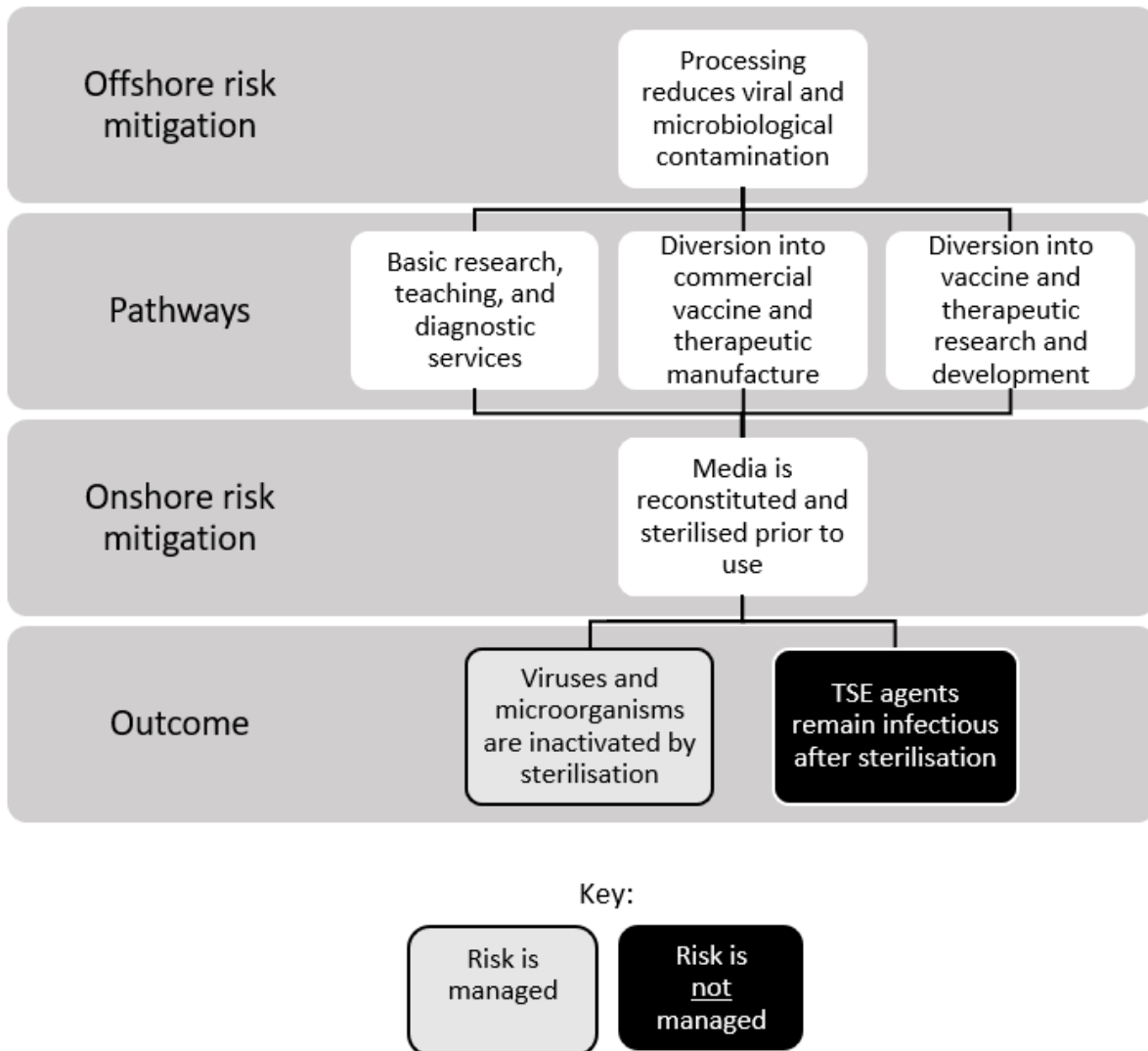
Considerations relevant to this pathway are:

- This pathway focuses on the clinical phases of vaccine and therapeutic research and development. Preclinical studies generally involve laboratory use of microbiological media. Preclinical studies are considered under Pathway 1.
- Microorganisms cultivated for incorporation into a vaccine/therapeutic product are purified prior to inclusion in the product. This is expected to leave very little, if any, microbiological media in the final product.

- The users of dehydrated microbiological media in this pathway are most likely private commercial entities within the biotechnology sector. These companies must adhere to relevant guidelines and standards during product development in order to achieve product registration.
- Products imported into Australia for use in vaccine and therapeutic research and development in target animal species are required to comply with the following department policies which outline stringent sourcing, extraneous agent testing, and sterilisation requirements for ingredients and finished products:
 - [Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines 1999](#)
 - [Specific quarantine requirements for the importation of inactivated veterinary vaccines 1997](#)
 - [Guidelines for managing the risk of transmitting spongiform encephalopathies \(TSEs\) via veterinary vaccines and other in vivo veterinary products 2012](#)
- Clinical phases of research and development will require compliance with some or all of the following which mandate stringent documentation, product characterisation, reproducibility, quality assurance, and quality control:
 - [Australian Code of Good Manufacturing Practice for Veterinary Chemical Products 2007](#)
 - Good Laboratory Practice (GLP)
 - Good Clinical Practice (GCP)

Risk mitigation measures intrinsic to this pathway (Figure 1):

- Sterility of the microbiological media prior to use in culturing/isolating microorganisms is required to ensure there are no contaminating microorganisms being cultivated alongside the target microorganism. This is a crucial aspect of quality control of the investigational product during the clinical phases of development.
- Sterility of the final product, particularly for parenteral products and to a lesser degree for oral products, is necessary to ensure iatrogenic infection in the recipient animals, and subsequent product failure, does not occur.

Figure 1: Schematic diagram demonstrating Pathways 1-3 for dehydrated microbiological media

2.4.2 Pathways resulting in environmental exposure of microbiological media

Pathway 4: Inappropriate handling and disposal

This pathway covers the inappropriate handling and disposal of dehydrated microbiological media from the laboratory. This pathway has three different branches:

- The media is transported to the laboratory where it is disposed of in the general rubbish prior to reconstitution and sterilisation. In this branch, dehydrated media is neither diluted through reconstitution nor sterilised.
- The media is transported to the laboratory where dehydrated media is reconstituted. This results in a dilution factor of at least 1:20. Reconstituted dehydrated microbiological media is disposed of into the municipal wastewater treatment system prior to sterilisation.
- Dehydrated microbiological media is transported to the laboratory where it is reconstituted and sterilised according to the manufacturer's instructions or the specific needs of the end user prior to disposal into the municipal wastewater system or in the rubbish.

This pathway also covers media that is disposed of inappropriately from other locations, such as warehouses, or intentional diversion of microbiological media into animal feed. Inappropriate disposal from a warehouse may happen if a bulk batch of media is damaged or found to be unsuitable for distribution. It is possible that damaged consignments held in distribution warehouses may be discarded as waste and sent to landfill.

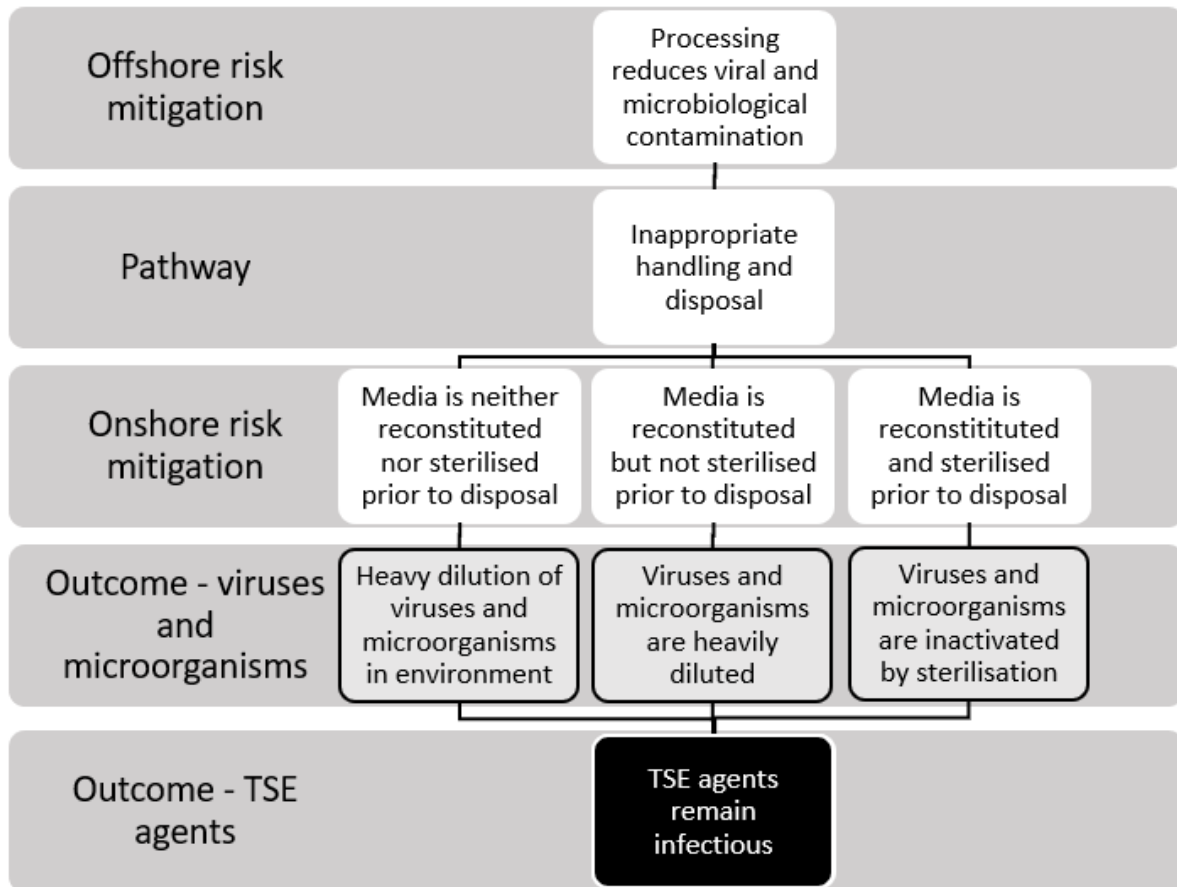
Considerations relevant to this pathway are:

- For the first two branches of this pathway, sterilisation of dehydrated microbiological media has not occurred prior to disposal.
- Dehydrated microbiological media discarded from distribution warehouses would possibly be discarded in bulk volumes, and would not have undergone reconstitution or sterilisation.
- The scope of this review is limited to importation of dehydrated microbiological media in volumes of ≤ 5 kg per individually packaged unit.
- Dehydrated microbiological media is very expensive which provides a major disincentive for disposal prior to use.
- The ruminant feed ban prohibits feeding of any meal derived from vertebrate animal origin to ruminants. Swill feeding is illegal in Australia. However, people discarding media in this pathway may not realise microbiological media contains animal-derived ingredients.
- Microbiological media has a very low nutritional value. This makes it undesirable and unsuitable for use in livestock feed.
- Reconstitution and disposal into the municipal sewer results in a large dilution factor reducing the likelihood of pathogens remaining in sufficient titres to constitute an infectious dose.
- Aquatic pathogens are generally very temperature labile and will not survive desiccation. They are unlikely to survive the microbiological media processing prior to export in sufficient titres to constitute an infectious dose. Disposal into waterways through the municipal sewer will result in further dilution of any viable pathogens.
- Most laboratories in Australia are located in urban and suburban environments, whereas most livestock and feral animals are located in rural environments. This limits the access of susceptible livestock and feral animals to inappropriately disposed microbiological media.

Risk mitigation measures intrinsic to this pathway (Figure 2):

- Dehydrated microbiological media is only imported in volumes ≤ 5 kg per individually packaged unit.
- Media disposed into landfill is likely to remain in its packaging, providing a physical barrier between the media and foraging animals. Any media that breaches its packaging will be diluted by environmental factors.
- There is a large dilution factor for pathogens when microbiological media is disposed into the municipal sewer.
- Microbiological media disposed through the third branch of the pathway has been sterilised.

Figure 2: Schematic diagram demonstrating Pathway 4 for dehydrated microbiological media



Key:



Pathway 5: Environmental contamination

This pathway covers dehydrated microbiological media that contaminates the environment in large quantities. An example of this pathway would be a truck accident in transit resulting in media spilling from its packaging into the environment.

Considerations relevant to this pathway are:

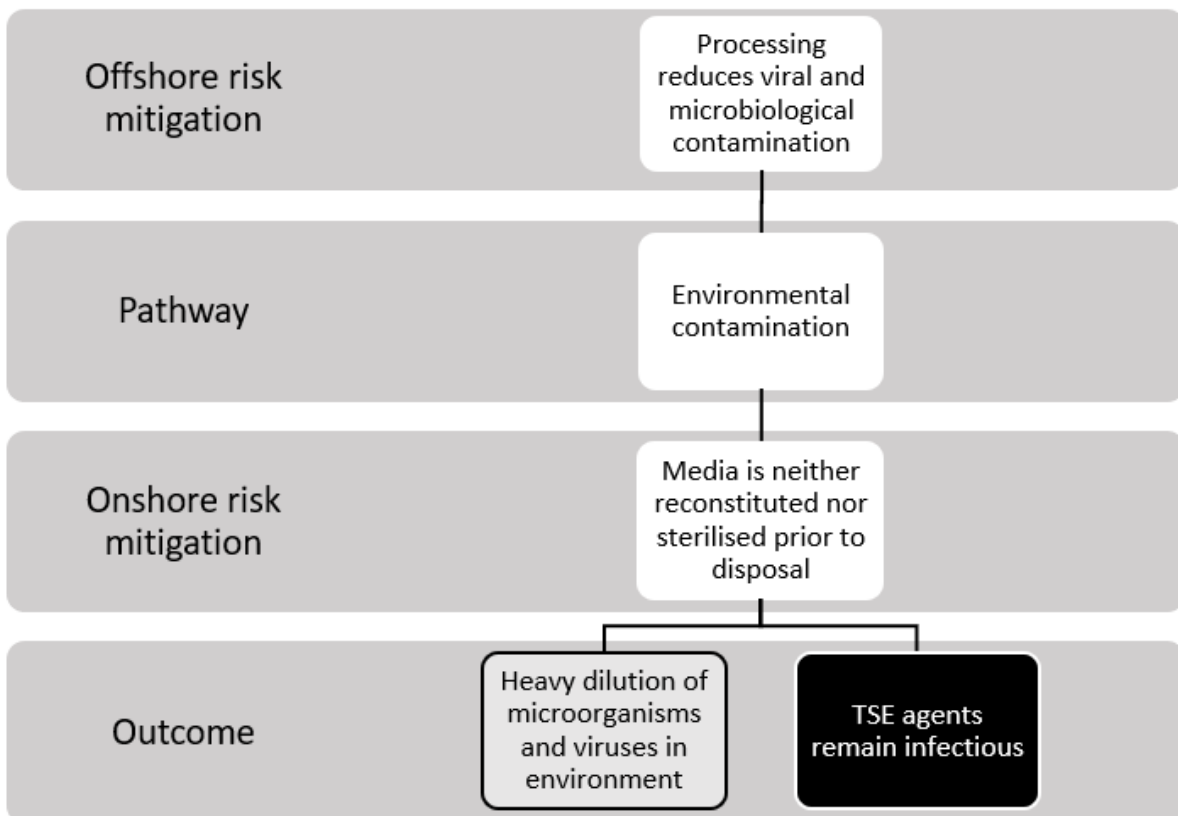
- Dehydrated microbiological media in this pathway is neither reconstituted nor sterilised.
- The scope of this review is limited to importation of dehydrated microbiological media in volumes of ≤ 5 kg per individually packaged unit.
- In the unlikely event of a truck accident it is highly unlikely that media would breach all layers of packaging as well as the trailer holding the load.

- A truck accident resulting in microbiological media spillage is likely to result in contamination of the road and immediately adjacent land. Contamination is unlikely to extend much further than this.

Risk mitigation measures intrinsic to this pathway (Figure 3):

- Dehydrated microbiological media is highly processed prior to import.
- Dehydrated microbiological media is only imported in volumes ≤ 5 kg per individually packaged unit.

Figure 3: Schematic diagram demonstrating Pathway 5 for dehydrated microbiological media



Key:



2.5 Literature review and review of risk assessment

The result of the risk assessment determines if the biosecurity risk would exceed Australia's ALOP if dehydrated or pre-sterilised microbiological media were imported with no restrictions. This is known as the 'unrestricted risk'. If the unrestricted risk is determined to exceed Australia's ALOP, risk management measures, applied as import conditions, are required to manage the biosecurity risk.

Details of the risk assessment process relevant to the importation of animals and animal products are provided in Chapter 2.1 of the Terrestrial Code.

A review of the risk factors relevant to the hazards retained for further review was conducted to identify any significant changes in disease agent attributes or geographic distribution that would be relevant to biosecurity considerations for Australia.

A literature review of peer-reviewed scientific information was conducted for each retained hazard. Information outlined in the literature review was restricted to that relevant to dehydrated or pre-sterilised microbiological media. If definitive information on risk factors was not found through literature review or contact with relevant experts, then any uncertainties were identified and documented.

Based on the literature review, a risk assessment was conducted and a conclusion was reached for each hazard about whether the importation of dehydrated or pre-sterilised microbiological media posed a biosecurity risk to Australia. Assumptions and judgements that were made in drawing conclusions for each hazard retained for further review were documented in the relevant risk assessment section ([Section 4](#)).

2.5.1 Risk assessment framework

For each hazard retained for risk assessment, a qualitative evaluation of the biosecurity risk associated with the importation of dehydrated or pre-sterilised microbiological media for each identified pathway was undertaken, and included the following:

- entry assessment - the likelihood of the hazard entering Australia via imported dehydrated or pre-sterilised microbiological media
- exposure assessment - the likelihood of susceptible species being exposed to the hazard via imported dehydrated or pre-sterilised microbiological media
- consequence assessment - the likelihood of establishment and/or spread of the outbreak scenario and the overall effect of establishment and/or spread.

In accordance with the Terrestrial Code, if any stage of the risk assessment estimated a negligible risk for a particular pathway, the risk assessment did not need to continue.

Based on the risk assessment, a conclusion was reached for each hazard about whether the importation of dehydrated or pre-sterilised microbiological media results in an unrestricted risk estimate that achieved Australia's ALOP.

In this review, the likely consequences have been derived by making separate assessments of establishment and/or spread; and direct and indirect effects. This was considered necessary for a robust assessment to allow for differences in risk between the five identified pathways for laboratory

use and environmental exposure of dehydrated and pre-sterilised microbiological media. By separating these assessments, the review recognises the difference in risk between the pathways, which may result in different likely outbreak scenarios. The pathways differ in the following aspects:

- the level of external regulatory oversight (they may be highly regulated or unregulated)
- the likelihood of the pathway resulting in exposure of susceptible species to dehydrated or pre-sterilised microbiological media.

2.5.2 Entry assessment

Entry assessment describes the biological pathways for introducing hazards into the importing country, and estimates the likelihood of that occurring. It considers biological factors of the hazard and the species of origin; country factors such as prevalence and animal health systems in the country of export; and commodity factors such as the quantity of media imported; the likelihood of imported microbiological media containing ingredients from the relevant animal species; and processing treatments during manufacture.

The entry pathway evaluated the following factors affecting the presence of the hazard:

- the worldwide prevalence and distribution of the hazard
- the tissue tropism of the hazard
- the likelihood of microbiological media containing ingredients from the relevant animal species
- the incubation period of the hazard
- the effect of the standard processes used in commercial production of dehydrated and pre-sterilised microbiological media on the hazard.

For each hazard identified, a qualitative likelihood (Table 1) was assigned to describe the likelihood of the hazard entering Australia in dehydrated or pre-sterilised microbiological media.

Table 1: Qualitative likelihoods used for entry, exposure, and establishment and/or spread assessments

Likelihood	Descriptive definition
High	The event would be very likely to occur
Moderate	The event is equally likely to occur or not occur
Low	The event would be unlikely to occur
Very low	The event would be very unlikely to occur
Extremely low	The event would be extremely unlikely to occur
Negligible	The event would almost certainly not occur

2.5.3 Exposure assessment

Exposure assessment describes the biological pathways necessary for exposure of susceptible species to each identified hazard from imported dehydrated or pre-sterilised microbiological media, and estimates the likelihood of the exposure occurring. It estimates the likelihood of susceptible species in Australia being directly exposed to and infected with the hazard introduced via imported dehydrated or pre-sterilised microbiological media.

The exposure assessment commences when dehydrated or pre-sterilised microbiological media products are cleared for import at the Australian border, and exposure was assessed under the assumption that entry had occurred and the imported dehydrated or pre-sterilised microbiological media was contaminated with the hazard. For each hazard, an exposure assessment was conducted for each of the five identified exposure pathways ([Section 2.4](#)). These pathways are considered a fundamental aspect of the exposure assessment.

Factors considered in determining whether hazards in imported dehydrated or pre-sterilised microbiological media may expose susceptible species include:

- the survival of the hazard in stored dehydrated microbiological media and pre-sterilised microbiological media
- the effect of risk mitigation measures that are required for microbiological media to be fit for purpose, including reconstitution and sterilisation
- the expected level of expertise and training of staff working in the facilities where dehydrated and pre-sterilised microbiological media would be used in the different pathways
- accessibility of the product to susceptible species, including product disposed as waste or product contaminating the environment
- applicable legislation or other regulatory oversight.

All states and territories have legislation regulating feeding animal-derived material or anything contaminated by animal-derived material to ruminants and banning swill feeding of pigs. However, people discarding microbiological media may not realise it contains animal-derived ingredients.

There is also legislation placing the onus on property owners to prevent wildlife or feral animals from accessing waste sites on their property (QLD DAF 2019). Most Australian states and territories now have legislation or codes of practice governing the design, management and security of landfills, which may reduce opportunities for scavenging animals to access community waste at these sites (EPA Victoria 2015; NSW EPA 2016; QLD DAF 2019).

A qualitative likelihood (Table 1) was assigned to describe the likelihood of the exposure occurring for each hazard.

This risk assessment determined that there were two groups of potentially susceptible species in Australia. The exposure groups recognised in this risk assessment were:

- susceptible domestic animals
- susceptible wild animals.

Likelihood of entry and exposure

For each hazard, the likelihood of entry and exposure was estimated for each pathway by combining the likelihood of entry and the corresponding likelihood of exposure using the matrix in Figure 4.

Figure 4: Matrix for combining entry assessment and exposure assessment qualitative likelihoods

Likelihood of entry	<i>High</i>	Negligible	Extremely low	Very low	Low	Moderate	High
	<i>Moderate</i>	Negligible	Extremely low	Very low	Low	Low	Moderate
	<i>Low</i>	Negligible	Extremely low	Very low	Very low	Low	Low
	<i>Very low</i>	Negligible	Extremely low	Extremely low	Very low	Very low	Very low
	<i>Extremely low</i>	Negligible	Negligible	Extremely low	Extremely low	Extremely low	Extremely low
	<i>Negligible</i>	Negligible	Negligible	Negligible	Negligible	Negligible	Negligible
		<i>Negligible</i>	<i>Extremely low</i>	<i>Very Low</i>	<i>Low</i>	<i>Moderate</i>	<i>High</i>
		Likelihood of exposure					

This resulted in determination of the overall likelihood of entry and exposure for each hazard.

2.5.4 Consequence assessment

Once exposure of a susceptible population has occurred, a number of possible outbreak scenarios could follow. These represent a continuum ranging from no outbreak to widespread establishment. This review grouped all likely outbreak scenarios into four categories (Table 2).

Table 2: Nomenclature for outbreak scenarios

Outbreak scenario	Descriptive definition
Scenario 1	the disease agent does not establish or is not recognised within the exposed population
Scenario 2	the disease agent establishes within the directly exposed population only, is identified and is eradicated, or is self-limiting without further spread
Scenario 3	the disease agent establishes within the directly exposed population, spreads to other populations, and may be eradicated
Scenario 4	the disease agent establishes within the directly exposed population, spreads to other populations, and becomes endemic.

In this risk review, for each pathway, all possible outbreak scenarios were evaluated for plausibility based on the epidemiology of each disease agent. The most likely outbreak scenario for each hazard, resulting from the exposure of susceptible species, was considered (described in the relevant disease section).

The likelihood of the outbreak scenario occurring was then determined for each pathway to obtain a likelihood of establishment and/or spread.

When determining the likelihood of establishment and/or spread within the outbreak scenario, qualitative descriptors were used as described in Table 1.

2.5.5 Overall effects of establishment and/or spread

Effects attributable to the identified outbreak scenario/s were addressed in terms of direct and indirect effects on human, animal, and plant life and health on a national scale, including adverse health, environmental, and socioeconomic effects.

The significance of effects at the overall national level were assessed in terms of seven (two direct and five indirect) criteria and are not repeated in individual risk assessments.

Direct effects

- Life or health (including production effects) of susceptible species, including public health consequences.
- The living environment, including life and health of wildlife, and any effects on the non-living environment.

Indirect effects

- New or modified eradication, control, monitoring or surveillance and compensation strategies or programs for animal disease management.
- Domestic trade or industry, including changes in consumer demand and effects on other industries reliant on directly affected industries.
- International trade, including loss of markets, meeting new technical requirements to enter or maintain markets and changes in international consumer demand.
- The environment, including biodiversity, endangered species and the integrity of ecosystems.
- Communities, including reduced tourism, reduced rural and regional economic viability and loss of social amenity, and any 'side effects' of control measures.

The overall effect of establishment and/or spread (combination of direct and indirect effects) associated with the outbreak scenario/s took into account the geographic level (Table 3), and the magnitude (Table 4) of these effects.

Table 3: Geographic level descriptive definitions

Geographic level	Descriptive definition
Local	A community, locality or town
Regional	A recognised geographic area (such as far north Queensland)
State or territory	A single Australian state or territory
National	All Australian states and territories

Table 4: Magnitude of direct and indirect effects descriptive descriptions

Magnitude	Descriptive definition
Highly significant	Extremely serious and irreversible and likely to have permanent economic effects.
Significant	Serious and substantive, but reversible and unlikely to have permanent economic effects
Minor significance	Recognisable, but minor and reversible
Indiscernible	Not usually distinguishable from normal day-to-day variation

Based on the geographic level and magnitude of effects, the overall effect of establishment and/or spread was determined using the rules described in Table 5.

Table 5: Descriptions for determining overall effect of establishment and/or spread

Effect	Descriptive definition
Extreme	The effect is likely to be highly significant at the national level. Implies that economic stability, societal values or social well-being would be seriously affected.
High	The effect is likely to be significant at the national level and highly significant within affected zones. Implies that the effect would be of national concern. However, serious effects on economic stability, societal values or social well-being would be limited to a given zone.
Moderate	The effect is likely to be recognised on a national level and significant within affected zones. The effect is likely to be highly significant to directly affected parties.
Low	The effect is likely to be recognised within affected zones and significant to directly affected parties. It is not likely that the effect will be recognised at the national level.
Very low	The effect is likely to be minor to directly affected parties. The effect is unlikely to be recognised at any other level.
Negligible	The effect is unlikely to be recognised at any level within Australia.

Likely consequences

The likely consequences were determined by combining the likelihood of establishment and/or spread associated with the outbreak scenario with the overall effect of establishment and/or spread using the matrix shown in Figure 5.

Figure 5: Matrix for combining the likelihood and overall effect of establishment and/or spread

Likelihood of establishment and/or spread	<i>High</i>	Negligible	Very low	Low	Moderate	High	Extreme
	<i>Moderate</i>	Negligible	Very low	Low	Moderate	High	Extreme
	<i>Low</i>	Negligible	Negligible	Very low	Low	Moderate	High
	<i>Very low</i>	Negligible	Negligible	Negligible	Very low	Low	Moderate
	<i>Extremely low</i>	Negligible	Negligible	Negligible	Negligible	Very low	Low
	<i>Negligible</i>	Negligible	Negligible	Negligible	Negligible	Negligible	Very low
		<i>Negligible</i>	<i>Very Low</i>	<i>Low</i>	<i>Moderate</i>	<i>High</i>	<i>Extreme</i>
		Overall effect of establishment and spread					

2.5.6 Risk estimation

The risk estimation determines whether the importation represents an unrestricted biosecurity risk that achieves Australia's ALOP for each hazard.

Combination of the likelihood of entry and exposure with the likely consequences for each pathway was undertaken using the risk estimation matrix in Figure 6.

Figure 6: Risk estimation matrix

Likelihood of entry and exposure	<i>High</i>	Negligible risk	Very low risk	Low risk	Moderate risk	High risk	Extreme risk
	<i>Moderate</i>	Negligible risk	Very low risk	Low risk	Moderate risk	High risk	Extreme risk
	<i>Low</i>	Negligible risk	Negligible risk	Very low risk	Low risk	Moderate risk	High risk
	<i>Very low</i>	Negligible risk	Negligible risk	Negligible risk	Very low risk	Low risk	Moderate risk
	<i>Extremely low</i>	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Very low risk	Low risk
	<i>Negligible</i>	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Very low risk
		<i>Negligible</i>	<i>Very Low</i>	<i>Low</i>	<i>Moderate</i>	<i>High</i>	<i>Extreme</i>

Likely consequences

This resulted in the unrestricted risk estimate, which was considered the final output of the risk assessment. An unrestricted risk was determined for each pathway and presented in a table at the end of each risk assessment section ([Section 4](#)). If the unrestricted risk estimate did not achieve Australia's ALOP, specific risk management was considered necessary for the hazard.

2.6 Review of risk management

This risk review focused on determining whether risk management was warranted for each of the hazards identified as posing a biosecurity risk through the importation of dehydrated or pre-sterilised microbiological media. Following each risk assessment, if the unrestricted risk was 'negligible' or 'very low', then it achieved Australia's ALOP and risk management was not required. If the unrestricted risk was 'low', 'moderate', 'high' or 'extreme', it did not achieve Australia's ALOP and risk management measures were required.

The review is based on scientific information, including expert advice, operational feasibility and practicality to determine whether the measures were appropriate. If it was concluded that previous risk management measures were overly restrictive or could not achieve Australia's ALOP, alternative and/or complementary risk management measures were proposed to provide an appropriate risk management option.

2.7 Risk communication

Risk communication is defined in the Terrestrial Code as 'the interactive transmission and exchange of information and opinions throughout the risk analysis process concerning risk, risk-related factors and risk perceptions among risk assessors, risk managers, risk communicators, the general public and other interested parties' (WOAH 2022e).

In conducting import risk analyses and risk reviews, the department consults with the Department of Health and Aged Care to ensure that public health considerations are included in the development of Australia's animal biosecurity policies. Consultation with external stakeholders is a standard procedure for all import risk analyses and risk reviews to enable stakeholder assessment and feedback on draft conclusions and recommendations about Australia's animal biosecurity policies.

3 Hazard identification

The list of hazards (disease agents) of potential biosecurity concern comprised disease agents from the following:

- Causative disease agents for the diseases listed by the WOAHA for the following species from which microbiological media ingredients are derived: domestic cattle (*Bos taurus* and *Bos indicus*), sheep (*Ovis aries*), pigs (*Sus scrofa*), goats (*Capra hircus*), horses (*Equus caballus*), rabbits (*Oryctolagus cuniculus*), birds (Class Aves), crustaceans (Phylum Arthropoda, Subphylum Crustacea), and finfish (Class Actinopterygii, Chondrichthyes, and Sarcopterygii).
- Causative disease agents for the diseases listed on the department's [National list of notifiable animal diseases for the animal species](#) mentioned above.
- Other disease agents of the above-mentioned species identified in previous import risk analyses and reviews including for chicken meat, turkey meat, sausage casings, dairy products, beef, ovine and caprine semen and embryos, horses, pig meat, marine finfish, ornamental finfish, prawns and prawn products, and salmon conducted by the department.

The method of hazard identification and refinement is described in [Section 2.3](#).

The preliminary list of hazards identified that were excluded from risk review based on their susceptibility to a treatment equivalent to a moist heat treatment of 100°C for 30 minutes; autoclaving at 121°C for 15 minutes at 15 psi; or ionising radiation to achieve a minimum absorbed dose of 50 kGy are listed in [Appendix A](#). The specific treatments, or equivalent combinations of treatments, were considered attained by the offshore processing methods outlined in [Section 2.2.1](#), or the preparation and sterilisation of dehydrated microbiological media that occurs in Australia following importation.

The hazards retained for risk review after hazard identification and refinement are listed in Table 6.

Table 6: Hazard identification and refinement

Disease agent / Disease	Susceptible species	WOAH-listed disease	Adverse consequences in Australia	Present in Australia	Present in exporting countries	Retained for risk review
Bovine spongiform encephalopathy protease-resistant prion protein (PrP ^{BSE}) / Bovine spongiform encephalopathy (BSE)	Domestic and zoological bovids, domestic and zoological felids, non-human primates, goats, humans	Yes	Yes	No	Yes	Yes
Scrapie protease-resistant prion protein (PrP ^{Sc}) / Scrapie	Sheep and goats	Yes	Yes	No	Yes	Yes

3.1 Disease agents retained for risk review

The disease agents retained for risk review on the basis of the information provided in Table 6 were:

- Bovine spongiform encephalopathy protease-resistant prion protein (PrP^{BSE})
- Scrapie protease-resistant prion protein (PrP^{Sc})

4 Risk reviews

4.1 Bovine spongiform encephalopathy protease-resistant prion protein (PrP^{BSE})

4.1.1 Background

Infection with the bovine spongiform encephalopathy (BSE) protease-resistant prion protein (PrP^{BSE}) may result in BSE, which is a disease of bovines. PrP^{BSE} can also cause transmissible spongiform encephalopathies (TSEs) in other species, including zoological bovids, domestic and zoological felids, non-human primates, goats, and humans (Bruce et al. 1997; Eloit et al. 2005; Hill et al. 1997; Jeffrey et al. 2006; Sigurdson & Miller 2003). Classical BSE was first detected in the United Kingdom in 1986 as an epidemic, and subsequently has been detected throughout much of the world, with most cases in Europe. PrP^{BSE} has been detected in felines in Australia on two occasions; one case was diagnosed in 1991 in a cheetah imported into Broome Zoo (Peet & Curran 1992), and the second was in 2002 in an Asiatic golden cat imported into Melbourne Zoo (Young & Slocombe 2003). PrP^{BSE} has never been detected in bovines in Australia.

Atypical BSE arises spontaneously in herds worldwide and affects older cattle (> 8 years old) (DAFF 2012). It has been detected as an incidental finding during intensive surveillance for classical BSE. When assessing BSE risk status recognition, the WOAH excludes atypical BSE as it is believed to occur in all cattle populations at a very low rate. Given the extremely low incidence and lack of field evidence of oral transmissibility, atypical BSE will not be considered further in this review.

Infection with PrP^{BSE} causes an invariably fatal, progressive neurological disease caused by spongiform degeneration of the central nervous system (CNS) grey matter. It is characterised by a prolonged incubation time (2 to >10 years; average around 5 years) (Aguilar-Calvo et al. 2015; AHA 2021b). Survival times range from weeks to months following onset of clinical signs (AHA 2021b). PrP^{BSE} causes variant Creutzfeldt-Jakob disease (vCJD) in humans (Bruce et al. 1997; Hill et al. 1997).

PrP^{BSE} is extremely resistant to inactivation and the primary mode of PrP^{BSE} transmission is by ingestion of contaminated animal tissues/products (Aguilar-Calvo et al. 2015; Chesebro 2003). Economic loss is directly linked to mass slaughter of affected herds and loss of meat production and, indirectly, to the restriction on the export of animals and their by-products.

In 2006, a theoretical case of BSE in Australia was estimated to result in a cumulative loss to the national economy of \$2.9 billion to \$5.2 billion over a four year period, with further costs imposed by the requirement for increased surveillance and disposal of [specified risk material](#) to ensure its exclusion from animal feed (Yainshet, Cao & Elliston 2006).

Classical BSE is a bovine WOAH-listed disease (WOAH 2022c). Transmissible spongiform encephalopathies are nationally notifiable diseases. PrP^{BSE} is zoonotic.

4.1.2 Technical information

Agent properties

PrP^{BSE} is a very small infectious particle known as a prion. Prions are composed of protein only and nucleic acids are not required for prion infectivity (Bellinger-Kawahara et al. 1987; Oesch et al. 1985; Safar et al. 2005).

PrP^{BSE} is a misfolded isoform of the cellular prion protein, PrP^C. PrP^{BSE} is highly resistant to the thermal and chemical treatments considered suitable to inactivate most pathogens due to the following properties (Aguilar-Calvo et al. 2015; Meyer et al. 1986; Pan et al. 1993; Stahl et al. 1987; Taylor 1999):

- low detergent solubility
- low susceptibility to hydrolysis by proteases
- increased accumulation in host tissues compared with PrP^C
- altered tissue distribution in the host's central nervous system compared with PrP^C.

Inactivation of prion infectivity has only been demonstrated following extreme treatments such as 20,000 ppm sodium hypochlorite for 1 hour (Fichet et al. 2004) which is highly corrosive to many surfaces, or 1N NaOH for 60 minutes followed by autoclaving at 121°C for 30 minutes (Taguchi et al. 1991). The WOAHP recommends porous load autoclaving at 134°C to 138°C for 18 minutes at 208 kPa; however, it recognises that this will not result in complete inactivation in all situations (WOAHP 2022b). Although there are reports of other treatments successfully inactivating prions, many of these have been demonstrated to be insufficient for complete inactivation in subsequent studies (Taylor 1999). Inactivation studies of prions are further complicated by the sometimes marked difference in susceptibility to inactivation treatments observed between different prion strains and sample types (e.g. brain macerates or intact brain tissue) (Taylor 1999). Many of these verified treatments are suitable solely for small scale use within a laboratory or research environment.

Transmission

The primary mode of PrP^{BSE} transmission is by ingestion of contaminated animal tissues/products (Aguilar-Calvo et al. 2015; Chesebro 2003). The infectious dose for PrP^{BSE} is very low (Phillips, Bridgeman & Ferguson-Smith 2000).

Although not established, there is evidence to support the possibility of a very low rate of maternal transmission of PrP^{BSE} (Donnelly 1998; Wilesmith et al. 1997). Horizontal transmission through environmental contamination is not an established mode of transmission of PrP^{BSE} (Ferguson et al. 1997).

PrP^{BSE} has demonstrated a remarkable ability to cross the species barrier. At least 15 animal species were naturally infected with PrP^{BSE} during the BSE epidemic due to ingestion of contaminated feed. Affected species included zoological bovids, domestic and zoological felids, and non-human primates (Sigurdson & Miller 2003). Natural transmission of PrP^{BSE} has also been demonstrated in goats (Eloit et al. 2005; Jeffrey et al. 2006) and humans (Bruce et al. 1997; Hill et al. 1997). PrP^{BSE} is also experimentally transmissible to many species (Aguilar-Calvo et al. 2015). For transmissibility studies and bioassays, transgenic mice are usually used to increase the likelihood of a successful inoculation.

Experimental inoculation in rodents is usually achieved via the intracerebral route; however, the oral and intraperitoneal routes can also result in infection (Maignien et al. 1999; Wang et al. 2015).

Immunity

PrP^{BSE} does not evoke a specific immune response (WOAH 2022b).

Distribution

BSE was first detected in the United Kingdom in 1986, and has since been detected on most continents, including Asia, Europe, and North America. It has never been detected in Australia (WOAH 2023a).

The implementation of successful control measures following the initial outbreak of BSE in the United Kingdom has seen a decrease in the prevalence of BSE worldwide, with the WOA estimating a prevalence approaching zero cases per million cattle (WOAH 2023a).

Pathogenesis

The incubation of BSE exceeds 2 years (Aguilar-Calvo et al. 2015), and may be greater than 10 years (WOAH 2022b). Survival times range from weeks to months following onset of clinical signs (AHA 2021b).

Following oral ingestion, PrP^{BSE} accumulates in the gut associated lymphoid tissue of the ileocaecal junction and jejunum, Peyer's patches in the ileum, and palatine tonsils. PrP^{BSE} then spreads via the enteric nervous system to the central nervous system (CNS), and then to various parts of the peripheral nervous system (Costassa et al. 2016).

Clinical signs

Clinical signs observed in cattle most commonly include apprehension, ataxia, and hyperaesthesia. Other clinical signs include alopecia, cachexia, tremors, temperament changes such as lethargy or aggression, and other gait abnormalities (Aguilar-Calvo et al. 2015).

Pathology

Histopathological changes include CNS grey matter vacuolation; astrocytosis; and neuronal degeneration (Aguilar-Calvo et al. 2015; Wells & Wilesmith 1995). PrP^{BSE} deposition is mostly confined to the CNS; however, low infectivity of various lymphoid tissues including the tonsils and Peyer's patches of the small intestine, distal ileum, jejunum, and ileocaecal junction have also been reported (Aguilar-Calvo et al. 2015). BSE infectivity has also been reported in skeletal muscle, and has been attributed to spread of PrP^{BSE} through the peripheral nervous system (Okada et al. 2014).

Testing

There is currently no suitable test available to detect the presence of PrP^{BSE} in biological commodities such as dehydrated and pre-sterilised microbiological media.

PrP^{BSE} infectivity in a biological sample can be demonstrated using a mouse bioassay; however, this is impractical for routine diagnostic purposes due to the long incubation period of BSE (WOAH 2022b). Laboratory methods such as protein misfolding cyclic amplification (PMCA) (Murayama et al. 2010), quaking induced conversion (QuIC) (Green 2019), and surround optical fibre immunoassay (SOFIA) (Chang et al. 2009) have demonstrated high sensitivity for detecting protease-resistant prion proteins in biological samples such as urine (Chen et al. 2010), blood (Lacroux et al. 2014), and cerebrospinal fluid (Schmitz et al. 2016). However, they have not been formally evaluated for use in

ante-mortem surveillance systems in animals (WOAH 2022b) or for the detection of PrP^{BSE} in biological commodities. These methods can have sensitivities measured in the order of femtograms or attograms (Orrù et al. 2012). Other methods that have been investigated and show some potential for detection of protease-resistant prion proteins in various substrates are flow cytometry (Trieschmann et al. 2005), infrared spectroscopy (Lasch et al. 2003), and nanoscale liquid chromatography-mass spectrometry (Onisko et al. 2007).

No diagnostic test is currently available for live animals (WOAH 2022b).

Treatment

There is no treatment available for any TSEs.

Control

The WOAH has developed a three-tier system for categorising countries according to their BSE risk status: negligible BSE risk, controlled BSE risk, or undetermined BSE risk (WOAH 2022a).

The WOAH categorisation of negligible risk is based on the following:

- negligible risk with regard to the BSE agent for at least 7 years
- intensive active surveillance over a 7-year period and maintained over time
- no indigenous case of classical BSE born less than 11 years ago
- evidence of an effective ruminant-to-ruminant feed ban for at least 8 years.

The WOAH categorisation of controlled risk is based on the following:

- at least a controlled risk with regard to the BSE agent
- intensive active surveillance over a 7-year period and maintained over time.

The BSE risk of a country or zone is considered to be undetermined if it cannot be demonstrated to meet the requirements for negligible or controlled BSE risk.

The WOAH-reported BSE status of member countries is based on criteria outlined in the Terrestrial Code. This includes the outcome of a risk assessment; ongoing awareness programmes for veterinarians, farmers and other cattle workers; compulsory notification and investigation of all cattle showing signs of clinical BSE; and examination, carried out in accordance with the WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Terrestrial Manual), of brain or other tissues samples collected within the framework of surveillance and monitoring systems. All countries not listed as negligible or controlled BSE risk will be considered undetermined BSE risk.

For Australia to continue to be officially recognised as having a 'negligible risk' status for BSE in accordance with the Terrestrial Code, Australia maintains a TSE Freedom Assurance Program (TSEFAP). The purpose of the TSEFAP is to increase market confidence that Australian animals and animal products are free from TSEs.

One key project under the TSEFAP is the National Transmissible Spongiform Encephalopathies Surveillance Program (NTSESP), designed to demonstrate Australia's ability to meet the requirements for a BSE negligible risk country, and provide early detection of these diseases should they occur. Additionally, Australia has an inclusive ban on the feeding to all ruminants of all meals, including

meat and bone meal (MBM), derived from all vertebrates, including fish and birds. This ban on restricted animal material (RAM) was introduced in 1996 and legislated in all states and territories in 1997. It provides assurance to international markets that appropriate measures are in place to ensure RAM is not being fed to ruminant livestock species (AHA 2021a).

Australia currently implements surveillance designed to allow the detection of at least one BSE case per 50,000 in the adult cattle population at a confidence level of 95 %.

Fluids and tissues derived from TSE susceptible species have been categorised according to three risk categories which are taken from the [Guidelines for managing the risk of transmitting transmissible spongiform encephalopathies \(TSEs\) via veterinary vaccines and other in vivo veterinary products 2012](#):

- Category A (high infectivity): Brain, spinal cord, eye, retina, optic nerve, trigeminal ganglia, spinal ganglia, pituitary gland, dura mater, pineal gland, skull, vertebral column, distal ileum.
- Category B (lower infectivity): Ileum (proximal), lymph nodes, proximal colon, spleen, tonsil, cerebrospinal fluid, adrenal gland, distal colon, stomach, nasal mucosa, peripheral nerves, liver, lung, pancreas, thymus, oesophagus, placenta, kidney (sheep), salivary gland, blood, blood vessels, bone marrow, mammary gland (sheep/goat), milk (sheep/goat), uterus.
- Category C (no detectable infectivity): Faeces, heart, mammary gland (bovine), milk (bovine), ovary, saliva, seminal vesicle, skeletal muscle, kidney (bovine), testis, thyroid, foetal tissue, bile, bone, cartilaginous tissue, connective tissue, hair, skin, urine, semen (bovine), embryo (bovine), tongue, tendon, trachea, adipose tissue.

The department considers this system to be effective and practical when applied to the extensive range of possible microbiological media ingredients and it has been adopted for use in this review.

4.1.3 Current biosecurity measures

Animal biosecurity requirements are in place for PrP^{BSE} for multiple biological commodities.

Generally, BSE risk management measures limit imports to:

- Countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status; and/or
- Commodities/products containing or made from tissues/secretions/excretions that have been scientifically assessed as not being sites for deposition of PrP^{BSE}; and/or
- End uses that do not expose susceptible species to assessed commodities/products (e.g. laboratory use, therapeutic use in non-susceptible species).

Australia has guidelines for managing the animal biosecurity risk of transmissible spongiform encephalopathies in products imported for use in animals, including veterinary vaccines and other *in vivo* veterinary products (DAFF 2012). Specific measures in place for mitigation of PrP^{BSE} in bovine products for *in vivo* use are listed below. Many of these ingredients are likely to be incorporated into various types of dehydrated and pre-sterilised microbiological media:

- There are no restrictions on the *in vivo* use of bovine materials, other than neural tissue, from negligible BSE risk countries.

- Bovine neural material is not permitted to be used in the manufacture of products for *in vivo* use in TSE-susceptible target species, regardless of the country of origin of the source animals.
- Bovine neural material from an undetermined BSE risk country is not permitted to be used directly or indirectly in the manufacture of products for use in any species.
- Bovine colostrum from undetermined BSE risk countries is not permitted to be used in the production of veterinary vaccines and therapeutics for use in naturally or experimentally TSE susceptible species.
- Bovine colostrum from controlled BSE risk countries may only be used in the production of veterinary vaccines and therapeutics if they are either:
 - destined for use in species not susceptible to TSEs, or
 - assessed on a case-by-case basis as acceptable after taking into consideration factors including country and/or herd of origin, manufacturing process, potential for cross contamination, target species, and method of administration.
- Bovine blood and blood derivatives from controlled BSE risk countries may only be used in the production of veterinary vaccines and therapeutics if destined for use in species not susceptible to TSEs.
- Bovine blood, blood derivatives, serum or serum derivatives sourced from undetermined BSE risk countries is not permitted to be used in the production of veterinary vaccines and therapeutics destined for use in species susceptible to TSEs.
- Bovine bone-derived material sourced from controlled BSE risk countries may only be used if specific sourcing and processing requirements are met. Material shall not be derived from vertebrae from animals greater than 30 months of age, skulls, spinal cord, or other specified risk material, and must not be cross-contaminated with other higher risk tissues.
- Bone-derived material from undetermined BSE risk countries, in addition to the requirements for bone-derived material from controlled BSE risk countries, shall be destined only for use in species not susceptible to TSEs, or destined only for non-parenteral use.
- Gelatine from negligible BSE risk countries shall not be derived from skulls or spinal cord.
- Bovine hide-derived gelatine and collagen produced from raw material sourced from controlled or undetermined BSE risk countries are acceptable, provided that appropriate assurance is given that cross-contamination with Category A and B tissues has not occurred.
- Tallow from controlled BSE risk countries for parenteral veterinary therapeutic use in TSE susceptible target species shall contain less than 0.15 % protein impurities, originate from bovine animals that have passed ante- and post-mortem inspection, and not have been prepared using specified risk material.
- Bovine tissue extracts and peptones sourced from controlled BSE risk countries may be used in the production of veterinary vaccines and therapeutics only if no specified risk material is used in the production of the product AND one of the following applies:
 - the product is destined for use in species not susceptible to TSEs, or
 - no Category A or B specified risk material is used in production, or

- a clearance study has been undertaken and the production process has been found to be effective at clearing TSE agent from the product.
- Bovine-derived peptones and tissue extracts derived from Category B tissues and sourced from undetermined BSE risk countries is not permitted for *in vivo* use.

In addition to the specific requirements outlined for different ingredients, PrP^{BSE} dilution is considered as a form of mitigation of PrP^{BSE} in bovine-derived products. The use of bovine-derived ingredients in composite products provides a dilution factor for PrP^{BSE}, as does multiple passaging of microorganisms or infectious agents using TSE-free material that does not permit prion replication. Acceptable levels of dilution include:

- a cumulative dilution of approximately 10¹⁰ for bacterial master seeds used in vaccine production
- a cumulative dilution of approximately 10¹⁸ for viral master seeds used in vaccine production.

4.1.4 Conclusion

PrP^{BSE} causes significant fatal neurodegenerative clinical disease in cattle and other species, including humans. BSE is a WOAHL-listed disease of cattle and is nationally notifiable in Australia. A BSE outbreak would represent a major economic and social threat to Australia's agricultural industries and environment. The prolonged incubation period makes early detection of a biosecurity incursion very difficult. The resistance of PrP^{BSE} to thermal, chemical or physical inactivation treatments make elimination of contaminating PrP^{BSE} in dehydrated and pre-sterilised microbiological media very difficult. PrP^{BSE} is not present in Australia and may be present in microbiological media containing ingredients derived from infected animals.

Based on the preceding factors, the department concluded that further risk assessment of PrP^{BSE} in dehydrated and pre-sterilised microbiological media was required.

4.1.5 Risk assessment

Entry assessment

The following factors were considered relevant to the estimate of the likelihood of PrP^{BSE} being present in imported microbiological media:

- Considering atypical and classical BSE together, the WOAHL estimates the prevalence of BSE in worldwide cattle populations to be approaching zero cases per million cattle. The two most recent cases of classical BSE reported to WOAHL were diagnosed in 2018 and 2021 (WOAHL 2023b).
- BSE has a long incubation period (approximately 2 to 10 years) so animals infected with PrP^{BSE} may appear clinically normal at slaughter.
- Bovine tissue is the most commonly used animal tissue in microbiological media.
- The protein digests incorporated into microbiological media are not always defined and could contain any type of bovine tissue, potentially including specified risk material.
- PrP^{BSE} displays a more restricted tissue distribution in infected cattle than that seen with other protease-resistant prion proteins infecting other species, including PrP^{Sc} in sheep.

- The processes used in the commercial manufacture of microbiological media, such as heat treatments, acid hydrolysis, or enzymatic digestion, will not inactivate PrP^{BSE}.
- A few microbiological media products have an absolute requirement for inclusion of Category A tissues.
- Microbiological media is a composite product providing a dilution factor for any infectious agents that may be present in animal-derived ingredients.

Based on this information, the likelihood of entry of PrP^{BSE} associated with dehydrated and pre-sterilised microbiological media from any country was estimated to be **very low** using the definitions in Table 1.

Exposure assessment

Factors relevant to the estimate of the likelihood that susceptible species in exposure groups would be exposed to PrP^{BSE} via contaminated microbiological media were considered.

General considerations relevant to all pathways:

- Multiple species are naturally susceptible to infection with PrP^{BSE}, including domestic and zoological bovids, domestic and zoological felids, goats, non-human primates, and humans.
- PrP^{BSE} demonstrates high environmental stability. The infectious titre will not decline appreciably over time.

Basic research, industrial use, teaching, and diagnostic services:

- A large part of this pathway encompasses *in vitro* laboratory work, whereby there is no direct pathway into an animal.
- *In vivo* work mostly involves laboratory animals held in laboratory animal housing. Although PrP^{BSE} is experimentally transmissible to laboratory animals, most *in vivo* studies in laboratory animals would not result in exposure of susceptible species outside of laboratory facilities.
- Research studies involving species naturally susceptible to TSEs are far less common than studies involving laboratory animals.
- Most research studies involving livestock will not involve the direct administration of dehydrated and pre-sterilised microbiological media or its derivatives.
- Current approved disposal methods for contaminated laboratory waste will not inactivate PrP^{BSE}.
- It is very unlikely that disposed media will be accessible to and ingested by susceptible species.

Based on this information, the likelihood of exposure of BSE-susceptible species to PrP^{BSE} associated with dehydrated and pre-sterilised microbiological media from any country imported for basic research, industrial use, teaching, and diagnostic services was estimated to be **very low**.

Diversion into commercial vaccine/therapeutic production:

- This pathway is highly regulated by companies internally (e.g. by internal quality assurance units), and externally (e.g. by government bodies including the department, the Therapeutic Goods Administration, and the APVMA).

- The commercial vaccine or therapeutic product manufactured using the dehydrated or pre-sterilised microbiological media will be administered directly into large numbers of animals, often to an entire herd.
- Due to the prolonged incubation period of BSE, it is likely that the contaminated vaccine/therapeutic product will be used on very large numbers of animals, potentially over many years, prior to detection of clinical disease in exposed animals.
- It may be difficult to detect instances where this diversion pathway has occurred.

Based on this information, the likelihood of exposure of susceptible species to PrP^{BSE} through the use of dehydrated or pre-sterilised microbiological media from any country imported under Pathway 1 and diverted into commercial vaccine/therapeutic production was estimated to be **high**.

Diversion into vaccine/therapeutic research and development:

- The investigational product produced using microbiological media will be administered directly to target animal species (e.g. companion animals and livestock). This will likely include administration to multiple animals in pen studies using research flocks/herds, and field studies using privately owned animals.
- Use of the investigational product may be geographically widespread and not confined to research facilities.
- Due to the prolonged incubation period of BSE, it is likely that the contaminated investigational vaccine/therapeutic product will be used in large numbers of animals prior to detection of clinical disease in exposed animals.
- Despite the high level of regulation associated with this pathway, it may be difficult to detect instances where this diversion pathway has occurred.

Based on this information, the likelihood of exposure of BSE-susceptible species to PrP^{BSE} through the use of dehydrated or pre-sterilised microbiological media from any country imported under Pathway 1 and diverted into vaccine/therapeutic research and development was estimated to be **high**.

Inappropriate handling and disposal:

- The majority of laboratories in Australia are in urban/suburban environments, making exposure of BSE-susceptible species to PrP^{BSE} in contaminated microbiological media that has been disposed of inappropriately extremely unlikely.
- Microbiological media has a very low nutritional value particularly when considered on a weight per cost basis. This makes it undesirable and unsuitable for use in livestock feed.
- Dehydrated microbiological media is very expensive which provides a major disincentive for disposal prior to use.
- It is highly unlikely that a BSE-susceptible species would be exposed to PrP^{BSE} following disposal into the municipal sewer.
- The inappropriate disposal of microbiological media from distribution warehouses is highly unlikely to occur due to the high value of the goods.

- Dehydrated microbiological media sent to landfill is likely to remain packaged.
- State and territory legislation or codes of practice governing the design, management, and security of landfill sites contribute to managing the risk of disposed media being ingested by susceptible species.

Based on this information, the likelihood of exposure of BSE-susceptible species to PrP^{BSE} associated with inappropriate handling and disposal of dehydrated or pre-sterilised microbiological media from any country was estimated to be **extremely low**.

Environmental contamination:

- Most shipping ports and distribution warehouses are in urban/suburban areas. Although long haul carriage of media by trucks may occur, the majority of transport of bulk consignments would occur between urban sites within the same metropolitan area.
- It is very unlikely that a truck accident resulting in environmental exposure of dehydrated or pre-sterilised microbiological media would occur in a situation that would enable a BSE-susceptible species to be exposed to PrP^{BSE} in the spilled material.

Based on this information, the likelihood of exposure of BSE susceptible species to PrP^{BSE} associated with dehydrated or pre-sterilised microbiological media from any country through environmental contamination was estimated to be **extremely low**.

The likelihood of exposure of BSE-susceptible species to PrP^{BSE} associated with dehydrated or pre-sterilised microbiological media for each pathway is summarised in Table 7.

Table 7: Likelihood of exposure of BSE-susceptible species to PrP^{BSE} in Australia

Pathway	Likelihood of exposure
Basic research, industrial use, teaching, and diagnostic services	Very low
Diversion into commercial vaccine/therapeutic production	High
Diversion into vaccine/therapeutic research and development	High
Inappropriate handling and disposal	Extremely low
Environmental contamination	Extremely low

Estimation of the likelihood of entry and exposure

The likelihood of entry of PrP^{BSE} to Australia and the likelihood of its exposure to BSE-susceptible species was estimated using the matrix of rules described in Figure 4. The estimate of the likelihood of entry was very low and the likelihood of exposure for each identified pathway is listed in Table 7. As a result, the likelihood of entry and exposure of PrP^{BSE} was estimated for each identified pathway (Table 8).

Table 8: Likelihood of entry and exposure of PrP^{BSE}

Pathway	Likelihood of entry and exposure
Basic research, industrial use, teaching, and diagnostic services	Extremely low

Pathway	Likelihood of entry and exposure
Diversion into commercial vaccine/therapeutic production	Very low
Diversion into vaccine/therapeutic research and development	Very low
Inappropriate handling and disposal	Extremely low
Environmental contamination	Extremely low

Likelihood of establishment and/or spread, associated with the outbreak scenario

Factors considered relevant to the establishment and/or spread associated with exposure of susceptible domestic and wild animals to PrP^{BSE} were:

- BSE is WOAHL-listed, nationally notifiable, and zoonotic.
- Neither environmental contamination nor direct horizontal transmission between naturally susceptible infected individuals are known transmission routes for PrP^{BSE}.
- *In vivo* work mostly involves laboratory animals held in laboratory animal housing. Although PrP^{BSE} is experimentally transmissible to laboratory animals, most *in vivo* studies in laboratory animals would not result in infection.
- The main route of transmission is via feedstuff contaminated with infective tissues from PrP^{BSE} infected animals.
- The standard sterilisation procedures considered appropriate for disposal of laboratory waste will not inactivate PrP^{BSE} infectivity.
- PrP^{BSE} has a very low infectious dose.
- There would be a large dilution factor involved if contaminated microbiological media were released into the municipal sewer.
- The Australian Ruminant Feed Ban was legislated in 1997 and prohibits the feeding to all ruminants of all meals, including meat and bone meal, derived from all vertebrates, including fish and birds. This eliminates the pathway for transmission of PrP^{BSE} between susceptible livestock.
- BSE has a long incubation (2 to >10 years; approximately 5 years on average) so an incursion would not be detected for at least 2 years after initial exposure to the contaminated dehydrated or pre-sterilised microbiological media.
- There is no effective treatment for BSE and once clinical signs develop the disease is invariably fatal.

The use of microbiological media contaminated with PrP^{BSE} in basic research, industrial use, teaching and diagnostic services has the potential to infect a small number of animals within isolated research facilities/laboratories. Animals used in basic research, industrial use, teaching and diagnostic services are predominantly laboratory animals that are not naturally susceptible to infection with PrP^{BSE}. Even if these animals were exposed to PrP^{BSE} and infection developed, there is no pathway for transmission to other animals. The most likely outbreak scenario following exposure to PrP^{BSE} through basic research, industrial use, teaching, and diagnostic services was considered to be

scenario 1: the disease agent does not establish or is not recognised within the directly exposed population.

Diversion of microbiological media contaminated with PrP^{BSE} into commercial vaccine/therapeutic production has the potential to infect a large number of animals over a large geographical area. Due to the long incubation period of BSE, a large number of animals will likely be exposed prior to detection of PrP^{BSE} contamination. In the absence of infected tissues being fed to other animals in accordance with the ruminant feed ban, horizontal transmission is not expected to occur. Maternal transmission is only expected to occur at a very low rate. The most likely outbreak scenario following exposure to PrP^{BSE} through diversion of microbiological media into commercial vaccine/therapeutic production was considered to be **scenario 2:** the disease agent establishes within the directly exposed population only, is identified and is eradicated. The population exposed to PrP^{BSE} through contaminated microbiological media in this pathway has the potential to be a very large population.

Diversion of microbiological media contaminated with PrP^{BSE} into use in vaccine/therapeutic research and development has the potential to infect a large number of animals within research facilities or individual flocks/herds used for field studies. Administration may be to naturally susceptible species in pen or field studies. Due to the long incubation period of BSE, the PrP^{BSE}-contaminated microbiological media may be used for multiple field studies prior to detection of clinical signs in affected animals resulting in many animals being exposed prior to detection of PrP^{BSE} contamination. In the absence of infected tissues being fed to other animals in accordance with the ruminant feed ban, horizontal transmission is not expected to occur. Maternal transmission is only expected to occur at a very low rate. The most likely outbreak scenario following exposure to PrP^{BSE} through diversion into use in vaccine/therapeutic research and development was considered to be **scenario 2:** the disease agent establishes within the directly exposed population only, is identified and is eradicated.

Inappropriate handling and disposal of microbiological media contaminated with PrP^{BSE} is not expected to result in establishment and/or spread, as environmental contamination is not a factor in the epidemiology of BSE. The most likely outbreak scenario following exposure to PrP^{BSE} through inappropriate handling and disposal of microbiological media was considered to be **scenario 1:** the disease agent does not establish or is not recognised within the directly exposed population.

Environmental contamination of PrP^{BSE}-contaminated microbiological media is not expected to result in establishment and/or spread, as environmental contamination is not a factor in the epidemiology of BSE. The most likely outbreak scenario following exposure to PrP^{BSE} through environmental contamination of PrP^{BSE}-contaminated microbiological media was considered to be **scenario 1:** the disease agent does not establish or is not recognised within the directly exposed population.

Based on these considerations, the likelihood of establishment and/or spread, of PrP^{BSE} was determined for each pathway as shown in Table 9.

Table 9: Likelihood of establishment and/or spread of PrP^{BSE}

Pathway	Most likely outbreak scenario	Likelihood of establishment and/or spread
Basic research, industrial use, teaching, and diagnostic services	Scenario 1	Very low

Pathway	Most likely outbreak scenario	Likelihood of establishment and/or spread
Diversion into commercial vaccine/therapeutic production	Scenario 2	High
Diversion into vaccine/therapeutic research and development	Scenario 2	Moderate
Inappropriate handling and disposal	Scenario 1	Very low
Environmental contamination	Scenario 1	Very low

Determination of the effects resulting from the outbreak scenario:

For the most likely outbreak scenario for each pathway, the direct and indirect effects of PrP^{BSE} were estimated taking into account the geographic level (Table 3) and the magnitude (Table 4) of these effects. Based on the level and magnitude of effects, the overall effect of establishment and/or spread was determined using Table 5 for each pathway. The following factors were considered relevant to a conclusion on the effects of the establishment and/or spread of PrP^{BSE}.

- PrP^{BSE} is WOAH-listed, nationally notifiable and zoonotic.
- Natural transmission of PrP^{BSE} has been observed in multiple species, including domestic and zoological bovids, domestic and zoological felids, goats, non-human primates, and humans.
- Most laboratory research is undertaken using laboratory organisms. Natural transmission of PrP^{BSE} between infected laboratory organisms is not expected to occur.
- BSE has a prolonged incubation period, precluding early detection and eradication of the disease.
- There is no information regarding the susceptibility of non-avian Australian wildlife to PrP^{BSE}. As many non-avian Australian wildlife are not carnivorous and there is no evidence to suggest they are susceptible to TSEs, natural transmission to most wildlife species is not considered likely.
- Australia's BSE status is important for export certification and provides significant benefit for Australia's trade status. The link between BSE and variant Creutzfeldt Jakob disease (vCJD) would cause immediate and long-lasting trade barriers should BSE be detected in Australian cattle.
- A case of BSE in Australia would result in downgrading of Australia's BSE status from 'negligible' to 'controlled'. It would take many years for negligible status to be regained. Australia's reputation as an exporter of high quality and safe bovine products would be damaged into the foreseeable future.
- In 2006, a theoretical case of BSE in Australia was estimated to result in a cumulative loss to the national economy of \$2.9 billion to \$5.2 billion over a four year period, with further costs imposed by the requirement for increased surveillance and disposal of specified risk material to ensure its exclusion from animal feed.
- The mass destruction and disposal of affected animals would be distressing for the local communities, and there would likely be concern over the possibility of vCJD transmission to humans in the years prior to the onset of clinical disease in affected cattle.
- The link between BSE and vCJD has far-reaching negative impacts in exposed human populations, including negative and long-lasting effects on blood, tissue, and organ donation

programs. Up until 2022, Australia excluded blood donations from people who resided in the United Kingdom for ≥ 6 months between 1980 and 1996. Cases of BSE in Australia would have immediate and potentially permanent impacts on blood and organ donation programs.

- Reliable testing for PrP^{BSE} infection in live animals is not available.
- The mortality rate is 100% in all species, including humans, once clinical signs are observed.
- There is no treatment for BSE, vCJD, or other encephalopathies arising from infection with PrP^{BSE}.

For basic research, industrial use, teaching, and diagnostic services; inappropriate handling and disposal; and environmental contamination pathways the most likely outbreak scenario is **scenario 1** (the disease agent does not establish or is not recognised within the directly exposed population). Infection in the laboratory is unlikely to be recognised or to spread outside of the laboratory. Due to this, the effects are likely to be indiscernible for susceptible species, public health, wildlife, the environment, and communities. The effect on the economy and trade are therefore expected to be indiscernible. The overall effect of establishment and/or spread for the outbreak scenario is unlikely to be recognised at any level within Australia and was estimated to be **negligible**.

For diversion into commercial vaccine/therapeutic production and diversion into vaccine/therapeutic research and development pathways the most likely outbreak scenario is **scenario 2** (the disease agent establishes within the directly exposed population only, is identified and is eradicated). Confirmation of eradication is expected to take years due to the prolonged incubation of BSE. An outbreak of BSE, or equivalent disease in other susceptible species, is likely to have significant effects at the national level. The effects are likely to be highly significant for human health due to the role of PrP^{BSE} in vCJD. A single case of BSE is likely to have highly significant economic effects due to prolonged loss of trade and market access and the requirement for increased surveillance and carcass disposal. Eradication is likely, but it will take many years before Australia could regain a WOAHP negligible risk status for BSE. The effects are expected to be indiscernible for wildlife due to the lack of a pathway for most wildlife species, and unlikely host species amongst Australian native species. The effects on the environment are likely to be indiscernible. The overall effect of establishment and/or spread for the outbreak scenario is likely to be significant at the national level with serious effects on economic stability and social well-being in affected zones and was estimated to be **high**.

Based on the geographic level and magnitude of effects, the overall effect of establishment and/or spread is shown in Table 10.

Table 10: Overall effects associated with the outbreak scenario of PrP^{BSE}

Pathway	Overall effects
Basic research, industrial use, teaching, and diagnostic services	Negligible
Diversion into commercial vaccine/therapeutic production	High
Diversion into vaccine/therapeutic research and development	High
Inappropriate handling and disposal	Negligible

Pathway	Overall effects
Environmental contamination	Negligible

Due to the outcome of negligible for basic research, industrial use, teaching, and diagnostic services; inappropriate handling and disposal; and environmental contamination, the risk assessment was discontinued for these pathways. The likely consequences (using Figure 5) and therefore the unrestricted risk (using Figure 6) would be negligible which achieves Australia's ALOP. Therefore, no specific risk management is considered necessary for PrP^{BSE} in dehydrated or pre-sterilised microbiological media for these pathways.

Estimation of likely consequences

The estimate of the likelihood of establishment and/or spread for the scenario for each pathway (Table 9) was combined with the overall effects associated with the outbreak scenario for each pathway (Table 10) using Figure 5 to obtain an estimation of likely consequences for each pathway (Table 11).

Table 11: Likely consequences of PrP^{BSE}

Pathway	Likely consequences
Diversion into commercial vaccine/therapeutic production	High
Diversion into vaccine/therapeutic research and development	High

4.1.6 Risk estimation

For each pathway, the likelihood of entry and exposure (Table 8) was combined with the likely consequences of establishment and/or spread (Table 11) using Figure 6 which resulted in a risk estimation outlined in Table 12.

Table 12: Unrestricted risk estimate for PrP^{BSE}

Pathway	Unrestricted risk estimate
Diversion into commercial vaccine/therapeutic production	Low
Diversion into vaccine/therapeutic research and development	Low

The unrestricted risk estimate of **low** does not achieve Australia's ALOP. Therefore specific risk management is considered necessary for PrP^{BSE} in dehydrated or pre-sterilised microbiological media for the following pathways:

- Diversion into commercial vaccine/therapeutic production
- Diversion into vaccine/therapeutic research and development

4.2 Scrapie protease-resistant prion protein (PrP^{Sc})

4.2.1 Background

Infection with the scrapie protease-resistant prion protein (PrP^{Sc}) may result in scrapie. Classical scrapie is host specific and naturally infects sheep and goats (Jeffrey & Gonzalez 2007). Scrapie is considered to have an almost worldwide distribution; Australia and New Zealand are the only countries considered free from classical scrapie.

Atypical scrapie arises spontaneously in older sheep and goats and is poorly transmissible under natural conditions (Fediaevsky et al. 2010). The WOAAH considers atypical scrapie to be a non-contagious condition that occurs spontaneously and sporadically (WOAH 2022f). Atypical scrapie will not be considered further in this review.

Infection with PrP^{Sc} causes an invariably fatal, progressive neurological disease caused by spongiform degeneration of the central nervous system (CNS) grey matter. It is characterised by a prolonged incubation time (2 to 5 years) (Aguilar-Calvo et al. 2015). Survival times range from weeks to months following onset of clinical signs (AHA 2020b).

PrP^{Sc} transmission occurs both horizontally and vertically and environmental contamination with infectious PrP^{Sc} provides an important source of infection. PrP^{Sc} is extremely resistant to inactivation (Taylor 1999). Economic loss is directly linked to mass slaughter of affected flocks and loss of production and, indirectly, to the restriction on the export of animals and their by-products.

In 2017, a theoretical case of scrapie in Australia was estimated to cost \$75 million if a 3-month sheep meat export trade ban was imposed, and this figure grew to \$2.2 billion in the case of a sheep meat ban being extended until Australia regained negligible-risk status (15 years on average) (Hafi, Eather & Garner 2017).

Classical scrapie is a WOAAH-listed disease of sheep and goats (WOAH 2022c). Transmissible spongiform encephalopathies are nationally notifiable diseases.

4.2.2 Technical information

Agent properties

PrP^{Sc} is a very small infectious particle known as a prion. Prions are composed of protein; nucleic acids are not required for prion infectivity (Bellinger-Kawahara et al. 1987; Oesch et al. 1985; Safar et al. 2005).

PrP^{Sc} is a misfolded isoform of the cellular prion protein, PrP^C. PrP^{Sc} is highly resistant to the thermal and chemical treatments considered suitable to inactivate most pathogens due to the following properties (Aguilar-Calvo et al. 2015; Meyer et al. 1986; Pan et al. 1993; Stahl et al. 1987; Taylor 1999):

- low detergent solubility
- low susceptibility to hydrolysis by proteases
- increased accumulation in host tissues compared with PrP^C
- altered tissue distribution in the host's central nervous system compared with PrP^C.

Inactivation of prion infectivity has only been demonstrated following extreme treatments such as 20,000 ppm sodium hypochlorite for 1 hour (Fichet et al. 2004) which is highly corrosive to certain surfaces, or 1N NaOH for 60 minutes followed by autoclaving at 121°C for 30 minutes (Taguchi et al. 1991). Although there are reports of other treatments successfully inactivating prions, many of these have been demonstrated to be insufficient for complete inactivation in subsequent studies (Taylor 1999). Inactivation studies of prions are further complicated by the sometimes marked difference in susceptibility to inactivation treatments observed between different prion strains and sample types (e.g. brain macerates or intact brain tissue) (Taylor 1999).

Transmission

Scrapie transmission occurs within and between flocks, and genetic variations among sheep determine susceptibility to infection (Detwiler & Baylis 2003). Horizontal transmission accounts for most scrapie cases in heavily infected flocks. The most likely route of infection is oral (Detwiler & Baylis 2003). PrP^{Sc} is excreted in urine, faeces, saliva, and through the skin (Gough & Maddison 2010). Transmission to lambs occurs vertically through the placenta (Gough & Maddison 2010) and horizontally through milk (Konold et al. 2008). The infectious dose required for transmission of PrP^{Sc} is very low (Fryer & McLean 2011).

PrP^{Sc} can bind to soil particles and retain infectivity for decades (Brown & Gajdusek 1991; Seidel et al. 2007). Persistent infectivity has been demonstrated on many objects and materials (Konold et al. 2015; Weissmann et al. 2002) and has been demonstrated to last at least 16 years (Georgsson, Sigurdarson & Brown 2006). Environmental transmission through oral exposure is an important factor in scrapie epidemiology.

Iatrogenic scrapie has been caused by administration of PrP^{Sc}-contaminated louping ill virus and *Mycoplasma agalactiae* vaccines (Caramelli et al. 2001; Detwiler & Baylis 2003). These were not due to contaminated microbiological media used in production, but due to the inclusion of formalin-treated ovine brain, spinal cord, and spleen in the louping ill virus vaccine; and homogenised, filtered ovine brain, mammary gland, and lymph node in the *Mycoplasma agalactiae* vaccine.

Immunity

PrP^{Sc} does not evoke a specific immune response (WOAH 2022f).

Distribution

Classical scrapie has been reported throughout most of the world. Australia and New Zealand are the only countries considered by the WOAH as being free from classical scrapie (WOAH 2022f).

Pathogenesis

Scrapie has a long incubation period (2 to 5 years) and is invariably fatal once clinical signs develop. Survival times range from 2 weeks to 6 months following the onset of clinical signs (Aguilar-Calvo et al. 2015).

Following entry into the gut associated lymphoid tissue, PrP^{Sc} spreads to other lymphoreticular tissue including the spleen, lymph nodes and tonsils, then to the enteric nervous system and the CNS. Following replication in the CNS there is centrifugal spread of PrP^{Sc} via the peripheral nervous system to sites of secondary replication. There is prolonged persistence and replication within the lymphoid tissues throughout disease incubation (Gough & Maddison 2010).

Clinical signs

Clinical signs include incoordination, gait abnormalities progressing to severe hindlimb ataxia, hyperaesthesia, hyperexcitability, altered mentation, neurological deficits, pruritus causing self-trauma, alopecia and wool loss, progressive loss of body condition, recumbency, and death (Aguilar-Calvo et al. 2015; Detwiler & Baylis 2003; Konold & Phelan 2014).

Pathology

Histopathological changes generally include non-inflammatory spongiform changes, neuronal degeneration, and astrocytosis (Hadlow, Kennedy & Race 1982). Outside of the nervous system, PrP^{Sc} has been detected in the lymph nodes, spleen, tonsils, distal ileum, proximal colon, muscles, nictitating membrane, mammary glands, placenta, skin, pancreas, heart, and urinary bladder (Aguilar-Calvo et al. 2015).

Testing

There is currently no test available to detect the presence of PrP^{Sc} in biological commodities such as dehydrated or pre-sterilised microbiological media.

PrP^{Sc} infectivity in a biological sample can be demonstrated using a mouse bioassay; however, the prolonged incubation period makes this impractical for routine diagnostic purposes.

The standard scrapie cell assay (SSCA) has shown promise for *in vitro* diagnostics and can demonstrate protease-resistant prion protein infectivity in environmental samples, thus making it potentially useful in screening of biological samples. However, it has many limitations and is currently not used for this purpose (Van der Merwe et al. 2015).

Other *in vitro* methods such as protein misfolding cyclic amplification (Chen et al. 2010), quaking induced conversion (Orrù et al. 2009), and surround optical fibre immunoassay (Chang et al. 2009) have demonstrated high sensitivity for detecting protease-resistant prion proteins in biological samples such as urine (Chen et al. 2010), blood (Chen et al. 2010), and cerebrospinal fluid (Schmitz et al. 2016; Wilham et al. 2010). However, they have not been formally evaluated for use in ante-mortem surveillance systems in animals or for the detection of PrP^{Sc} in biological commodities. These methods can have sensitivities measured in the order of femtograms or attograms (Orrù et al. 2012). Other methods that have been investigated and show some potential for detection of protease-resistant prion proteins in various substrates are flow cytometry (Trieschmann et al. 2005), infrared spectroscopy (Lasch et al. 2003), and nanoscale liquid chromatography-mass spectrometry (Onisko et al. 2007).

Treatment

There is no treatment available for any TSEs.

Control

The PRNP gene encodes both PrP^C and PrP^{Sc}. It is highly polymorphic in sheep and specific genotypes correlate to host susceptibility or resistance (Goldmann 2018). Alleles that confer some degree of resistance to scrapie in goats have also been identified (Lacroux et al. 2014).

Australia's National TSE Surveillance Project (NTSESP) sampling design for scrapie is consistent with the WOA's recommendations, and is designed to enable detection of scrapie with a confidence level of 99% if it comprised 1% of sheep neurological cases (AHA 2020a). Additionally, Australia has

an inclusive ban on the feeding to all ruminants of all meals, including meat and bone meal (MBM), derived from all vertebrates, including fish and birds. This ban on restricted animal material (RAM) was introduced in 1996 and legislated in all states and territories in 1997. It provides assurance to international markets that appropriate measures are in place to ensure RAM is not being fed to ruminant livestock species (AHA 2021a).

Fluids and tissues derived from TSE susceptible species have been categorised according to three risk categories which are taken from the [Guidelines for managing the risk of transmitting transmissible spongiform encephalopathies \(TSEs\) via veterinary vaccines and other in vivo veterinary products 2012](#):

- Category A (high infectivity): Brain, spinal cord, eye, retina, optic nerve, trigeminal ganglia, spinal ganglia, pituitary gland, dura mater, pineal gland, skull, vertebral column, distal ileum.
- Category B (lower infectivity): Ileum (proximal), lymph nodes, proximal colon, spleen, tonsil, cerebrospinal fluid, adrenal gland, distal colon, stomach, nasal mucosa, peripheral nerves, liver, lung, pancreas, thymus, oesophagus, placenta, kidney (sheep), salivary gland, blood, blood vessels, bone marrow, mammary gland (sheep/goat), milk (sheep/goat), uterus.
- Category C (no detectable infectivity): Faeces, heart, mammary gland (bovine), milk (bovine), ovary, saliva, seminal vesicle, skeletal muscle, kidney (bovine), testis, thyroid, foetal tissue, bile, bone, cartilaginous tissue, connective tissue, hair, skin, urine, semen (bovine), embryo (bovine), tongue, tendon, trachea, adipose tissue.

The department considers this system to be effective and practical when applied to the extensive range of possible dehydrated or pre-sterilised microbiological media ingredients and it has been adopted for use in this review.

4.2.3 Current biosecurity measures

Animal biosecurity requirements are in place for scrapie for multiple biological commodities.

Generally, scrapie risk management measures limit imports to:

- Countries recognised by the department as free from scrapie; and/or
- Commodities/products containing or made from tissues/secretions/excretions that have been scientifically assessed as not being sites for deposition of PrP^{Sc}; and/or
- End uses that do not expose susceptible species to assessed commodities/products (e.g. therapeutic use in non-susceptible species); and/or
- Case-by-case assessment.

Australia has guidelines for managing the animal biosecurity risk of transmissible spongiform encephalopathies in products imported for use in animals, including veterinary vaccines, other veterinary therapeutics, and *in vivo* veterinary products (DAFF 2012). Specific measures in place for mitigation of PrP^{Sc} in ovine products for *in vivo* use are listed below. Many of these ingredients are likely to be incorporated into various types of dehydrated or pre-sterilised microbiological media:

- There are no TSE restrictions on the use of ovine or caprine materials, other than neural tissue, from countries free of classical scrapie.

- Ovine/caprine neural material from any species naturally susceptible to TSEs, regardless of country of origin, is not permitted to be used directly or indirectly in the manufacture of products for use in TSE susceptible target species.
- Milk and its derivatives, other than milk sugars, from sheep or goats in classical scrapie affected countries may not be used in the production of veterinary vaccines and therapeutics for use in naturally or experimentally TSE susceptible species.
- Colostrum from sheep or goats in classical scrapie affected countries may not be used in the production of veterinary vaccines and therapeutics for use in naturally or experimentally TSE-susceptible species.
- Processing of wool derivatives produced from slaughtered animals in scrapie affected countries should include either treatment at pH > 13 at ≥ 60°C for at least 1 hour or molecular distillation at ≥ 22°C.
- Bone-derived material sourced from sheep and goats shall not be derived from vertebrae from animals greater than 30 months of age, skulls, spinal cord, or other specified risk material; shall not be cross-contaminated with other higher risk tissues; shall be subjected to a process that includes all of the following steps:
 - pressure washing (degreasing); and
 - acid demineralisation; and
 - prolonged acid or alkaline treatment; and
 - filtration; and
 - sterilisation at 138°C for a minimum of 4 seconds; or
 - is outlined as satisfactory in the Scientific Steering Committee report on gelatin or in EMEA/410/01 Rev. 3, s6.2(ii) (EMEA 2011).
- Sheep and goat blood, blood derivatives, serum, or serum derivatives sourced from classical scrapie-free countries may be used without TSE restrictions.
- Sheep and goat blood, blood derivatives, serum, or serum derivatives sourced from countries affected with classical scrapie may not be used in the production of veterinary vaccines and therapeutics destined for use in species susceptible to TSEs.
- Peptones and tissue extracts derived from Category B tissues from sheep or goats in scrapie-affected countries are not permitted to be used in TSE susceptible target species.
- Ovine/caprine ingredients used in inactivated veterinary vaccines must not be sourced from scrapie affected countries.

In addition to the specific requirements outlined for different ingredients, PrP^{Sc} dilution is considered as a form of mitigation of PrP^{Sc} in ovine/caprine-derived products. The use of ovine/caprine-derived ingredients in composite products provides a dilution factor for PrP^{Sc}, as does multiple passaging of microorganisms or infectious agents using TSE-free material that does not permit prion replication. Acceptable levels of dilution include:

- a cumulative dilution of approximately 10¹⁰ for bacterial master seeds used in vaccine production

- a cumulative dilution of approximately 10^{18} for viral master seeds used in vaccine production.

4.2.4 Conclusion

PrP^{Sc} causes significant fatal neurodegenerative clinical disease in sheep and goats. Scrapie is a WOAH-listed disease of sheep and goats and is nationally notifiable in Australia. A scrapie outbreak would represent a major economic and social threat to Australia's agricultural industries and environment. The prolonged incubation period makes early detection of a biosecurity incursion very difficult. Persistence of PrP^{Sc} in the environment and its resistance to chemical treatments make eradication very difficult once established. The resistance of PrP^{Sc} to thermal, chemical or physical inactivation treatments make elimination of contaminating PrP^{Sc} in dehydrated or pre-sterilised microbiological media very difficult. PrP^{Sc} is not present in Australia and may be present in microbiological media containing ingredients derived from infected animals.

Based on the preceding factors, the department concluded that further risk assessment of PrP^{Sc} in dehydrated or pre-sterilised microbiological media was required.

4.2.5 Risk assessment

Entry assessment

- Scrapie has a long incubation period (approximately 2 to 5 years) so animals infected with PrP^{Sc} may appear clinically normal at slaughter.
- Ovine/caprine tissue is rarely used in microbiological media production.
- Where ovine/caprine tissue is included in microbiological media, the protein digests are not always defined and could contain any type of ovine/caprine tissue, potentially including specified risk material.
- PrP^{Sc} displays widespread tissue distribution in infected sheep/goats. This may increase the likelihood of ovine/caprine tissue containing infectious PrP^{Sc} being used in the manufacture of dehydrated or pre-sterilised microbiological media.
- The processes used in the commercial manufacture of microbiological media, such as heat treatments, acid hydrolysis, or enzymatic digestion, will not inactivate PrP^{Sc}.
- Some microbiological media products have an absolute requirement for inclusion of Category A tissues.
- Microbiological media is often a composite product providing a dilution factor for any infectious agents that may be present in animal-derived ingredients.
- Scrapie is present across most of the world, with only Australia and New Zealand recognised by the WOAH as being scrapie-free.

Based on this information, the likelihood of entry of PrP^{Sc} associated with dehydrated or pre-sterilised microbiological media from any country was estimated to be **very low** using the definitions in Table 1.

Exposure assessment

General considerations relevant to all pathways:

- Sheep and goats are the only species known to be naturally susceptible to infection with scrapie. Australia is one of the world's biggest sheep producers, with 2019 figures estimating a national flock of approximately 75 million, accounting for 6.3% of the world's sheep population.
- PrP^{Sc} demonstrates environmental stability for many years.

Basic research, industrial use, teaching, and diagnostic services:

- A large part of this pathway encompasses *in vitro* work, whereby there is no direct pathway to an animal.
- When livestock are used in research and teaching the most commonly studied species is sheep.
- Most research studies involving livestock will not involve administration of dehydrated or pre-sterilised microbiological media or its derivatives.
- Current approved disposal methods for contaminated laboratory waste will not inactivate PrP^{Sc}.
- It is very unlikely that disposed media will be accessible to and ingested by susceptible species.

Based on this information, the likelihood of exposure of Australian sheep and goats to PrP^{Sc} through the use of dehydrated or pre-sterilised microbiological media from any country imported under Pathway 1 was estimated to be **low**.

Diversion into commercial vaccine/therapeutic production:

- This pathway is highly regulated both internally (e.g. by internal quality assurance units) and externally (e.g. by government bodies such as the Australian Pesticides and Veterinary Medicines Authority and the Department of Agriculture, Fisheries and Forestry).
- The commercial vaccine or therapeutic product manufactured using the dehydrated or pre-sterilised microbiological media will be administered directly into large numbers of animals, often to an entire herd.
- Due to the prolonged incubation period of scrapie, it is likely that the contaminated vaccine/therapeutic product will be used on very large numbers of animals, potentially over many years, prior to detection of clinical disease in exposed animals.
- It may be difficult to detect instances where this diversion pathway has occurred.

Based on this information, the likelihood of exposure of Australian sheep and goats to PrP^{Sc} through the use of dehydrated or pre-sterilised microbiological media from any country imported under Pathway 1 and diverted into commercial vaccine/therapeutic production was estimated to be **high**.

Diversion into vaccine/therapeutic research and development:

- The investigational product produced using microbiological media will be administered directly to target animal species (e.g. companion animals and livestock). This will likely include administration to multiple animals in pen studies using research flocks/herds, and field studies using privately owned animals.
- Use of the investigational product may be geographically widespread and not confined to research facilities.

- Due to the prolonged incubation period of scrapie, it is likely that the contaminated investigational vaccine/therapeutic product will be used in large numbers of animals prior to detection of clinical disease in exposed animals.
- Despite the high level of regulation associated with this pathway, it may be difficult to detect instances where this diversion pathway has occurred.

Based on this information, the likelihood of exposure of Australian sheep and goats to PrP^{Sc} through the use of dehydrated or pre-sterilised microbiological media from any country imported under Pathway 1 and diverted into use for vaccine/therapeutic research and development was estimated to be **high**.

Inappropriate handling and disposal:

- The majority of laboratories in Australia are in urban/suburban environments, making exposure of scrapie-susceptible species to PrP^{Sc} in contaminated microbiological media that has been disposed of inappropriately extremely unlikely.
- Microbiological media has a very low nutritional value particularly when considered on a weight per cost basis. This makes it undesirable and unsuitable for use in livestock feed.
- Dehydrated microbiological media is very expensive which provides a major disincentive for disposal prior to use.
- It is highly unlikely that a scrapie-susceptible species would be exposed to PrP^{Sc} following disposal into the municipal sewer.
- The inappropriate disposal of microbiological media from distribution warehouses is highly unlikely to occur due to the high value of the goods.
- Dehydrated microbiological media sent to landfill is likely to remain packaged.
- State and territory legislation or codes of practice governing the design, management, and security of landfill sites contribute to managing the risk of disposed media being ingested by susceptible species.
- Contamination of the environment with PrP^{Sc} is an important factor in the epidemiology of scrapie, and PrP^{Sc} can remain infectious in the environment for many years.

Based on this information, the likelihood of exposure of Australian sheep and goats to PrP^{Sc} associated with dehydrated or pre-sterilised microbiological media from any country through inappropriate handling and disposal was estimated to be **extremely low**.

Environmental contamination:

- Most shipping ports and distribution warehouses are in urban/suburban areas. Although long haul carriage of media by trucks may occur, the majority of transport of bulk consignments would occur between urban sites within the same metropolitan area.
- It is very unlikely that a truck accident resulting in environmental exposure of dehydrated or pre-sterilised microbiological media would occur in a situation that would enable a scrapie-susceptible species to be exposed to PrP^{Sc} in the spilled material.

Based on this information, the likelihood of exposure of Australian sheep or goats to PrP^{Sc} associated with dehydrated or pre-sterilised microbiological media from any country through environmental contamination was estimated to be **extremely low**.

The likelihood of exposure of scrapie-susceptible species to PrP^{Sc} associated with dehydrated or pre-sterilised microbiological media for each pathway is summarised in Table 13.

Table 13: Likelihood of exposure of scrapie-susceptible species to PrP^{Sc} in Australia

Pathway	Likelihood of exposure
Basic research, industrial use, teaching, and diagnostic services	Low
Diversion into commercial vaccine/therapeutic production	High
Diversion into vaccine/therapeutic research and development	High
Inappropriate handling and disposal	Extremely low
Environmental contamination	Extremely low

Estimation of the likelihood of entry and exposure

The likelihood of entry of PrP^{Sc} to Australia and the likelihood of its exposure to scrapie-susceptible species was estimated using the matrix of rules described in Figure 4. The estimate of the likelihood of entry was very low and the likelihood of exposure for each identified pathway is listed in Table 13. As a result, the likelihood of entry and exposure of PrP^{Sc} was estimated for each identified pathway (Table 14).

Table 14: Likelihood of entry and exposure of PrP^{Sc}

Pathway	Likelihood of entry and exposure
Basic research, industrial use, teaching, and diagnostic services	Very low
Diversion into commercial vaccine/therapeutic production	Very low
Diversion into vaccine/therapeutic research and development	Very low
Inappropriate handling and disposal	Extremely low
Environmental contamination	Extremely low

Likelihood of establishment and/or spread associated with the outbreak scenario

Factors considered relevant to the establishment and/or spread, associated with exposure of susceptible domestic and wild animals to PrP^{Sc} were:

- Scrapie is WOAHL-listed and nationally notifiable.
- Both horizontal and vertical routes are important in PrP^{Sc} transmission, allowing PrP^{Sc} to establish itself in a population and spread between animals once introduced.
- *In vivo* work involves laboratory animals held in laboratory animal housing. Although PrP^{Sc} is experimentally transmissible to laboratory animals, most *in vivo* studies in laboratory animals would not result in successful infection.

- PrP^{Sc} has a very low infectious dose.
- The standard sterilisation procedures considered appropriate for disposal of laboratory waste will not inactivate PrP^{Sc} infectivity.
- There would be a large dilution factor involved if contaminated microbiological media were released into the municipal sewer.
- Environmental contamination with PrP^{Sc} plays an important role in the epidemiology of scrapie. Eradication in Australia would be very difficult once established.
- Scrapie has a long incubation (approximately 2 to 5 years on average) so an incursion would not be detected for at least 2 years after initial exposure to the contaminated dehydrated or pre-sterilised microbiological media.
- There is no effective treatment for scrapie and once clinical signs develop the disease is invariably fatal.

The use of microbiological media contaminated with PrP^{Sc} in basic research, industrial use, teaching and diagnostic services has the potential to infect a small number of animals within isolated research facilities/laboratories. Animals used in basic research, industrial use, teaching and diagnostic services are predominantly laboratory animals that are not naturally susceptible to infection with PrP^{Sc}. Even if these animals were exposed to PrP^{Sc} and infection developed, there is no pathway for the infection to be transmitted to other animals. The most likely outbreak scenario following exposure to PrP^{Sc} through basic research, industrial use, teaching, and diagnostic services was considered to be **scenario 1**: the disease agent does not establish or is not recognised within the directly exposed population.

Diversion of microbiological media contaminated with PrP^{Sc} into commercial vaccine/therapeutic production has the potential to infect a large number of animals over a large geographical area. Due to the prolonged incubation period of scrapie, a large number of animals will likely be exposed prior to detection of PrP^{Sc} contamination. Following infection of one animal, horizontal and vertical transmission are likely to occur, and spread to other flocks is likely through the normal movement of sheep/goats during the incubation period. Environmental contamination is expected which will lead to further transmission, and the persistence of infective PrP^{Sc} in the environment will make eradication very difficult. The most likely outbreak scenario following exposure to PrP^{Sc} through diversion of microbiological media into commercial vaccine/therapeutic production was considered to be **scenario 4**: the disease agent establishes within the directly exposed population and spreads to other populations.

Diversion of microbiological media contaminated with PrP^{Sc} into use in vaccine/therapeutic research and development has the potential to infect many animals within research facilities or individual flocks/herds used for field studies. Administration may be to naturally susceptible species in pen or field studies. Due to the long incubation period of scrapie, the PrP^{Sc}-contaminated microbiological media may be used for multiple field studies prior to detection of clinical signs in affected animals resulting in many animals being exposed prior to detection of PrP^{Sc} contamination. Animals used in research studies may be sold and moved prior to the onset of clinical disease, resulting in PrP^{Sc} contamination of their new environment. The most likely outbreak scenario following exposure to PrP^{Sc} through diversion into use in vaccine/therapeutic research and development was considered to

be **scenario 4**: the disease agent establishes within the directly exposed population and spreads to other populations. The department notes this is consistent with the demonstrated international experience of a scrapie contaminated *Mycoplasma agalactiae* vaccine used in Italy (Bertolini et al. 2012).

Inappropriate handling and disposal of microbiological media contaminated with PrP^{Sc} may result in establishment and/or spread, as environmental contamination is an important factor in the epidemiology of scrapie. The most likely outbreak scenario following exposure to PrP^{Sc} through inappropriate handling and disposal of microbiological media was considered to be **scenario 4**: the disease agent establishes within the directly exposed population and spreads to other populations.

Environmental contamination of PrP^{Sc}-contaminated microbiological media may result in establishment and/or spread, as environmental contamination is an important factor in the epidemiology of scrapie. The most likely outbreak scenario following exposure to PrP^{Sc} through environmental contamination of PrP^{Sc}-contaminated microbiological media was considered to be **scenario 4**: the disease agent establishes within the directly exposed population and spreads to other populations.

Based on these considerations, the likelihood of establishment and/or spread of PrP^{Sc} was determined for each pathway as shown in Table 15.

Table 15: Likelihood of establishment and/or spread of PrP^{Sc}

Pathway	Most likely outbreak scenario	Likelihood of establishment and/or spread
Basic research, industrial use, teaching, and diagnostic services	Scenario 1	Low
Diversion into commercial vaccine/therapeutic production	Scenario 4	High
Diversion into vaccine/therapeutic research and development	Scenario 4	Moderate
Inappropriate handling and disposal	Scenario 4	Very low
Environmental contamination	Scenario 4	Very low

Determination of the effects resulting from the outbreak scenario:

For the most likely outbreak scenario for each pathway, the direct and indirect impacts of PrP^{Sc} were estimated taking into account the geographic level (Table 3) and the magnitude (Table 4) of these effects. Based on the level and magnitude of effects, the overall effect of establishment and/or spread was determined using Table 5 for each pathway. The following factors were considered relevant to a conclusion on the effects of the establishment and/or spread, of PrP^{Sc}.

- PrP^{Sc} is WOAH-listed and nationally notifiable.
- Scrapie has a prolonged incubation period, precluding early detection and eradication of the disease.
- Scrapie is host-specific and native Australian wildlife are unlikely to be susceptible to infection.
- Australia's scrapie status is important for export certification and provides significant benefit for Australia's trade status. As one of only two countries worldwide that are recognised as being

scrapie-free, Australia's sheep products hold high value for purposes requiring scrapie-free product.

- A case of scrapie would degrade the value of Australia's sheep products, as it would no longer be deemed a superior product to that available elsewhere.
- Due to the persistence of infective PrP^{Sc} in the environment, and the importance of environmental contamination in the epidemiology of scrapie, eradication of PrP^{Sc} once established will be very difficult. If eradicable, modelling has suggested eradication would take an average of 8 years, and it would take another 7 years to regain negligible-risk status. Modelling suggests eradicable outbreaks may last up to 50 years.
- In 2017, a theoretical case of scrapie in Australia was estimated to cost \$75 million if a 3 month sheep meat ban was imposed, and this figure grew to \$2.2 billion in the case of a sheep meat ban being extended until Australia regained negligible-risk status (15 years on average).
- The mass destruction and disposal of affected animals would be distressing for the local communities.
- Reliable testing for PrP^{Sc} infection in live animals is not available.
- The mortality rate is 100% once clinical signs are observed.
- There is no treatment for scrapie.

For basic research, industrial use, teaching, and diagnostic services the most likely outbreak scenario is **scenario 1** (the disease agent does not establish or is not recognised within the directly exposed population). The effects are likely to be indiscernible for susceptible species, public health, wildlife, the environment, and communities. The effect on the economy and trade are expected to be indiscernible. The overall effect of establishment and/or spread for the outbreak scenario is unlikely to be recognised at any level within Australia and was estimated to be **negligible**.

For diversion into commercial vaccine/therapeutic production, diversion into vaccine/therapeutic research and development, inappropriate handling and disposal, and environmental contamination, the most likely outbreak scenario is **scenario 4** (the disease agent establishes within the directly exposed population and spreads to other populations). Eradication is expected to be very difficult or impossible. Confirmation of eradication, if possible, is expected to take decades due to the prolonged incubation of scrapie.

An outbreak of scrapie is likely to have significant effects at the national level. The effects are likely to have minimal significance for human health as scrapie is not zoonotic. However, there may be alarm amongst people and a rejection of consumable sheep/goat products due to perceived risk based on the link between BSE and vCJD. Significant economic effects are expected due to prolonged loss of trade and market access, and the requirement for increased surveillance and carcass disposal. The effects are expected to be indiscernible for wildlife due to a lack of known host species amongst Australian native species. The effects on the environment are likely to be indiscernible. The overall effect of establishment and/or spread for the outbreak scenario is likely to be significant at the national level with serious effects on economic stability and social well-being in affected zones and was estimated to be **high**.

Based on the geographic level and magnitude of effects, the overall effect of establishment and/or spread is shown in Table 16.

Table 16: Overall effect associated with the outbreak scenario of PrP^{Sc}

Pathway	Direct and indirect effects
Basic research, industrial use, teaching, and diagnostic services	Negligible
Diversion into commercial vaccine/therapeutic production	High
Diversion into vaccine/therapeutic research and development	High
Inappropriate handling and disposal	High
Environmental contamination	High

Due to the outcome of negligible for basic research, industrial use, teaching, and diagnostic services, the risk assessment was discontinued for this pathway. The likely consequences (using Figure 5) and therefore the unrestricted risk (using Figure 6) would be **negligible** which achieves Australia's ALOP. Therefore, no specific risk management is considered necessary for PrP^{Sc} in dehydrated or pre-sterilised microbiological media for this pathway.

Estimation of the likely consequences

The estimate of the likelihood of establishment and/or spread for the scenario for each pathway (Table 15) was combined with the overall effect associated with the outbreak scenario for each pathway (Table 16) using Figure 5 to obtain an estimation of likely consequences for each pathway (Table 17).

Table 17: Likely consequences of PrP^{Sc}

Pathway	Consequences
Diversion into commercial vaccine/therapeutic production	High
Diversion into vaccine/therapeutic research and development	High
Inappropriate handling and disposal	Low
Environmental contamination	Low

4.2.6 Risk estimation

For each pathway, the likelihood of entry and exposure (Table 14) was combined with the likely consequences of establishment and/or spread (Table 17) using Figure 6, which resulted in a risk estimation outlined in Table 18.

Table 18: Unrestricted risk estimate for PrP^{Sc}

Pathway	Unrestricted risk estimate
Diversion into commercial vaccine/therapeutic production	Low
Diversion into vaccine/therapeutic research and development	Low
Inappropriate handling and disposal	Negligible

Pathway	Unrestricted risk estimate
Environmental contamination	Negligible

The unrestricted risk estimate of negligible for the following pathways achieves Australia's ALOP. Therefore, specific risk management is not considered necessary for PrP^{Sc} in dehydrated or pre-sterilised microbiological media for these pathways:

- Inappropriate handling and disposal
- Environmental contamination.

The unrestricted risk estimate of **low** for the following pathways does not achieve Australia's ALOP. Therefore, specific risk management is considered necessary for PrP^{Sc} in dehydrated or pre-sterilised microbiological media:

- Diversion into commercial vaccine/therapeutic production
- Diversion into vaccine/therapeutic research and development.

5 Proposed biosecurity risk management measures for the importation of dehydrated or pre-sterilised microbiological media

This review concluded that risk management for dehydrated and pre-sterilised microbiological media imported for laboratory use is required for the protease-resistant prion proteins, PrP^{BSE} and PrP^{Sc}.

The following provides the proposed biosecurity measures for dehydrated or pre-sterilised microbiological media imported into Australia for laboratory use.

5.1 Baseline risk management measures

Baseline risk management measures will be applied to all dehydrated or pre-sterilised microbiological media products imported into Australia for laboratory use. The baseline risk management measures for dehydrated or pre-sterilised microbiological media are:

- Assurance that the goods are dehydrated microbiological media or pre-sterilised microbiological media
- Dehydrated microbiological media is imported in volumes of ≤ 5 kg per individually packaged unit.

5.2 Additional animal biosecurity measures

To manage the animal biosecurity risk of bovine-derived ingredients used in the manufacture of dehydrated or pre-sterilised microbiological media, the following animal biosecurity measures will apply:

- 1) Material does not contain Category A (high infectivity) bovine tissue as listed on the department's list of [Transmissible Spongiform Encephalopathy \(TSE\) risk categories of tissues and fluids](#)

AND

Goods are manufactured in countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status, as listed on the [Bovine Spongiform Encephalopathy \(BSE\) Country List](#)

OR

- 2) Material is collected in countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status, as listed on the [Bovine Spongiform Encephalopathy \(BSE\) Country List](#)

AND

Goods are manufactured in countries recognised by the department as having a negligible or controlled bovine spongiform encephalopathy (BSE) risk status, as listed on the [Bovine Spongiform Encephalopathy \(BSE\) Country List](#)

To manage the animal biosecurity risk of ovine- or caprine-derived ingredients used in the manufacture of dehydrated or pre-sterilised microbiological media, the following animal biosecurity measures will apply:

- Material is sourced from ovines/caprines born, raised and slaughtered/born, raised and residing in Australia/New Zealand only.

If all of the above cannot be met, assessment on a case-by-case basis is required.

5.3 Review of processes

5.3.1 Review of policy

The department reserves the right to review the biosecurity measures after the first year of trade, or when there is reason to believe that the disease or sanitary status of an approved country/zone has changed, or if there is evidence of new or emerging diseases. The department may also review the biosecurity measures if there is any change in the nature or understanding of a disease/disease agent (hazard), entry pathways or exposure pathways.

6 Appendix A: Summary of disease agents excluded based on susceptibility to sterilisation with standard processes

Multiple species

<i>Alphainfluenzavirus influenzae</i> (influenza, avian influenza, equine influenza, swine influenza)	<i>Anaplasma phagocytophilum</i> (tick borne fever, granulocytic anaplasmosis)	<i>Bacillus anthracis</i> (Anthrax)
<i>Bluetongue virus</i> (Bluetongue)	<i>Bordetella bronchiseptica</i> (Infectious bronchitis)	<i>Borrelia burgdorferi</i> (Lyme disease)
<i>Borrelia theileri</i> (bovine borreliosis)	<i>Brachyspira</i> spp.	<i>Brucella abortus</i> , <i>B. melitensis</i> , <i>B. ovis</i> , <i>B. suis</i> (Brucellosis)
<i>Burkholderia pseudomallei</i> (melioidosis)	<i>Campylobacter coli</i> (campylobacteriosis)	<i>Campylobacter jejuni</i> (campylobacteriosis)
<i>Chlamydia abortus</i> , <i>C. pecorum</i> (chlamydiosis)	<i>Chlamydia psittaci</i> (psittacosis, ornithosis)	<i>Clostridium</i> spp.
<i>Corynebacterium pseudotuberculosis</i> (caseous lymphadenitis)	<i>Coxiella burnetii</i> (Q fever)	<i>Cryptosporidium parvum</i> (cryptosporidiosis)
<i>Eastern equine encephalitis virus</i> (eastern equine encephalitis)	<i>Ehrlichia ruminantium</i> (heartwater)	<i>Epizootic hemorrhagic disease virus</i> (epizootic haemorrhagic disease)
<i>Erysipelothrix rhusiopathiae</i> (erysipelas)	<i>Escherichia coli</i>	<i>Foot-and-mouth disease virus</i> (foot-and-mouth disease)
<i>Francisella tularensis</i> (tularemia)	<i>Getah virus</i>	<i>Henipavirus hendraense</i> (Hendra virus disease)
<i>Histophilus somni</i> (histophilosis)	<i>Leptospira</i> spp. (leptospirosis)	<i>Listeria</i> spp. (listeriosis)
<i>Lyssavirus rabies</i> (rabies)	<i>Mammalian orthoreovirus</i>	<i>Mycobacterium avium</i> subsp. <i>paratuberculosis</i> / (Paratuberculosis, Johne's disease)

Dehydrated and pre-sterilised microbiological media

<i>Mycobacterium tuberculosis</i> (bovine tuberculosis)	<i>Mycoplasma capricolum</i> (contagious caprine pleuropneumonia)	<i>Orthobornavirus bornaense</i> (Borna disease)
<i>Orthobunyavirus akabaneense</i> (Akabane disease)	<i>Orthobunyavirus cacheense</i> (Cache Valley fever)	<i>Orthobunyavirus schmallenbergense</i>
<i>Orthobunyavirus shuniense</i>	<i>Orthoflavivirus encephalitis</i> (tick-borne encephalitis)	<i>Orthoflavivirus japonicum</i> (Japanese encephalitis)
<i>Orthoflavivirus loupingi</i> (louping ill, ovine encephalomyelitis)	<i>Orthoflavivirus nilense</i> (West Nile fever)	<i>Orthoflavivirus wesselsbronense</i> (Wesselsbron disease)
<i>Orthonairovirus haemorrhagiae</i> (Crimean-Congo haemorrhagic fever)	<i>Pasteurella</i> spp. (fowl cholera, atrophic rhinitis, bovine haemorrhagic septicaemia)	<i>Phlebovirus riftense</i> (Rift Valley fever)
<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Typhimurium DT104	<i>Staphylococcus</i> spp.	<i>Streptococcus</i> spp.
<i>Toxoplasma gondii</i> (toxoplasmosis)	<i>Trypanosoma brucei</i> , <i>T. congolense</i> , <i>T. vivax</i> (trypanosomosis (tsetse-transmitted))	<i>Trypanosoma evansi</i> (surra)
<i>Varicellovirus suidalpha1</i> (Aujeszky's disease, pseudorabies)	<i>Vesicular exanthema of swine virus</i> (vesicular exanthema of swine)	<i>Vesiculovirus alagoas</i> , <i>Vesiculovirus cocal</i> , <i>Vesiculovirus indiana</i> , <i>Vesiculovirus newjersey</i> (vesicular stomatitis)
<i>Yersinia enterocolitica</i> (yersiniosis)	<i>Yersinia pestis</i> (plague)	

Avian

<i>Avastrovirus 2</i> (avian nephritis, infectious stunting syndrome, baby chick nephritis)	<i>Avian coronavirus</i> (Avian infectious bronchitis)	<i>Avian leukosis virus</i> (lymphoid leukosis)
<i>Avian orthoreovirus</i>	<i>Avian paraavulavirus 3</i>	<i>Avibacterium paragallinarum</i> (infectious coryza)
<i>Avibirnavirus gumboroense</i> (infectious bursal disease, Gumboro disease)	<i>Bordetella avium</i> (avian bordetellosis)	<i>Borrelia anserina</i> (avian spirochetosis)
<i>Clostridium colinum</i> (ulcerative enteritis)	<i>Fowl aviadenovirus A</i> (adenoviral gizzard erosion)	<i>Fowl aviadenovirus B</i>
<i>Fowl aviadenovirus C</i> (hepatitis hydropericardium syndrome)	<i>Fowl aviadenovirus D</i> , <i>Fowl aviadenovirus E</i> (inclusion body hepatitis)	<i>Fowlpox virus</i> (fowlpox)

Dehydrated and pre-sterilised microbiological media

<i>Gyrovirus chickenanemia</i> (chicken infectious anemia)	<i>Iltovirus gallidalpha1</i> (infectious laryngotracheitis)	Lymphoproliferative disease virus (lymphoproliferative disease)
<i>Malacoplasma iowae</i>	<i>Mardivirus gallidalpha2</i> (Marek's disease, fowl paralysis)	<i>Metaavulavirus yucaipaense</i>
<i>Metapneumovirus avis</i> (turkey rhinotracheitis, swollen head syndrome)	<i>Mycoplasma gallisepticum</i> (avian mycoplasmosis)	<i>Mycoplasma synoviae</i> (avian mycoplasmosis)
<i>Ornithobacterium rhinotracheale</i>	<i>Orthoavulavirus javaense</i> (Newcastle disease)	<i>Reticuloendotheliosis virus</i>
<i>Riemerella anatipestifera</i>	<i>Salmonella enterica</i> subs. <i>arizonae</i> (Arizonosis)	<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Enteritidis
<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Gallinarum biovar Gallinarum (fowl typhoid)	<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Gallinarum biovar Pullorum (pullorum disease)	<i>Tremovirus A</i> (avian encephalomyelitis)

Bovine

<i>Actinomyces bovis</i> (Lumpy jaw)	<i>Aichivirus B</i>	<i>Anaplasma bovis</i> , <i>Anaplasma marginale</i> (Bovine anaplasmosis)
<i>Babesia bigemina</i> , <i>B. bovis</i> , <i>B. divergens</i> (Bovine babesiosis)	<i>Besnoitia besnoiti</i> (Bovine besnoitiosis)	<i>Bocaparvovirus unguulate1</i> (bovine parvovirus infection)
<i>Bovine atadenovirus D / Bovine mastadenovirus A, B, C</i> (Bovine respiratory disease (infectious bovine rhinotracheitis, infectious pustular vulvovaginitis, bovine reproductive disease))	<i>Bovine immunodeficiency virus</i>	<i>Bovine leukemia virus</i> (enzootic bovine leukosis)
<i>Campylobacter fetus</i> subsp. <i>venerealis</i> (bovine genital campylobacteriosis)	<i>Enterovirus E</i> , <i>Enterovirus F</i> (bovine enterovirus infection)	<i>Ephemerovirus febris</i> (bovine ephemeral fever)
<i>Epsilonpolyomavirus bovis</i>	<i>Jembrana disease virus</i> (Jembrana disease)	<i>Lumpy skin disease virus</i> (lumpy skin disease)
<i>Macavirus alcelaphinegamma1</i> (Malignant catarrhal fever)	<i>Morbillivirus pecoris</i> (Rinderpest)	<i>Mycoplasma mycoides</i> subsp. <i>mycoides</i> small colony (SC) type (contagious bovine pleuropneumonia)

Dehydrated and pre-sterilised microbiological media

<i>Mycoplasma</i> <i>bovis</i> (bovine mycoplasmosis)	<i>Orthobunyavirus ainoense</i> (Aino disease)	<i>Orthopneumovirus bovis</i> (bovine respiratory syncytial disease, bovine respiratory disease complex)
<i>Pestivirus bovis</i> , <i>Pestivirus tauri</i> , <i>Pestivirus brazilense</i> (bovine viral diarrhoea)	<i>Respirovirus bovis</i>	<i>Rhadinovirus bovinegamma4</i>
<i>Theileria</i> spp. (East Coast fever, oriental theileriosis, tropical theileriosis)	<i>Tritrichomonas foetus</i> (trichomoniasis)	<i>Varicellovirus bovinealpha1</i>

Equine

<i>Actinobacillus equuli</i> (sleepy foal disease)	<i>African horse sickness virus</i> (African horse sickness)	<i>Alphaarterivirus equid</i> (equine viral arteritis)
<i>Babesia caballi</i> (equine babesiosis)	<i>Betacoronavirus 1</i>	<i>Burkholderia mallei</i> (glanders)
<i>Ehrlichia risticii</i> (Potomac horse fever)	<i>Equine encephalosis virus</i> (equine encephalosis)	<i>Equine infectious anemia virus</i> (equine infectious anaemia)
Equine mastadenovirus A	Equine mastadenovirus B	Equine rhinitis A virus
<i>Equine torovirus</i>	<i>Erbovirus A</i>	<i>Histoplasma capsulatum</i> (histoplasmosis, epizootic lymphangitis)
<i>Horsepox virus</i> (horsepox)	<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Abortusequi	<i>Taylorella equigenitalis</i> (contagious equine metritis)
<i>Theileria equi</i> (equine piroplasmosis)	<i>Trypanosoma equiperdum</i> (dourine)	<i>Varicellovirus equidalpha1</i> (equine rhinopneumonitis, equine herpes myeloencephalopathy)
<i>Varicellovirus equidalpha3</i> (equine coital exanthema)	<i>Varicellovirus equidalpha4</i> (equine rhinopneumonitis)	<i>Varicellovirus equidalpha8</i>
<i>Varicellovirus equidalpha9</i>	<i>Venezuelan equine encephalitis virus</i> (Venezuelan equine encephalitis)	<i>Western equine encephalitis virus</i> (western equine encephalitis)

Ovine/caprine

<i>Caprine arthritis encephalitis virus</i> (caprine arthritis encephalitis)	<i>Dichelobacter nodosus</i> (ovine footrot)	<i>Goatpox virus</i> (sheep and goat pox)
<i>Jaagsiekte sheep retrovirus</i> (ovine pulmonary adenocarcinoma)	<i>Morbillivirus caprinae</i> (peste-des-petits ruminants)	<i>Mycoplasma agalactiae</i> (contagious agalactia)

Dehydrated and pre-sterilised (microbiological media

<i>Orf virus</i> (orf disease, scabby mouth)	<i>Orthonairovirus nairobiense</i> (Nairobi sheep disease)	<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Abortusovis
<i>Sheeppox virus</i> (sheep and goat pox)	<i>Visna-maedi virus</i> (Maedi-visna)	

Porcine

<i>Actinobacillus pleuropneumoniae</i> (Porcine pleuropneumonia)	<i>Actinobacillus suis</i> (Actinobacillosis)	<i>Actinobaculum suis</i>
<i>African swine fever virus</i> (African swine fever)	<i>Alphacoronavirus 1</i> (transmissible gastroenteritis)	<i>Betaarterivirus suis 1 & 2</i> (porcine reproductive and respiratory syndrome)
<i>Betacoronavirus 1</i> (porcine hemagglutinating encephalomyelitis)	<i>Brachyspira hyodysenteriae</i> (swine dysentery)	<i>Cardiovirus A</i> (encephalomyocarditis)
<i>Enterovirus B</i> (swine vesicular disease)	<i>Glaesserella parasuis</i> (Glässer disease)	<i>Henipavirus nipahense</i>
<i>Lawsonia intracellularis</i> (porcine proliferative enteropathy)	<i>Mesomycoplasma hyopneumoniae</i> (porcine enzootic pneumonia)	<i>Mesomycoplasma hyorhinis</i> (fibrinous polyarthritis and polyserositis)
<i>Metamycoplasma hyosynoviae</i> (fibrinous polyarthritis)	<i>Mycoplasma suis</i> (infectious anaemia of pigs, porcine eperythrozoonosis)	<i>Orthorubulavirus suis</i> (blue eye disease)
<i>Pestivirus suis</i> (classical swine fever)	<i>Circovirus porcine2</i>	<i>Porcine cytomegalovirus</i>
<i>Porcine epidemic diarrhea virus</i> (porcine epidemic diarrhoea)	<i>Porcine mastadenovirus A, B, C</i>	<i>Protoparvovirus ungulate1</i> (stillbirth, mummification, embryonic death, and infertility (SMEDI) syndrome)
<i>Rotavirus A, B, C, E</i>	<i>Schaalia hyovaginalis</i> (porcine actinomycosis)	<i>Streptococcus suis</i>
<i>Swinepox virus</i> (swine pox)	<i>Teschovirus A</i> (teschovirus encephalomyelitis)	

Lagomorph

<i>European brown hare syndrome virus</i>	<i>Myxoma virus</i> (myxomatosis)	<i>Rabbit fibroma virus</i>
<i>Rabbit hemorrhagic disease virus</i> (rabbit haemorrhagic disease)	<i>Treponema cuniculi</i> (rabbit syphilis)	

Dehydrated and pre-sterilised microbiological media

Aquatics		
<i>Achlya</i> spp.	<i>Acineta</i> spp.	<i>Acinetobacter</i> spp.
<i>Aerococcus viridans</i> var. <i>homari</i> (gaffkemia)	<i>Aeromonas</i> spp.	<i>Ambystoma tigrinum</i> virus
<i>Aparavirus tauraense</i>	<i>Aphanomyces</i> spp.	<i>Apiosoma</i> spp.
Apostome ciliates, including <i>Ascophrys</i> spp., <i>Gymnodinioides</i> spp., <i>Synophrya</i> spp. and <i>Hyalophysa</i> spp.	Aquabirnaviruses (genus <i>Aquabirnavirus</i>)	Aquatic epicomensal bacteria, including <i>Cytophaga</i> spp., <i>Flavobacterium</i> spp., <i>Leucothrix</i> spp., and <i>Thiothrix</i> spp.
Aquatic megalocytiviruses (genus <i>Megalocytivirus</i>)	<i>Aspergillus awamori</i> (black gill infection)	<i>Atkinsiella dubia</i>
<i>Bacillus licheniformis</i>	<i>Bacillus mycoides</i>	Baculovirus <i>penaei</i> (BP) (tetrahedral baculovirosis)
Beihai shrimp virus genotype 1	Betanodaviruses (genus <i>Betanodavirus</i>) (viral encephalopathy and retinopathy, viral nervous necrosis)	<i>Brooklynella hostilis</i>
Candidatus <i>Hepatobacter penaei</i> (necrotising hepatopancreatitis)	<i>Carnobacterium</i> spp.	<i>Ceratonova shasta</i>
<i>Chlamydia</i> spp. (Epitheliocystis)	<i>Chryseobacterium joostei</i>	Ciliates (including <i>Ichthyophthirius multifiliis</i>)
<i>Citrobacter freundii</i>	<i>Cladosporium</i> spp.	<i>Clostridium perfringens</i>
Covert mortality nodavirus (viral covert mortality disease / covert mortality disease / 'bottom death' disease)	Crangon crangon flavivirus	Crustacea hepe-like virus 1 (CHEV1)
<i>Cryptobia</i> spp.	<i>Cryptocaryon irritans</i>	<i>Cyivirus cyprinidallo3</i> (koi herpesvirus disease)
<i>Decapod iridescent virus 1</i>	<i>Dermocystidium</i> spp.	<i>Edwardsiella tarda</i>
<i>Eimeria</i> spp.	<i>Enterobacter cloacae</i>	<i>Enterococcus</i> spp.
<i>Enterocytozoon hepatopenaei</i> (hepatopancreatic microsporidiosis (HPM) and enterosporidiosis)	<i>Enteromyxum</i> spp.	<i>Ephelota</i> spp.

Dehydrated and pre-sterilised microbiological media

<i>Epizootic haematopoietic necrosis virus</i>	Erythrocytic necrosis virus	<i>Exophiala</i> spp.
Farfantepenaeus duorarum nodavirus	<i>Flavobacterium</i> spp.	<i>Flexibacter</i> spp.
<i>Fusarium</i> spp. (burn spot disease, black spot disease, black gill disease and fusariosis)	<i>Gammanudivirus cracrangonis</i>	<i>Gammanudivirus pemonodonis</i>
<i>Gilbertella persicaria</i>	<i>Glugea</i> spp.	<i>Goussia gadi</i>
Gregarines, including <i>Cephalolobus</i> spp., <i>Nematopsis</i> spp., and <i>Paraophioidina</i> spp.	<i>Haliphthoros</i> spp.	<i>Haplosporida</i> spp. (hepatopancreatic haplosporidiosis)
Haplosporidian-like parasite (red gill disease)	<i>Hematodinium</i> spp.	<i>Henneguya</i> spp.
<i>Hepanhamaparvovirus decapod1</i>	<i>Hexamita</i> spp.	<i>Ichthyophonus hoferi</i>
<i>Isavirus salaris</i> (infectious salmon anaemia)	Infectious myonecrosis virus	Infectious precocity virus (Infectious precocity virus disease, iron prawn syndrome)
<i>Inodosporus</i> spp.	<i>Kudoa</i> spp.	<i>Lactococcus</i> spp. (white muscle disease)
Laem Singh virus	<i>Lagenidium</i> spp.	<i>Leptolegnia</i> spp.
<i>Leptomitus</i> spp.	<i>Leptomonas</i> spp.	<i>Loma salmonae</i>
<i>Lymphocystis disease virus 1 and 2</i>	Macrobrachium nipponense reovirus	Macrobrachium rosenbergii Taihu virus (disease of seven days)
Macrobrachium rosenbergii nodavirus	<i>Metanophrys sinensis</i>	<i>Micrococcus</i> spp.
<i>Microsporidia</i> spp.	Mourilyan virus	<i>Mycobacterium</i> spp.
<i>Mycoplasma</i> spp.	<i>Myxobolus</i> spp.	<i>Neoparamoeba perurans</i> (Amoebic gill disease)
<i>Nimanivirus lahi</i>	<i>Nitzschia</i> spp.	<i>Nocardia</i> spp.
<i>Novirhabdovirus piscine</i> (viral haemorrhagic septicaemia)	<i>Novirhabdovirus salmonid</i> (infectious haematopoietic necrosis)	<i>Nucleospora salmonis</i>

Dehydrated and pre-sterilised microbiological media

<i>Okavirus flavicapitis</i> (yellowhead disease)	Oncorhynchus masou virus	<i>Ovipleistophora arlo</i>
<i>Piscine orthoreovirus</i> (erythrocytic inclusion body syndrome)	<i>Parauronema</i> spp.	<i>Parvicapsula</i> spp.
<i>Pasteurella</i> spp.	<i>Penaeus monodon</i> metalloidensovirus	<i>Penaeus monodon</i> nucleopolyhedrovirus
<i>Penaeus vannamei</i> nodavirus (white tail disease, white muscle disease)	<i>Penstylhamaparvovirus decapod1</i>	Peritrichous and loricate ciliates, including <i>Cothurnia</i> spp., <i>Epistylis</i> spp., <i>Lagenophrys</i> spp., <i>Rhabdostyla</i> spp., <i>Vorticella</i> spp., <i>Zoothamnium</i> spp.
<i>Photobacterium</i> spp.	Pilchard herpesvirus	<i>Piscirickettsia salmonis</i>
<i>Pleistophora</i> spp.	<i>Proteus penneri</i>	<i>Providencia</i> spp.
<i>Pseudomonas</i> spp.	<i>Pythium</i> spp.	Ranaviruses (genus <i>Ranavirus</i>)
<i>Renibacterium salmoninarum</i>	<i>Salmon pancreas disease virus</i>	<i>Salmovirus salmonidallo1</i>
<i>Saprolegnia</i> spp. (Saprolegniosis)	<i>Sherwanella algae</i>	<i>Sirolopidium</i> spp.
Spawner-isolated mortality virus	<i>Sphaerospora</i> spp.	<i>Sphaerothecum destruens</i>
<i>Spirillum</i> spp.	<i>Spiroplasma</i> spp.	<i>Sprivirus cyprinus</i>
<i>Staphylococcus</i> spp.	<i>Streptococcus</i> spp.	<i>Tenacibaculum maritimum</i>
<i>Tetracapsuloides bryosalmonae</i>	<i>Thalassomyces</i> spp.	<i>Thelohanellus</i> spp.
<i>Trichodina</i> spp.	<i>Trichodinella</i> spp.	<i>Trypanosoma anura</i>
<i>Unicapsula</i> spp.	<i>Veronaea botryosa</i> (systemic phaeohyphomycosis)	<i>Vibrio</i> spp. (acute hepatopancreatic necrosis disease, glass post-larvae, translucent post-larvae disease, highly lethal <i>Vibrio</i> disease)
Wenzhou shrimp viruses	<i>White spot syndrome virus</i> (white spot disease)	<i>Yersinia ruckeri</i> – Hagerman strain (Enteric redmouth disease, Yersiniosis)

Glossary

Term or abbreviation	Definition
ALOP	Appropriate level of protection
appropriate level of protection (ALOP) for Australia	The <i>Biosecurity Act 2015</i> defines the appropriate level of protection (or ALOP) for Australia as a high level of sanitary and phytosanitary protection aimed at reducing biosecurity risks to very low, but not to zero.
approved arrangements	An approved arrangement is an arrangement for which an approval is in force under the <i>Biosecurity Act 2015</i> .
AS/NZS 2243.3: Safety in laboratories, Part 3: Microbiological safety and containment	The Australian and New Zealand Standard for the requirements, responsibilities and general guidelines relating to the safe handling and containment of microorganisms and infectious agents within laboratories.
AUSVETPLAN	Australian Veterinary Emergency Plan
Australian territory	Australian territory as referenced in the <i>Biosecurity Act 2015</i> refers to Australia, Christmas Island and Cocos (Keeling) Islands.
BA	Biosecurity advice
bacteriophage	A virus that infects and replicates inside a bacterium.
BICON	Australian Biosecurity Import Conditions System
biosecurity	The prevention of the entry, establishment or spread of unwanted pests and infectious disease agents to protect human, animal or plant health or life, and the environment.
biosecurity import risk analysis (BIRA)	The <i>Biosecurity Act 2015</i> defines a BIRA as an evaluation of the level of biosecurity risk associated with particular goods, or a particular class of goods, that may be imported, or proposed to be imported, into Australian territory, including, if necessary, the identification of conditions that must be met to manage the level of biosecurity risk associated with the goods, or the class of goods, to a level that achieves the ALOP for Australia. The risk analysis process is regulated under legislation.
biosecurity measures	The <i>Biosecurity Act 2015</i> defines biosecurity measures as measures to manage any of the following: biosecurity risk, the risk of contagion of a listed human disease, the risk of listed human diseases entering, emerging, establishing themselves or spreading in Australian territory, and biosecurity emergencies and human biosecurity emergencies.
biosecurity risk	The <i>Biosecurity Act 2015</i> refers to biosecurity risk as the likelihood of a disease or pest entering, establishing or spreading in Australian territory, and the potential for the disease or pest causing harm to human, animal or plant health, the environment, economic or community activities.
BSE	Bovine spongiform encephalopathy
EADRA	Emergency animal disease response agreement
ELISA	enzyme-linked immunosorbent assay
endemic	Belonging to, native to, or prevalent in a particular geography, area or environment.
eukaryote	An organism consisting of a cell/cells containing a distinct membrane-bound nucleus.
FAO	Food and Agriculture Organization of the United Nations
goods	The <i>Biosecurity Act 2015</i> defines goods as an animal, a plant (whether moveable or not), a sample or specimen of a disease agent, a pest, mail or any other

Term or abbreviation	Definition
	article, substance or thing (including, but not limited to, any kind of moveable property).
host	An organism that harbours a parasite, mutual partner, or commensal partner, typically providing nourishment and shelter.
import permit	Official document authorising a person to bring or import particular goods into Australian territory in accordance with specified import requirements.
Infectious agent	Infectious agent includes any of the following (whether naturally occurring or synthetically created): <ul style="list-style-type: none"> (a) a virus; (b) a prion; (c) a plasmid; (d) a viroid; (e) a thing that is a part of an infectious agent. <p>Examples: For the purposes of paragraph (e), capsids, envelopes, enzymes, genetic material coding for an infectious agent, proteins.</p>
<i>in vitro</i> use	Laboratory use that does not involve use in/administration to an animal or human.
<i>in vivo</i> use	Use within/administration to an animal or human.
IRA	Import risk analysis
ISO/IEC 15189 – Medical laboratories – requirements for quality and competence	The international standard specifying requirements for quality and competence in medical laboratories, published by the International Organisation for Standardisation.
ISO/IEC 17025 – General requirements for the competence of testing and calibration laboratories	The international standard specifying the requirements for quality and competence in medical laboratories, published by the International Organisation for Standardisation.
ISO/IEC 17043 – Conformity assessment - General requirements for proficiency testing	The international standard specifying the general requirements for the competence of providers of proficiency testing schemes and for the development and operation of proficiency testing schemes, published by the International Organisation for Standardisation.
kGy	kilogray
kPa	kilopascal
laboratory animal	An animal that is used in a laboratory or research institution for scientific or research purposes.
laboratory organism	A guinea pig, hamster, mouse, rabbit, rat or microorganism that is used in a laboratory.
laboratory use	<i>In vitro</i> use, or <i>in vivo</i> in laboratory organisms end use
MBM	Meat and bone meal
microorganism	Microorganism includes any of the following (whether naturally occurring or synthetically created): <ul style="list-style-type: none"> (a) a single celled organism (whether an animal or plant); (b) a bacterium;

Term or abbreviation	Definition
	(c) a protozoan;
	(d) a fungus;
	(e) a plant pathogen;
	(f) a thing that is a part of a microorganism.
	Examples: For the purposes of paragraph (f), envelopes, enzymes, genetic material coding for a microorganism, proteins.
mycovirus	A virus that infects and replicates inside a fungus.
non-regulated risk analysis	Refers to the process for conducting a risk analysis that is not regulated under legislation (<i>Biosecurity import risk analysis guidelines 2016</i>).
NTSESP	National Transmissible Spongiform Encephalopathies Surveillance Program
OIE	Previous name for the World Organisation for Animal Health.
pathogen	A biological agent that can cause disease to its host.
PCR	polymerase chain reaction
PRNP	The chromosomal gene encoding the cellular prion protein and protease resistant prion protein.
prokaryote	A single-celled organism that lacks a distinct membrane-bound nucleus.
protist	A eukaryotic organism that is not classified as a plant, animal or fungus.
Pr ^{Pc}	Cellular prion protein
Pr ^{PBSE}	Bovine spongiform encephalopathy protease-resistant prion protein
Pr ^{PSc}	Scrapie protease-resistant prion protein
psi	Pounds per square inch
quality assurance	The wide-ranging concept covering all aspects of the manufacturing process that individually or collectively influence the quality of a manufactured product. It is the sum total of the arrangements made to ensure that veterinary chemical products are consistently manufactured in an appropriate manner to the quality standards required for their intended use.
quality control	A system that is concerned with specifications, sampling and testing, and with the organisation, documentation and release procedures that ensure that the necessary and relevant tests are carried out so that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory.
quarantine	Official confinement of regulated articles for observation and research or for further inspection, testing or treatment.
RAM	Restricted animal material
replication-competent	Capable of infecting cells and replicating to produce infectious progeny.
restricted risk	Risk estimate with phytosanitary measure(s) applied.
risk analysis	Refers to the technical or scientific process for assessing the level of biosecurity risk associated with the goods, or the class of goods, and if necessary, the identification of conditions that must be met to manage the level of biosecurity risk associated with the goods, or class of goods to a level that achieves the ALOP for Australia.
specified risk material	Particular tissue or fluid types derived from cattle, sheep or goats that are most likely to pose a risk of infectivity if the source animal was infected with a

Term or abbreviation	Definition
	transmissible spongiform encephalopathy. Also referred to as BSE risk material, TSE risk material.
SPS Agreement	WTO Agreement on the Application of Sanitary and Phytosanitary Measures.
stakeholders	Government agencies, individuals, community or industry groups or organisations, in Australia or overseas, including the proponent/applicant for a specific proposal, that have an interest in the policy issues.
surveillance	An official process that collects and analyses information related to animal health.
Terrestrial Code	World Organisation for Animal Health Terrestrial Animal Health Code
Terrestrial Manual	World Organisation for Animal Health Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
TSE	Transmissible spongiform encephalopathy
TSEFAP	TSE Freedom Assurance Program
unrestricted risk	Unrestricted risk estimates apply in the absence of risk mitigation measures.
Unicellular organism	An organism that consists of a single cell.
vCJD	Variant Creutzfeldt Jakob disease
vector	An organism that does not cause disease itself, but which causes infection by conveying pathogens from one host to another.
virus	An acellular infectious agent that must parasitise an animal or human cell in order to replicate and produce infectious progeny.
WOAH	World Organisation for Animal Health
WTO	World Trade Organization

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