



## **SUMMARY OF INFORMATION REQUIRED FOR AQIS ASSESSMENT OF INACTIVATED VETERINARY VACCINES**

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## **A. Introduction**

This Summary of Information (SOI) document is to be used by applicants who wish to apply for an Import Permit for inactivated veterinary vaccines. The document not only outlines the information AQIS requires to assess these applications but also provides a reference as to how the information is to be presented to AQIS.

AQIS assesses Import Permit applications for inactivated veterinary vaccines according to the requirements of the following policies:

- 'Specific Quarantine Requirements for the Importation of Inactivated Veterinary Vaccines (an addendum to the guidelines for submissions to import veterinary vaccines), December 1997'; and
- 'Requirements for Minimising the Risk of Transmitting Transmissible Spongiform Encephalopathies (TSE's) via Veterinary Vaccines and Other InVivo Veterinary Products, August 2005'

Applicants will notice that under each section of the SOI there is a heading '**Guidance on Policy Requirements**'. The points under this heading are a useful summary of the relevant policy requirements. **The points are for guidance only.** Applicants who require clarification on specific points of policy must refer to the relevant policy document or contact the 'AQIS BIP Vaccine Assessor' using [biologicals@aqis.gov.au](mailto:biologicals@aqis.gov.au).

Applicants will also notice the heading '**Evidentiary Requirements**' under each section of the SOI. AQIS assessing officers are required to review documents as the principle means of verifying compliance with relevant vaccine policy requirements. Those documents outlined under 'Evidentiary Requirements' must be presented by the applicant in support of their Import Permit application.

AQIS may impose requirements additional to those specified in this SOI where applicants/manufacturers have not demonstrated an appropriate level of control of biosecurity risk during the veterinary vaccine manufacturing process. Examples of additional requirements that may be imposed by AQIS are pathogen testing of vaccine intermediates/final product, increased documentation requirements or on-site audit requirements.

## **B. Dossier format**

AQIS requires supporting documentation to be presented in a format which will maximise the efficiency of the assessment process. All supporting documentation must be provided in an AQIS specific dossier which is supplementary to this SOI. AQIS will not accept dossiers that have been prepared for other regulatory agencies as supporting information for an AQIS Import Permit application.

Dossiers presented to AQIS must be annotated in a way which allows easy reference between the SOI and the dossier. As such AQIS requires the dossier to be indexed in the following way:

### **Index**

#### **Preliminary Information Requirements**

- 1. Standards of Manufacture/Sourcing of Ingredients**
- 2. Masterseed Viruses (MSV)**
- 3. Masterseed Bacteria (MSB)**
- 4. Master and Working Cell Seeds**
- 5. Working and Production Seeds – Viral and/or Bacterial**
- 6. Nutritive factors**
- 7. Trypsin and other enzymes of animal origin**
- 8. Fermentation broths and culture media**
- 9. Components of avian origin and embryonated eggs**
- 10. Other materials of animal origin**
- 11. Inactivation**
- 12. Final Product – Viral Vaccines**
- 13. Final Product – Bacterial Vaccines**

#### **Applicant's Declaration**

Within each section of the dossier applicants must provide documentation according to the **Evidentiary Requirements** outlined in this SOI. For example where the SOI requires applicants to provide a copy of a current certificate demonstrating compliance of the manufacturing facility with a code of Good Manufacturing Practice (cGMP) a copy of this certificate must be included in the '**1. Standards of Manufacture/Sourcing of Ingredients**' section of the dossier.

AQIS appreciates that not all sections of the dossier will be relevant to every vaccine product e.g. vaccines are not always manufactured using nutritive factors derived from serum. Where this is the case AQIS requires manufacturers to provide a declaration within the relevant section of the dossier confirming the absence of the particular component in vaccine manufacture.

Import Permit applications for new vaccine products which are submitted without a correctly formatted dossier will be rejected with no refund of application/assessment fees.

## **C. Equivalence**

As a signatory to the World Trade Organisation's Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) AQIS is empowered to enforce biosecurity risk management measures which are based on science. It is also an obligation under the SPS Agreement that AQIS considers risk management measures which might be considered equivalent to current, standard policy requirements.

This obligation extends to AQIS's veterinary vaccine assessments. Where a particular vaccine has been manufactured in a manner which is not compliant with current policy requirements applicants may present a case for equivalence to AQIS. Cases for equivalence may be presented as an appendix to the dossier submitted in support of the Import Permit application.

AQIS will review the case for equivalence and consider whether advice from Biosecurity Australia is necessary for a complete assessment of the case. Biosecurity Australia is the principle provider of scientific/technical policy advice to AQIS.

Once AQIS has collated and reviewed all relevant information in relation to the case, including advice from Biosecurity Australia, a determination will be made as to whether the measures outlined in the case for equivalence provide a level of biosecurity risk control which is equivalent to current policy requirements.

Where it is determined that the case does not provide an equivalent level of biosecurity risk control AQIS will not issue an Import Permit for the vaccine product.

It is difficult for AQIS to provide specific guidance on the format for cases for equivalence as their content will vary with each new vaccine product. **Prior to the submission of an Import Permit application** applicants will need to consider how the particular vaccine is not compliant with current policy requirements. Applicants will then need to define alternate measures which have been, or may be, implemented to demonstrate equivalence with these requirements.

In preparing a case for equivalence applicants must recognise that AQIS vaccine assessing officers consider all stages of the manufacturing process independently. The implication of this approach is that biosecurity risk control steps for one stage of the manufacturing process may not be considered effective in mitigating the biosecurity risk for another stage. For example the biosecurity risk of a masterseed which has not undergone extraneous agent testing as required by the policy may not be mitigated by the chemical inactivation step of the final bulk vaccine antigen.

Import Permit applications for non-compliant vaccine products which are not accompanied by a well considered and well drafted case for equivalence relating to the areas of non-compliance will be rejected by AQIS with no refund of application/assessment fees.

## **D. Preliminary Information Requirements**

### **1. Table for applicant to complete**

<b>Name of vaccine</b>	
<b>Target species</b>	
<b>List all antigens in final product</b>	
<b>Active against</b>	
<b>Manufacturer</b>	
<b>Importer</b>	
<b>List the name of the dossiers submitted in support of the application</b>	

### **2. Complete list of biological components**

Biological components are those derived from animals, plants and/or a microbial fermentation process. A complete list of biological components used in vaccine manufacture must be provided. This list defines the scope of the AQIS assessment.

#### **List of all biological components used in manufacture**

<b>Name and reference code for all masterseed organisms/viruses:</b>
<b>Name and reference code for all working and production seed organisms/viruses:</b>
<b>Name and reference code for all master and working cell seeds:</b>
<b>Complete list of biological products used in production:</b>

### **3. Flowchart of Production**

Manufacturers must provide a Flowchart of Production outlining each major step of the production process. The Flowchart of Production must make specific reference to each biological component used in manufacture at the point at which that biological component is used in manufacture.

### **4. Registration and volumes of sale of vaccine product in other countries**

For some assessments the registration of a vaccine product in another country may be used by AQIS to mitigate certain biosecurity risks. AQIS requests that applicants provide a table outlining the list of countries that have registered the vaccine product for distribution and use in their animal health industries. AQIS also requests that the table include figures on the volumes of sale for the vaccine product in each country.

## **E. Information Requirements**

### **1. Standards of Manufacture/Sourcing of Ingredients**

#### **1.1 Guidance on Policy Requirements**

- The manufacturing facility must comply with an appropriate code of Good Manufacturing Practice (cGMP) which is current. This is to ensure principles of quality assurance are built into every step of production e.g. final product quality, traceability of raw materials, appropriate records management practices;
- AQIS will assess the principles of quality assurance adopted by the manufacturing facility to ensure they are supportive of AQIS requirements i.e. the control of biosecurity risk;
- The manufacturing facility must be subject to regular audit and must be approved by the competent authority in the country of origin for the manufacture of veterinary vaccines;
- AQIS will not approve importation of vaccines manufactured in facilities which store and/or handle Annex 1 diseases (see Appendix 1) or other disease of biosecurity significance to Australia;
- Avian vaccines produced in facilities handling virulent avian influenza or Newcastle disease virus will not be approved;
- All sterilisation procedures must be validated and verified for the specific product, container type, configuration and volume and must be supported by cGMP standards and procedures;
- All materials of animal origin used in the production process must be sourced from countries with high standards of animal health and veterinary services;
- The source of all materials of animal origin used during production must be certified. This certification must be unequivocal and preferably be issued by the government of the source country. Manufacturer's certification may be accepted provided the manufacturer is operating under a quality assurance system accepted by AQIS as adequate to ensure compliance with Australian quarantine requirements. There must be an auditable trail from the country of origin of the source animals to the batch of finished vaccine destined for Australia;
- Annex 1 lists pathogens exotic to Australia which pose such a major economic and social threat to this country that sourcing of potentially contaminated products from affected countries will not be considered unless the product is effectively sterilised. In addition to country freedom, testing of certain products for pathogens listed in Annex 1 may be required especially where documentation concerning origin is unsatisfactory;
- Annex 2 (see Appendix 1) lists the prion diseases, scrapie and bovine spongiform encephalopathy (BSE). These agents are difficult to detect and generally extremely resistant to inactivation. Vaccines produced using products sourced from the relevant species in affected countries will not be approved;
- Annex 3 (see Appendix 1) lists other animal diseases which are either other exotic pathogens, potentially exotic strains of an endemic pathogen or are potential contaminants of economic and social concern to Australia. During assessment, AQIS may also identify other potential contaminants of concern.

#### **1.2 Evidentiary Requirements**

Manufacturers must provide:

**1.2.1** a copy of the current GMP certificate for their facility;

**1.2.2** a copy of all current certificates demonstrating approval of the facility to a quality management system e.g. ISO Standards;

**1.2.3** a copy of the registration/approval document issued to the facility by the government competent authority in the country of origin for the manufacture of veterinary vaccines;

**1.2.4** a complete list of microorganisms and/or viruses held at the facility;

**1.2.5** a case, a written declaration or procedural document demonstrating how the vaccine product is protected from contamination with microorganisms/viruses held at the manufacturing facility. Manufacturers must also provide a site floor plan in support of their case, declaration or procedural document;

**1.2.6** a complete list of products manufactured at the facility;

**1.2.7** a complete list of current Standard Operating Procedures in use within the manufacturing facility;

**1.2.8** evidence that all sterilisation procedures have been validated and verified for the specific vaccine product, container type, configuration and volume and must be supported by GMP standards and procedures. A copy of the Standard Operating Procedure outlining the sterilisation validation process is an example of the evidentiary requirement which may be submitted to AQIS to demonstrate compliance with the policy requirement.

**1.2.9** AQIS officers will conduct a documentation traceback audit of the vaccine manufacturing process to verify compliance of the manufacturer with AQIS quality system requirements. Manufacturers must be able to demonstrate a document control system which allows AQIS to review all relevant batch production records for a batch of vaccine that was recently manufactured and released from the manufacturing facility for distribution. The paper trail must include, but not be limited to, the following documents:

- the batch specific Certificate of Analysis for a batch of vaccine recently manufactured and released for distribution;
- copies of reports for tests undertaken on the final vaccine product (or bulk inactivated antigen prior to filling);
- copies of the manufacturing facility's raw material specifications for all biological products used in manufacture;
- copies of Certificates of Analysis for specific batches of animal derived product used to manufacture the vaccine batch;
- copies of in-process batch control records e.g. thermocouple data for autoclave sterilisers.

Manufacturers must provide copies of the complete document audit trail in the '1. Standards of Manufacture/Sourcing of Ingredients' section in the supporting dossier.

## 2. Masterseed viruses (MSVs)

### 2.1 Guidance on Policy Requirements

- All MSVs must be tested for:
  - bacterial and fungal contamination as per 9CFR 113.27(c) or Eu.Pharm (1997) 2.6.1; and
  - mycoplasmas as per 9CFR 113.28 or Eu.Pharm (1997) 2.6.7; and
  - extraneous viruses as per 9CFR 113.55 and 113.200; or as per European Pharmacopoeia - Vaccines for Veterinary Use (1997:0062); and
  - pathogens listed in Annex 1 and 3 (see Appendix 1) which are pathogenic to the species<sup>1</sup>
    - from which the virus was originally isolated
    - of all cell lines used for propagation and maintenance since original isolation of the virus
    - of all nutritive factors of animal origin previously used on these cell lines
    - for which the vaccine is intended; and
    - any other pathogen determined by AQIS during assessment of the application to be a potential contaminant.
- MSVs derived from bovines, ovines or caprines (or other species considered susceptible to TSE's) will be assessed according to the requirements of the TSE policy (see Introduction). Applicant should refer to the TSE policy for further information.

### 2.2 Evidentiary Requirements for MSVs

**2.2.1** Manufacturers must provide a full and well documented history of the master seed (in prose and tabulated form) which must include the species of origin, country of origin, date of isolation and passage history. The history must also identify all cell lines and nutritive media used for the transport, storage and propagation of the MSV.

#### Template for submission of tabulated MSV history

AQIS requires applicants to use the table below as a template for submission of the MSV history:

Seed designation	Passage	Biological raw materials		Comments
		Material	Lot numbers	
Original isolate	X – ?			
Pre-MSV	X - 1			
MSV	X			

<sup>1</sup> Note: AQIS may take into consideration countries of origin and potential for contamination before and after any processing or treatments.

A completed table must include specific details of all biological raw material e.g. nutritive factors, cell lines used in establishment of the MSV

**2.2.2** Manufacturers must also provide copies of test reports for all general and specific extraneous agent tests performed on the MSV. The reports must:

- be specific for the designated MSV that will be used to manufacture vaccine for the Australian market; and
- outline the protocol which was used to test for each extraneous pathogen.

### 3. Masterseed bacteria (MSB)

#### 3.1 Guidance on Policy Requirements

- All MSB must be tested for:
  - identity and purity such that the MSB is shown to contain only the species and strain of bacterium stated; and
  - pathogens listed in Annex 1 which occur in the country of origin of, and are pathogenic to the species:
    - from which the MSB was originally isolated; and
    - of all culture media ingredients of animal origin used since original isolation of the bacteria unless effectively sterilised; and
    - any other pathogen determined by AQIS on assessment of the application to be a potential contaminant.
- MSB derived from bovines, ovines or caprines (or other species considered susceptible to TSE's) will be assessed according to the requirements of the TSE policy (see Introduction). Applicant should refer to the TSE policy for further information.

#### 3.2 Evidentiary Requirements for MSB

**3.2.1** Manufacturers must provide a full and well documented history of the master seed (in prose and tabulated form) which must include the species of origin, country of origin, date of isolation and passage history. The history must also identify all culture media used for transport, storage and propagation of the bacteria.

##### Template for submission of tabulated form of MSB history

AQIS requires applicants to use the table below as a template for submission of the MSB history:

Seed designation	Passage	Biological raw materials		Comments
		Material	Lot numbers	
Original isolate	X – ?			
Pre-MSB	X - 1			
MSB	X			

A completed table must include specific details of all biological raw material e.g. fermentation broths, used in establishment of the MSB.

**3.2.2** Manufacturers must also provide copies of test reports for all general and specific extraneous pathogen tests, and non-pathogen related testing, performed on the MSB. The reports must:

- be specific for the designated MSB that will be used to manufacture vaccine for the Australian market; and
- outline the protocol for each test.

## 4. Master and Working Cell Seeds

### 4.1 Guidance on Policy Requirements

- Where it is necessary for primary cells to be used AQIS will only accept their use if they have been derived from specific pathogen free herds or flocks;
- The country of origin of the cell line must have been free of major exotic Annex 1 pathogens for the relevant species of origin at the time of creation of the cell line;
- If of ovine or caprine origin, country of origin must not be scrapie affected at the time of or within the 6 year period after the creation of the cell line;
- If of bovine origin, country of origin must not be BSE affected at the time of or within the 6 year period after the creation of the cell line;
- AQIS requires master and working cell seeds to be tested in accordance with the requirements of the Eu.Pharm (1997) Chapter 5.2.4 (*Cell cultures for the production of veterinary vaccines*);
- AQIS requires master and working cell seeds to undergo karyological and identity testing;
- All master cell seeds must be tested for:
  - bacterial and fungal contamination as per 9CFR 113.26 or Eu.Pharm (1997) 2.6.1; and
  - mycoplasmas as per 9CFR 113.28 or Eu.Pharm (1997) 2.6.7; and
  - extraneous pathogens as per 9CFR 113.51 for primary cell lines or as per 9CFR 113.52 for master and production (working) cell lines; and
  - extraneous pathogens as per European Pharmacopoeia - Vaccines for Veterinary Use (1997:0062 and 5.2.4); and
  - pathogens listed in Annex 1 and 3 (see Appendix 1) which are pathogenic to the species:
    - from which the cell line was originally isolated;
    - of all nutritive factors of animal origin previously used on the cell line since its creation;
    - for which the vaccine is intended.

Testing of the master and working cell seeds must be completed as described below:

	MCS	WCS	cells from WCS at highest passage level
general microscopy	+	+	+
bacteria/fungi	+	+	-
mycoplasma	+	+	-
viruses	+	+	-
identification of species	+	-	+
karyology	+	-	+

ie. Testing should be carried out on a culture of the MCS, WCS or on cells from the WCS at the highest passage level used for production and derived from a homogenous representative sample.

#### 4.2 Evidentiary Requirements for Master and Working Cell Seeds

4.2.1 Manufacturers must provide a full and well documented history of the master and working cell seed (in prose and tabulated form) which must include the species of origin, country of origin, date of creation and passage history. The history must also identify all nutritive factors used in creation of the seeds.

##### Template for tabulated form of master and working cell seed history

AQIS requires applicants to use the table below as a template for submission of the seed history:

Seed designation	Passage	Biological raw materials		Comments
		Material	Lot numbers	
Original cellular extract	X – ?			
Pre-master cell seed (MCS)	X - 1			
MCS	X			
Working cell seed	X + ?			

A completed table must include specific details of all biological raw material e.g. nutritive factors, used in creation of the seeds.

4.2.2 Manufacturers must also provide copies of test reports for all general and specific extraneous agent tests, and all non-pathogen related testing, performed on the MCS and WCS. The test reports for the MCS must be specific for the designated MCS that will be used to manufacture vaccine for the Australian market. The test reports for the WCS must be specific for the designated WCS currently being used in the manufacturing facility to manufacture vaccine. All test reports must outline the protocol for each test.

## **5. Working and Production seeds (viral or bacterial)**

### **5.1 Guidance on Policy Requirements**

- All working and production viruses and bacteria must be tested for potential pathogens as per relevant 9CFR or Eu.Pharm. requirement or as determined by AQIS on assessment of the application.

### **5.2 Evidentiary Requirements for Working and Production seeds (viral and bacterial)**

5.2.1 Manufacturers must provide a copy of the Standard Operating Procedure, or equivalent quality system document, outlining the testing undertaken on all working/production seeds used in vaccine manufacture. If not referenced in the Standard Operating Procedure the manufacturer must provide a declaration attesting to the specific standard against which the working/production seed has been tested e.g. 9CFR or Eu.Pharm.

## **F. Information Requirements for Production Process**

### **6. Nutritive factors e.g. serum, foetal serum, serum albumins, serum products**

#### **6.1 Guidance on Policy Requirements**

- The country and species of origin of all nutritive factors must be Government certified;
- AQIS will not approve a vaccine for import which is manufactured using nutritive factors sourced from a country affected by the relevant Annex 1 disease for the species of origin;
- Nutritive factors derived from bovines, ovines or caprines (or other species considered susceptible to TSE's) will be assessed according to the requirements of the TSE policy (see Introduction);
- Nutritive factors must be tested for:
  - bacterial and fungal contamination as per 9CFR 113.26 or Eu. Pharm. (1997) 2.6.1; and
  - mycoplasmas as per 9CFR 113.28 or Eu. Pharm. (1997) 2.6.7; and
  - other extraneous pathogens as per 9CFR 113.53 or Eu. Pharm. (1997:0062); and
  - pathogens listed in Annexes 1 and 3 which are pathogenic to the species of origin of the nutritive factor; and
  - bluetongue virus if of bovine or ovine origin (regardless of country of origin); and
  - any other pathogen determined by AQIS during assessment of the application to be a potential contaminant.

#### **6.2 Evidentiary Requirements**

**6.2.1** Manufacturers must provide a copy of the government certificate for all nutritive factors used in vaccine manufacture. Government certificates must be for a batch of nutritive factor recently used in manufacture and must attest to the country and species of origin;

**6.2.2** Manufacturers must also provide a copy of their raw material specification (RMS) or equivalent quality system document for all nutritive factors used in vaccine manufacture. The RMS document must outline all testing and/or treatment undertaken prior to use;

**6.2.3** Manufacturers must also provide a copy of the supplier's Certificate of Analysis or equivalent quality system document for all nutritive factors used in manufacture. The CofA must be specific to a batch recently used in manufacture and must outline any testing and/or treatment undertaken by the supplier.

Please note: Applicants may satisfy the requirements of **6.2.1 – 6.2.3** as part of the documentation traceback audit requirements of **1.2.9**.

## 7. Trypsin and other enzymes of animal origin

### 7.1 Guidance on Policy Requirements

- The country and species of origin of all animal derived enzyme products must be Government certified;
- AQIS will not approve a vaccine for import which is manufactured using animal derived enzyme products sourced from a country affected by the relevant Annex 1 disease for the species of origin;
- Animal derived enzymes derived from bovines, ovines or caprines (or other species considered susceptible to TSE's) will be assessed according to the requirements of the TSE policy (see Introduction);
- Animal derived enzymes must be tested for:
  - bacterial and fungal contamination as per 9CFR 113.26 or Eu.Pharm (1997) 2.6.1; and
  - mycoplasmas as per 9CFR 113.28 or Eu.Pharm (1997) 2.6.7; and
  - other extraneous pathogens as per 9CFR 113.53 or Eu. Pharm (1997) 5.2.5; and
  - if of porcine origin
    - porcine parvovirus;
    - porcine pestivirus (CSF);
    - porcine reproductive and respiratory syndrome (PRRS) virus;
    - transmissible gastroenteritis (TGE) virus; and
    - Aujeszky's disease (pseudorabies) virus.
  - if of bovine origin
    - bovine parvovirus;
    - bovine pestivirus (BVD);
    - vesicular stomatitis virus;
    - infectious rhinotracheitis virus

*Note: Testing for the porcine and bovine pathogens above is not necessary if the country of origin is free of the disease and the audit trail is conclusive for country of origin.*

- any other pathogen determined by AQIS during assessment of the application to be a potential contaminant.

### 7.2 Evidentiary Requirements

**7.2.1** Manufacturers must provide a copy of the government certificate for all enzymes of animal origin used in vaccine manufacture. Government certificates must be for a batch of enzymes recently used in manufacture and must attest to the country and species of origin;

**7.2.2** Manufacturers must also provide a copy of their raw material specification (RMS) or equivalent quality system document for all enzymes of animal origin used in vaccine manufacture. The RMS document must outline all testing and/or treatment undertaken on each batch prior to use;

**7.2.3** Manufacturers must also provide a copy of the supplier's Certificate of Analysis (CofA) or equivalent quality system document for all enzymes of animal origin used in manufacture. The CofA must be specific to a batch recently used in manufacture and must outline any testing and/or treatment undertaken by the supplier.

Please note: Applicants may satisfy the requirements of **7.2.1 – 7.2.3** as part of the documentation traceback audit requirements of **1.2.9**.

## 8. Fermentation broths and culture media

### 8.1 Guidance on Policy Requirements

- All ingredients used in the fermentation broth/production culture media must be provided to AQIS. The country and species of origin of each ingredient of animal origin must be specified along with details of any processing, treatments or testing of either the ingredients or final culture media/fermentation broth;
- Unless effectively sterilised (refer to 2.3.3 in policy) prior to use, meat extracts must not be sourced from countries affected by diseases listed in Annex 1 for the relevant species of origin. Additional testing will also be required by AQIS for the relevant Annex 1 pathogen(s) if sourced from such countries;
- Animal ingredients derived from bovines, ovines or caprines (or other species considered susceptible to TSE's) will be assessed according the requirements of the TSE policy (see Introduction);
- Unless effectively sterilised prior to use, either the individual ingredient of animal origin or the final fermentation broth/culture media must be tested for:
  - bacterial and fungal contamination as per 9CFR 113.26 or Eu.Pharm (1997) 2.6.1; and
  - mycoplasmas as per 9CFR 113.28 or Eu.Pharm (1997) 2.6.7; and
  - extraneous pathogens as per 9CFR 113.53 or Eu.Pharm (1997) 5.2.5; and
  - pathogens listed in Annex 1 and Annex 3 which are pathogenic to the species of origin of any fermentation/culture ingredients of animal origin; and
  - any other pathogens determined by AQIS to be a potential contaminant.

### 8.2 Evidentiary Requirements

**8.2.1** Manufacturers must provide a copy of their raw material specification (RMS) or equivalent quality system document for all fermentation broths/culture media used in vaccine manufacture. The RMS document must outline all testing and/or treatment undertaken on each batch prior to use;

**8.2.2** Manufacturers must also provide a copy of the supplier's Certificate of Analysis (CofA) or equivalent quality system document for all fermentation broths/culture media used in manufacture. The CofA must be specific to a batch recently used in manufacture and must outline:

- the country and species of origin of each ingredient of animal origin used in manufacture of the product; and
- any processing/treatments undertaken on the ingredients of animal origin or final culture medium/fermentation broth product; and
- all tests undertaken on the individual ingredients of animal origin or final culture medium/fermentation broth product.

Please note: Applicants may satisfy the requirements of **8.2.1 – 8.2.2** as part of the documentation traceback audit requirements of **1.2.9**.

## 9. Components of avian origin and embryonated eggs

### 9.1 Guidance on Policy Requirements

- Embryonated eggs and avian cell lines used for the growth and production of the inactivated vaccine should be derived from SPF flocks. The use of eggs from healthy non-SPF flocks free from the presence of certain agents and their antibodies will require additional assurances of safety and approval by AQIS. SPF flocks must be under veterinary supervision and approved by the relevant government authority in the country of origin;
- The principles, procedures and testing regime for SPF flocks must be as described in Eu.Pharm (1997) Chapter 5.2.2 (Chicken flocks free from specified pathogens for the production and quality control of vaccines). Flocks must also be tested for other avian pathogens listed in Annex 3 of the policy;
- Avian cell lines and non-SPF derived embryonated eggs must be sampled and tested for extraneous pathogens listed in Eu.Pharm (1997) Chapter 5.2.2 and in Annex 3;
- Other components/ingredients of avian origin must be derived from either:
  - a country free from clinical avian influenza and virulent Newcastle disease in their commercial poultry flocks provided the product is derived from such flocks; or
  - specific pathogen free (SPF) flocks; or
  - commercial poultry flock which vaccinates against avian influenza and Newcastle disease and there has been no outbreaks in the flock or within a 25 km radius for the preceding 3 months.
- Other components of avian origin must be tested for extraneous avian pathogens as listed in Eu.Pharm (1997) Chapter 5.2.2 and Annex 3 unless effectively sterilised (refer to 2.3.3 in policy);
- Avian cell lines and components of avian origin (unless effectively sterilised) must also be tested for bacteria, fungi, mycoplasma, salmonella and adventitious viruses as per 9CFR 113.26, 113.30, 113.31, 113.34;
- Components of avian origin and eggs must be tested for any other pathogens determined by AQIS during assessment of the application to be a potential contaminant.

### 9.2 Evidentiary Requirements

**9.2.1** When SPF eggs or avian cell lines derived from SPF eggs are used in manufacture, manufacturers must provide:

- a copy of the government health certificate demonstrating approval of the SPF flock by the competent authority in the country of origin;
- a copy of the government health certificate or equivalent government endorsed quality system document demonstrating current test results of the SPF flock testing program (Eu. Pharm. Chapter 5.2.2 and Annex 3);

**9.2.2** When non-SPF avian cell lines, embryonated eggs or other components of avian origin are used in manufacture, manufacturers must provide:

- a copy of their raw material specification (RMS) or equivalent quality system document for the components of avian origin used in vaccine manufacture. The RMS document must outline the country and species of origin and all testing/treatments undertaken; and
- a copy of the supplier's Certificate of Analysis (CofA) or equivalent quality system document for all components of avian origin used in manufacture. The CofA must be specific to a batch recently used in manufacture and must outline the country and species of origin and all testing/treatments undertaken by the supplier.

Please note: Applicants may satisfy the requirements of 9.2.1 – 9.2.2 as part of the documentation traceback audit requirements of 1.2.9.

## 10. Other material of animal origin

### 10.1 Guidance on Policy Requirements

- The country and species of origin, processing and any pathogen testing must be detailed with the application. Appropriate government health certification and other documentation providing an audit trail should be provided;
- Material of animal origin must not be sourced from countries affected by diseases listed in Annex 1 for the relevant species of origin unless effectively sterilised;
- Animal ingredients derived from bovines, ovines or caprines (or other species considered susceptible to TSE's) will be assessed according the requirements of the TSE policy (see Introduction);
- All other material of animal origin must be either effectively sterilised or be tested for:
  - bacterial and fungal contamination as per 9CFR 113.26 or Eu.Pharm (1997) 2.6.1; and
  - mycoplasmas as per 9CFR 113.28 or Eu.Pharm (1997) 2.6.7; and
  - extraneous pathogens as per 9CFR 113.53 or Eu.Pharm (1997) 5.2.5; and
  - pathogens listed in Annex 1 and Annex 3 which are pathogenic to the species of origin of the material of animal origin; and
  - any other pathogen determined by AQIS during assessment of the application to be a potential contaminant.

### 10.2 Evidentiary Requirements

#### 10.2.1 Manufacturers must provide either:

- a copy of the Government Certificate for all animal origin material used in vaccine manufacture. The Certificate must be for a batch recently used in manufacture and must attest to the country and species of origin of each material of animal origin; or
- a copy of the Certificate of Analysis (CofA), or equivalent quality system document, for all animal origin material used in vaccine manufacture. The document must be specific to a batch recently used in manufacture and must attest to the country and species of origin of each material of animal origin;

Applicants should take direction on the requirement for government certification or CofA from other areas of the SOI. For example, if manufacturers use a product of animal origin that contains or has been made using nutritive factors, government certification attesting to the country and species of origin of the nutritive factor will be required.

Alternatively if manufacturers use a product of animal origin that has been manufactured using a fermentation process AQIS will accept CofAs (or equivalent) attesting to the country and species of origin of animal origin ingredients. CofAs will need to be supported by an AQIS approved quality management system e.g. cGMP, in the manufacturing facility.

**10.2.2** Manufacturers must also provide a copy of their raw material specification (RMS) or equivalent quality system document for all animal origin ingredients used in vaccine manufacture. The RMS document must outline all testing and/or treatment undertaken on each batch;

**10.2.3** Manufacturers must also provide a copy of the supplier's Certificate of Analysis (CofA) or equivalent quality system document for all animal origin ingredients used in manufacture. The CofA must be specific to a batch recently used in manufacture and must outline any testing/treatments undertaken.

Please note: Applicants may satisfy the requirements of 10.2.1 – 10.2.3 as part of the documentation traceback audit requirements of 1.2.9.

## 11. Inactivation

### 11.1 Guidance on Policy Requirements

- The inactivating agent and inactivation procedure must be shown to inactivate the vaccine organism under conditions of vaccine manufacture;
- Complete inactivation must be achieved within 2/3 of the total inactivation time;
- Prior to inactivation, the bulk vaccine should be an homogenous suspension free from particles which may not be penetrated by the inactivating agent;
- A suitable test for the complete inactivation of vaccine organisms shall be carried out on the finished vaccine. The protocol for this test should normally be the same as the test carried out on the harvest material. If the presence of adjuvant or other substances render this impractical, then the test should be performed prior to the addition of the adjuvant. Bulk antigen so sampled shall not be stored except in the vessel from which the sample was taken.

### Additional Guidance on Policy Requirements for Viral Vaccines

- A test for complete inactivation shall be performed on the viral harvest immediately after the inactivation procedure and, if applicable, the neutralisation or removal of the inactivating agent. The test selected should be appropriate to the vaccine virus being used and should consist of at least 2 passages in cells, embryonated eggs or, where necessary in animals. The number of cell samples, eggs or animals should be sufficient to ensure appropriate sensitivity of the test. For cell cultures, at least 150 cm<sup>2</sup> of the cell culture monolayer should be inoculated with 1.0 ml of harvest. No evidence of the presence of any live virus or micro-organism should be observed.

### Additional Policy Requirements for Bacterial Vaccines

- A test for complete inactivation shall be performed on the bacterial harvest immediately after the inactivation procedure and, if applicable, the neutralisation or removal of the inactivating agent. The selected test should be appropriate to the vaccine bacteria being used and should consist of at least two passages in production media or in media prescribed in the relevant European Pharmacopoeia monograph. No evidence of any live micro-organism should be observed.

### 11.2 Evidentiary Requirements for Inactivation of Bacterial and Viral Vaccines

**11.2.1** Manufacturers must provide a copy of the inactivation kinetics study specific for the organism and the inactivant used in vaccine manufacture i.e. the inactivation kinetics study must be reflective of the conditions of vaccine manufacture. The study must also demonstrate complete inactivation of the bulk antigen within 2/3 of the total inactivation time;

**11.2.2** Manufacturers must also provide a declaration confirming that prior to inactivation the bulk antigen was an homogenous suspension free from particles. The declaration must also outline the process followed by the manufacturer when bulk antigen is found to have not been completely inactivated. The declaration must be on manufacturer's letterhead and must be signed and dated by a suitable member of the manufacturer's Quality Assurance/Control team;

**11.2.3** Manufacturers must also provide a copy of the Standard Operating Procedure, or equivalent quality system document, outlining the testing for complete inactivation performed on bulk antigen and/or finished product.

## 12. Final Product – Viral Vaccines

### 12.1 Guidance on Policy Requirements

- Every batch of the inactivated final bulk (or final container) viral vaccine must be sampled and tested in general in accordance with either 9CFR 113.200 or Eu. Pharm. 1997:0062;
- Every batch of the inactivated final bulk (or final container) viral vaccine must be sampled and tested for bacterial and fungal sterility as per 9CFR 113.26 or Eu. Pharm (1997) 2.6.1;
- Every batch of the inactivated final bulk (or final container) viral vaccine must be sampled and tested for freedom from mycoplasma as per 113.28 or as per Eu. Pharm (1997) 2.6.7;
- Every batch of the final bulk (or final container) viral vaccine must be sampled and tested for freedom from other extraneous pathogens by the following:
  - as per the Eu. Pharm. (1997) monograph for the specific inactivated viral vaccine; or
  - by any other method determined appropriate by AQIS;
- In addition, every batch of the final bulk (or final container) avian viral vaccine must be sampled and tested for freedom from the following:
  - avian leucosis viruses as per either Eu. Pharm (1997) 2.6.4 or 9CFR 113.31
  - extraneous viruses using fertilised eggs as per Eu. Pharm.(1997) 2.6.3 or 9CFR 113.34
  - salmonella as per either 9CFR 113.30 or other method determined appropriate by AQIS.
- Additional testing may be necessary as determined by AQIS on assessment of the application.

### 12.2 Evidentiary Requirements for Viral Vaccines

**12.2.1** Manufacturers must provide a copy of the Certificate of Analysis, or equivalent quality system document, for batches of final viral vaccine product. The document must demonstrate compliance with the testing requirements outlined above;

**12.2.2** Manufacturers must also provide a copy of a test report for a batch of vaccine that was recently manufactured and released by the manufacturer's Quality Control department.

## **13. Final Product – Bacterial Vaccines**

### **13.1 Guidance on Policy Requirements**

- Every batch of the inactivated final bulk (or final container) bacterial vaccine must be sampled and tested in general in accordance with either 9CFR 113.100 or Eu. Pharm. 1997:0062;
- Every batch of the inactivated final bulk (or final container) bacterial vaccine must be sampled and tested for bacterial and fungal sterility as per 9CFR 113.26 or Eu. Pharm (1997) 2.6.1;
- Every batch of the final bulk (or final container) viral vaccine must be sampled and tested for freedom from other extraneous pathogens by the following:
  - as per the Eu. Pharm. (1997) monograph for the specific inactivated viral vaccine; or
  - by any other method determined appropriate by AQIS
- Additional testing may be necessary as determined by AQIS on assessment of the application.

### **13.2 Evidentiary Requirements for Bacterial Vaccines**

**13.2.1** Manufacturers must provide a copy of the Certificate of Analysis, or equivalent quality system document, for batches of final product. The document must demonstrate compliance with the testing requirements outlined above;

**13.2.2** Manufacturers must also provide a copy of a test report for a batch of vaccine that was recently manufactured and released by the manufacturer's Quality Control department.

## **G. Applicant Declaration**

I declare that the information provided in this document and in supporting dossiers is accurate and that AQIS will be advised of any changes to the production process which affect the content of these documents.

I authorise the exchange of information, in relation to the vaccine product outlined in this Summary of Information document, between AQIS and the Australian Pesticides and Veterinary Medicines Authority (APVMA). I understand that this information will be used by AQIS and the APVMA for the purpose of ensuring compliance of the vaccine product with the regulatory requirements of each agency.

<b>Signature:</b>	
<b>Name:</b>	
<b>Date:</b>	
<b>Position:</b>	
<b>Company name and address:</b>	

## **Appendix 1 – Annex 1, 2 and 3 diseases**

### **ANNEX 1 -Exotic animal diseases of major economic and social concern**

<b>SPECIES</b>	<b>PATHOGEN/DISEASE</b>
<b>Bovine</b>	Foot and mouth disease virus Rinderpest virus
<b>Equine</b>	African horse sickness virus
<b>Ovine/Caprine</b>	Foot and mouth disease virus Rinderpest virus Peste des petits ruminants virus Ovine/caprine pox virus Pulmonary adenomatosis
<b>Porcine</b>	Foot and mouth disease virus Swine vesicular disease virus African swine fever virus Classical swine fever virus
<b>Avian</b>	Clinical avian influenza virus Virulent Newcastle disease virus <i>Note: Use of eggs from SPF flocks in affected country may be allowed subject to additional testing for ND and AI</i>
<b>Other species</b>	As determined by AQIS on application

### **ANNEX 2 - Exotic animal prions of major economic and social concern**

**(Relatively low infectivity but extremely high resistance to normal inactivation processes)**

<b>SPECIES</b>	<b>PATHOGEN/DISEASE</b>
<b>Bovine</b>	Bovine spongiform encephalopathy
<b>Ovine</b>	Scrapie

### ANNEX 3 - Other animal pathogens/diseases of economic and social concern

These pathogens/diseases are either exotic to Australia, potential for exotic strains of endemic pathogens or potential contaminants of concern.

SPECIES	PATHOGEN/DISEASE
<b>Bovine</b>	Adenovirus Akabane virus Bluetongue/EHD virus Bovine ephemeral fever virus Bovine herpesvirus 1, 2, 4 Bovine immunodeficiency virus Bovine parvovirus Bovine respiratory syncytial virus Bovine pestiviruses (Bovine Viral Diarrhoea) <i>Brucella abortus</i> Contagious bovine pleuro-pneumonia <i>Coxiella burnetti</i> (Q-fever) Enzootic bovine leucosis virus Infectious Bovine Rhinotracheitis virus Lumpy skin disease virus Parainfluenza virus 3 Rabies virus Rift Valley fever virus Rotavirus Vesicular stomatitis virus
<b>Equine</b>	Contagious equine metritis Epizootic lymphangitis Equine adenovirus Equine arteritis virus Equine encephalomyelitis viruses Equine herpes virus types 1,2,3, 4 Equine infectious anaemia virus Equine influenza virus Equine piroplasmosis Equine rhinopneumonitis virus Equine viral abortion Glanders Horse pox virus Pestivirus Potomac fever Rabies virus Surra Vesicular stomatitis virus

<b>Ovine/Caprine</b>	Adenovirus Akabane virus Bluetongue/EHD virus <i>Brucella melitensis</i> Caprine arthritis encephalitis Capripox virus Contagious agalactia Contagious caprine pleuro-pneumonia ( <i>Mycoplasma mycoides var capri</i> ) Contagious pustular dermatitis (Orf) Louping ill virus Maedi-visna virus Pestivirus Rabies virus Rift Valley fever virus Vesicular stomatitis virus
<b>Porcine</b>	Adenovirus Aujeszky's disease virus <i>Brucella suis</i> Haemagglutinating encephalomyelitis virus <i>Mycoplasma hyopneumoniae</i> Pestivirus (including Classical Swine Fever) Polioencephalomyelitis virus Porcine enteroviruses Porcine epidemic diarrhoea virus Porcine parvovirus Porcine respiratory corona virus Porcine respiratory and reproductive syndrome virus Rabies virus Rotavirus Swine influenza virus Swine pox virus Transmissible gastroenteritis virus Vesicular stomatitis virus
<b>Rabbit</b>	Rabbit haemorrhagic disease virus Rabies virus Shope fibroma virus Tularaemia Treponema
<b>Rodent</b>	Adenovirus Ectromelia virus ( <i>mice only</i> ) Encephalomyocarditis virus Korean haemorrhagic fever Lymphocytic choriomeningitis (Arena virus) Rabies virus Sendai virus

<b>Avian</b>	Avian adenovirus Avian encephalomyelitis virus Avian leucosis virus Avian nephritis virus Chicken anaemia agent Duck viral hepatitis Duck viral enteritis EDS 76 virus Fowl pox virus Infectious bronchitis virus Infectious bursal disease virus Infectious laryngotracheitis virus <i>M. gallisepticum</i> <i>M. synoviae</i> Marek's disease virus Reovirus Reticuloendotheliosis virus <i>S. enteritidis</i> <i>S. gallinarum</i> <i>S. pullorum</i> Turkey rhinotracheitis virus
<b>Canine/feline</b>	Aujeszky's disease virus Bluetongue virus <i>Brucella canis</i> Canine adenovirus 1, 2 Canine distemper virus Canine parvovirus <i>Ehrlichia canis</i> Feline calicivirus Feline immunodeficiency virus Feline infectious peritonitis virus Feline leukemia virus Feline panleukopaenia virus Feline rhinotracheitis virus <i>Leptospira interrogans var. canicola</i> Pestivirus Rabies virus
<b>Other species</b>	As determined by AQIS on application

## **Appendix 2 – Definitions**

**‘Effective sterilisation’** - means treating in such a way as to completely inactivate all conventional adventitious agents including viruses. Examples of effective sterilisation are autoclaving at 121°C for 15 minutes, 50kGray gamma irradiation or any other treatment which has been demonstrated to achieve a 6 log reduction in titre for all potential contaminants.

Additional points for consideration:

- Prions proteins are also a potential contaminant of concern for AQIS. Prion proteins are highly resistant to treatment and AQIS relies upon country freedom for the relevant species of origin;
- A level of titre reduction higher than 6 log will be required where there is reasonable likelihood of contamination e.g. if the average level of contamination in a product is 2 logs, treatment must achieve at least an 8 log (i.e. 6+2) reduction in titre.
- All sterilisation procedures should be validated, verified for the product, container type, configuration and volume and be supported by GMP standards and procedures. For example, in the case of autoclaving of culture media and other substrates, the autoclaving conditions should be validated for each media, for each container type and for each autoclave load configuration;
- **‘Government certificate’** – a document issued by the government agency/competent authority responsible for certification of agricultural products in the country of origin. International requirements for government certification are outlined on the website of the World Organisation for Animal Health ([www.oie.int](http://www.oie.int)). Further to the overarching international requirements for government to government certification AQIS requires the certificate to meet the following:
  - the certificate must have been issued and dated within the last 6 months; and
  - the certificate must be sealed with the stamp/seal of the issuing national competent authority.
- **‘Manufacturer’s declaration’** – a document issued by the manufacturer containing a written declaration as per the requirement outlined in the SOI. Manufacturer’s declarations must be on manufacturer’s letterhead and must be signed by a suitable member of the manufacturer’s quality assurance/control team and dated within the last 6 months.

## **Appendix 3 – Further information on testing to detect extraneous agents in masterseeds/raw materials**

A critical aspect of the AQIS assessment for Import Permit applications for vaccine products is the review of extraneous agent testing in masterseeds (masterseed viruses, masterseed bacteria, master cell seeds) and raw materials used in manufacture. It is a policy requirement that masterseeds/raw materials undergo testing to demonstrate, to an appropriate level of confidence, that they are free from extraneous agents.

In July 2011 Animal Biosecurity published the document 'Review of Published Tests to Detect Pathogens in Veterinary Vaccines Intended for Importation into Australia'. This Review document provides clarification on the tests that are considered acceptable for extraneous pathogen testing of masterseeds and raw materials for use in vaccine manufacture.

AQIS acknowledges however that there may be other validated unpublished test methods that are equally reliable and sensitive, including some test methods that remain commercial-in-confidence and are unpublished. These will be assessed by AQIS on case-by-case basis with input from Animal Biosecurity and may lead to an update of the Review document.

Applicants may view the document here.

### **How does AQIS use this document during the assessment of my Import Permit application?**

AQIS uses this document as the principle reference for determining whether testing (general or specific) is suitable for the purposes of detecting extraneous agents in masterseeds or raw materials used in manufacture of vaccines for the Australian market.

**Prior to submission of the vaccine Import Permit application** applicants must ensure that the test reports for masterseeds/raw materials submitted to AQIS in support of the application clearly outline the test method used for each test. In addition applicants should review the list of test methods currently accepted by AQIS to determine whether additional testing of masterseeds/raw materials will be required.

AQIS will accept a test demonstrating freedom of the masterseed/raw material which has been conducted in accordance with the requirements of the Review document. Where the document indicates that the test method is unsuitable for detection of extraneous agents AQIS will require additional testing to be undertaken in accordance with the requirements of the Review document. Applications which are submitted for vaccine manufactured using masterseeds/raw materials which have been tested using methods deemed unsuitable will be rejected by AQIS.

Where the masterseed/raw material has been tested using a method not referenced on the Review document AQIS will consult with Animal Biosecurity on the suitability of the method for detection of extraneous agents.

## **Appendix 4**

# **GUIDELINE FOR AQIS ASSESSMENT OF IMPORT PERMIT APPLICATIONS FOR VETERINARY VACCINES**

### **Introduction**

This Guideline sets out the principles followed by AQIS Biological Imports Program (BIP) in assessing applications to import new veterinary vaccines. It was built on the efficiencies gained from previous Veterinary Vaccine Subcommittee meetings and workshops to improve stakeholder knowledge of the application process.

### **Objectives**

The objective of this Guideline is to:

- improve the overall efficiency of the BIP veterinary vaccine assessment process;
- manage most effectively the significant work load with the available resources; and
- ensure fairness to all applicants in the order and manner in which assessments are processed through to completion.

### **Operational Practice**

The Guideline includes the following operational practices:

1. BIP will accept one request for a pre-submission meeting for any new vaccine (or vaccine related product) to discuss format requirements for the application. The aim of the meeting is to ensure applicants are confident to submit an application which is complete and meets all of AQIS's requirements. At the end of the meeting if it is determined that an applicant will not be able to submit an application which meets all of AQIS's requirements the application will not progress further.

The applicant will need to prepare an agenda for the meeting clearly outlining the points for discussion and the need for response.

BIP will accept applications for new vaccines (or vaccine related products) without a pre-submission meeting.

2. Only complete applications will be considered for review by BIP, subject to any prior arrangement with the BIP officer.

[An applicant's proposal to supply specific data, such as a current Good Manufacture Practice (GMP) certificate, by a specific time during the evaluation/assessment process will be considered on a case-by-case basis. BIP will not, however, extend this allowance to incomplete results of specific extraneous agent testing.]

Upon receipt of an Import Permit application for a veterinary vaccine, BIP will log the application and then screen it against the requirements outlined in the relevant Summary of Information document. Failure of compliance with any of the application requirements in the Summary of Information document, in the absence of any prior arrangement with the BIP officer, will result in rejection of the application. The application will hold no position in the queue until it is resubmitted in full. If the application is rejected, the initial application and assessment fee will not be refunded.

3. Applications will continue to be reviewed on the basis of 'first come, first served' as they take their place in the queue.

4. Vaccines for which there is a critical national need e.g. in the event of an emergency animal disease, as advised by Australia's Chief Veterinary Officer, will take priority over other vaccine assessments.
5. Data and applications will be reviewed on the basis of SORO (submit once, review once).
6. During the formal assessment process when an application is discovered to be deficient and the BIP officer believes the deficiency can be corrected with the presentation of additional documentation the applicant will be contacted by the BIP officer who will outline the deficiencies in a written letter. Following this notification the application will be placed at the end of the list of current applications under consideration by the BIP vaccine assessing officer.
7. The BIP officer will aim to identify all application deficiencies in the initial written outline of deficiencies. However where a deficiency is clearly identified which prohibits the product from importation into Australia e.g. unacceptably high levels of TSE risk, the BIP vaccine assessing officer will not complete a full review of the application and will therefore not identify all application deficiencies in writing to the applicant. Where the BIP officer believes that the deficiencies cannot be corrected with the presentation of additional documentation the application will be rejected.
8. A partial response to a deficiency letter means that the applicant has provided data or relevant scientific argument to address some but not all the deficiencies identified by the BIP vaccine assessing officer. A partial response will not reactivate the assessment of the application. Review of the information provided in response to a deficiency letter will only commence once a response has been received against all of the identified deficiencies.
9. If a COMPLETE response to a deficiency letter has not been received within 180 days from the date of issuing the letter, the application will be rejected and a resubmission will be required, unless an extension has been granted by the BIP officer at least 4 weeks before the end of the 180 day period. Extensions will be normally considered by the BIP officer on a case-by-case basis and for a period of no more than 4 weeks.
10. Applicants will be given the opportunity to provide a scientific argument in the form of a case for equivalence once e.g. BIP vaccine assessing officers will only consider a case for equivalence once for any extraneous agent in any one master seed or raw ingredient. Following assessment and determination of the suitability or otherwise of the case for equivalence no further information/data or published articles will be accepted for further review and the decision will be final and not open for reassessment.
11. BIP will consider requests from applicants to reprioritise the order of assessment of their applications. The reprioritised application can only take the place of another of their applications for which assessment has not yet commenced.