ATTACHMENT B

February 2004

QUARANTINE POLICY FOR THE IMPORTATION AND/OR USE OF FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN

SOURCE

This policy and associated import conditions have been adapted from the following June 1998 policies and conditions:

- "AQIS Contingency policy on the importation of fertile specific pathogen free eggs (domestic hen) for vaccine production",
- "Conditions for the importation of fertile specific pathogen free eggs (domestic hen) for vaccine production",
- "AQIS policy on the importation of fertile specific pathogen free eggs (domestic hen) for *in vitro* and *in vivo* laboratory work (within AAHL)", and
- "Conditions for the importation of fertile specific pathogen free eggs (domestic hen) for *in vitro* and *in vivo* laboratory work (within AAHL)".

DEFINITION

For the purpose of this policy, a specific pathogen free flock is one which meets the minimum requirements of Section 5.2.2 "Chicken flocks free from specified pathogens for the production and quality control of vaccines" of the European Pharmacopoeia. Depending on the intended end use of SPF eggs derived from the flock, additional requirements as detailed in this policy may be applied to the source SPF flock, the SPF eggs or products derived from the SPF eggs.

RATIONALE

Availability of SPF eggs is critical to:

- the production of some mammalian and human vaccines,
- the production of most inactivated avian vaccines,
- the production of live avian vaccines,
- disease diagnosis,
- biomedical research, and
- quarantine surveillance programs.

Currently only one facility in Australia produces a significant number of SPF eggs. If this SPF facility becomes infected or demand increases beyond production capability, the only option to ensure continued access to address these essential needs may be to import SPF eggs.

Under the European Pharmacopoeia requirements, once a source SPF flock is defined, no non-SPF birds can be added to it. Source SPF flocks are isolated flocks with appropriate biosecurity controls. All birds are tested at least once for the range of pathogens listed in the European Pharmacopoeia either at point of lay (introduced SPF birds) or by 20 weeks of age (new generation birds within established flock). After the

initial test, monthly tests are carried out on a 5% sample of the flock (but not less than 10 and need not be more than 200 birds) and a final test of birds is undertaken 4 weeks after the last collection of SPF eggs from the flock. Testing 1.25% of the flock on a weekly basis is considered equivalent to 5% monthly testing.

In vitro laboratory use

SPF eggs are needed for disease diagnosis requiring virus isolation, quarantine surveillance, quality control of many vaccines, and research and development in the biomedical and biotechnology fields. This work is conducted in laboratories and usually does not involve exposure to animals. As a general principle, all biological waste generated in laboratories is autoclaved, incinerated or otherwise disposed of safely.

While there are inherent quarantine risks associated with importation and use of the imported SPF eggs, these risks are significantly reduced if the SPF eggs and their derivatives are not exposed to susceptible species without additional risk assessment, do not leave the laboratory without AQIS approval and are properly disposed of. Restricting imported SPF eggs to laboratories which are Quarantine Approved Premises (QAP) for the purposes of handling imported SPF eggs ensures compliance with these control measures.

Restricting imports to SPF eggs from source SPF flocks that meet the requirements of Section 5.2.2 of the European Pharmacopeia should provide the necessary level of quarantine confidence to permit importation for *in vitro* use, subject to appropriate management controls on end use and disposal.

Vaccine production and other in vivo uses

There are inherent risks associated with vaccines, especially live vaccines, and substrates, including embryonated SPF eggs, used in vaccine production. A contaminated vaccine could rapidly spread an infectious agent nationally, making eradication very difficult. For these reasons, SPF eggs of non-Australian origin should only be used as a last resort, with preference given to use in the production of the lower risk vaccines. For example, if imported SPF eggs are to be used at all, they should be used in inactivated vaccines in preference to live vaccines and mammalian vaccines in preference to avian vaccines. SPF eggs of non-Australian origin should not be used in the production of live avian vaccines unless all other options are exhausted[1].

Inactivated vaccines are considered to be a significantly lower quarantine risk than live vaccines. However, there is still a potential for them to be contaminated as the use of the inactivant (eg formalin, etc) is based on its effectiveness against the vaccine organism and not against potential extraneous agents. Even if the extraneous agent is non-viable, a contaminated vaccine could also create false serological evidence of the presence of the disease in Australia jeopardising surveillance programs and our internationally recognised avian health status.

source SPF flocks and SPF eggs used to produce vaccines for use within Australia are expected to meet the requirements specified in the current European Pharmacopoeia

[1] Refer to the quarantine review of the import policy for the reasons why live avian vaccines are considered higher risk than other products.

(EP)[2]. AQIS requires, under the *Quarantine Act 1908*, that veterinary vaccines be demonstrated to be free of pathogens of quarantine concern to Australia. The Australian Pesticides and Veterinary Medicines Authority (APVMA) requires that veterinary vaccines be demonstrated free of all extraneous infectious agents. To avoid duplication, AQIS assessment of imported veterinary vaccines covers both quarantine and APVMA requirements in relation to freedom from all extraneous infectious agents. Additional testing will be required for exotic pathogens considered to be viable potential contaminants.

There have recently been problems overseas with chicken anaemia virus (CAV), avian adenovirus, avian leucosis virus and avian reovirus in source SPF flocks. There have also been reports of vaccines contaminated with avian reovirus and avian leucosis viruses as a result. These reports highlighted the potential risk associated with SPF eggs and the short comings of current surveillance and testing of both source SPF flocks and vaccines. Avian leucosis and CAV are endemic to Australia. However, there are exotic strains of avian reovirus and adenovirus of quarantine concern. Therefore, for all exotic pathogens which are also potential contaminants of live avian vaccines, it is considered necessary to increase the sampling rate and testing of source SPF flock applied close to the date of egg collection[3] or to use detection tests that are much more sensitive than those currently specified on final live avian vaccine by the European Pharmacopoeia.

Under Australia's commitment to the WTO Sanitary and Phytosanitary Agreement, restrictions exceeding those applied to domestic product cannot be imposed on imported product. Responsibility for assessment and registration of domestic vaccines rests with APVM. Therefore, Biosecurity Australia and AQIS cannot apply controls on CAV and avian leucosis above that applied by APVMA to domestic vaccines.

POLICY

1. The country of origin must be approved by the Director of Quarantine for the export and/or use of the SPF eggs. Approval will be based on a consideration of the quality of the country's veterinary services including diagnostic capability and the fundamental principles of an ethical, organisational and technical nature as described in the OIE Animal Health Code Chapters 1.3.3 and 1.3.4.

2. The source SPF flock must be approved by the relevant veterinary authority in the country of origin as an source SPF flock within the definition and requirements of the European Pharmacopoeia.

[2] The previous contingency policy also specified compliance with TGA Therapeutic Goods Order No 21. The APVMA has advised that TGO21 is no longer a legislative requirement and that compliance with EP is considered equivalent to meet APVMA requirements.

[3] There may be several weeks between egg collection and release of the final vaccine and testing of the flock undertaken during this time does provide considerable confidence. The preferred option is for this additional testing to be undertaken as close to the date of egg collection as possible (eg within 21 days prior to egg collection). AQIS may permit, on a case by case basis, the additional testing to be undertaken over an agreed period of not more than 8 weeks post egg collection and prior to release of the vaccine. Such permission would be on the understanding by the manufacturer that any positive test will result in the vaccine being rejected as it may be virtually impossible to determine whether the incursion was before or after egg collection.

3. The source SPF flocks from which the SPF eggs are derived must meet the minimum requirements specified by the most current European Pharmacopoeia[4].

4. Laboratories conducting the tests on the source SPF flock and, if applicable, the veterinary vaccines, must be accredited by the relevant government authority. Accreditation or approval should be based on an appropriate proficiency testing program. All tests undertaken for the purposes of this policy should be appropriately validated on a regular basis.

5. It is the importer's and end user's responsibility to ensure the source SPF flock, SPF eggs and the subsequent vaccines and other products meet the requirements of all other regulatory bodies including the Australian Pesticides and Veterinary Medicines Authority (APVMA) and Therapeutic Goods Administration (TGA).

6. All imports of SPF eggs of non-Australian origin regardless of end use must comply with the attached " Conditions for importation into Australia of fertile specific pathogen free eggs (*Gallus gallus*) of non-Australian origin"– *Condition Set A-1*.

7. All SPF eggs of non-Australian origin used overseas to produce veterinary vaccines and other veterinary *in vivo* products for use in Australia must comply with the relevant requirements in the attached "Conditions for fertile specific pathogen free eggs (*Gallus gallus*) of non-Australian origin for overseas use in veterinary vaccines destined for Australia".– *Condition Set A-2.*

8. All veterinary vaccines and other veterinary *in vivo* products produced in Australia on imported SPF eggs must comply with the attached "Conditions for the use of fertile specific pathogen free eggs (*Gallus gallus*) of non-Australian origin for veterinary vaccine production within Australia" – *Condition Set B-1*.

9. All veterinary vaccines and other veterinary *in vivo* products destined for use in Australia but produced overseas on SPF eggs of non-Australian origin must comply with the attached "Conditions for the use of fertile specific pathogen free eggs (*Gallus gallus*) of non-Australian origin for overseas veterinary vaccine production" – *Condition Set B-2.*

10. *In vitro* laboratory use of imported SPF eggs must be in accordance with the attached "Conditions for the *in vitro* laboratory use of fertile specific pathogen free eggs (*Gallus gallus*) of non-Australian origin" – *Condition Set C.*

11. Regulation of the use of SPF eggs in human vaccines and safety, including end product testing, of human vaccines rests with the TGA. However, AQIS is responsible for the quarantine import requirements of SPF eggs and regulation of all animal biosecurity issues associated with those eggs. All SPF eggs imported for human vaccine production must comply with the attached "Conditions for the

[4] Testing 1.25% of the flock per week will be considered equivalent to the 5% monthly testing specified in the European Pharmacopoeia.

use of fertile specific pathogen free eggs (*Gallus gallus*) of non-Australian origin for human vaccine production" - *Condition Set D.*

12. All facilities within Australia used for the holding, handling, using and/or testing of the imported SPF eggs must be Quarantine Approved Premises for the purpose of using imported SPF eggs.

13. The SPF eggs or veterinary vaccine produced on SPF eggs of non-Australian origin may not be imported until an import permit has been obtained from AQIS following an AQIS assessment including the source, facilities, procedures and relevant documentation.

    - Prior to the import permit being issued, copies of the source SPF flock's test results for the 4 month period immediately preceding the 21 day pre-collection period must be provided to AQIS.

    - Prior to the use of SPF eggs of non-Australian origin in vaccine production within Australia, copies of the results of testing of the source SPF flock for the required testing undertaken during the 21 day pre-collection period must be provided to AQIS. These results should also accompany the consignment of SPF eggs.

    - Prior to importation of a veterinary vaccine manufactured using SPF eggs of non-Australian origin, copies of the results of the required testing of the source SPF flock undertaken during the 21 day pre-collection period must be provided to AQIS. These results are required by AQIS prior to issuance of an AQIS import permit for the specific vaccine batch on which the SPF eggs were used.

14. Because of the inherent risks associated with vaccines and vaccine substrates, especially embryonated SPF eggs used in live avian vaccine production, the requirements of this policy for live avian vaccines were developed specifically to address a critical need

    - Prior to issuing an import permit for SPF eggs for live avian vaccine production or live avian vaccines manufactured on SPF eggs of non-Australian origin, a critical national need must be demonstrated. AQIS will seek advice from Biosecurity Australia on whether there is a critical national need and the likely duration of the critical need.

    - In determining if there is a critical national need, Biosecuirty Australia will consider the animal health risk to the national flock due the unavailability of the vaccine and the animal health risk due to the use of the SPF eggs of non-Australian origin. BA will also seek advice from:

        .. Australian SPF egg producers on whether there are insufficient SPF eggs available to meet vaccine production and other critical needs; and

.. Australian vaccine companies on whether there is insufficient stock of the vaccine to protect the national flock

.. peak national poultry associations on the impact to health and welfare of the national flock through non-availability of the vaccine(s).

- The import permit, if issued by AQIS, will be limited to the period considered necessary to meet this critical need.

15. Approval must be obtained from the Director of Quarantine prior to the release of the final vaccine (and any other products associated with the SPF eggs of non-Australian origin which have not been destroyed or sterilised in accordance with the approved SPF egg QA manual)

- To obtain this approval, all the relevant test results (ie the post-collection source SPF flock testing, egg and/or chicken tissue and final bulk vaccine testing) must be presented to AQIS.

16. If any investigation or test indicates the presence of a pathogen in the source SPF flock, SPF eggs in quarantine or an extraneous pathogen in the vaccine or other product derived from or in which the imported SPF eggs were used, the Director must be notified and the SPF eggs, tissue culture, derivatives, vaccine and/or other products will remain in quarantine.

- At the discretion of the Director and in consultation with the laboratory carrying out the investigations or test, and where necessary, other relevant authorities, further investigations and additional testing may be carried out to ascertain the cause of the positive result.

- Vaccine manufactured overseas will not be eligible for importation into Australia if the source SPF flock, SPF eggs, tissue culture and/or vaccine are found to be infected/contaminated with any pathogen of quarantine concern.

- The SPF eggs, tissue culture, vaccine and/or other products or derivatives may be destroyed, treated or re-exported at the discretion of the Director if it is confirmed that there is infection/contamination with any pathogen of quarantine concern.

- Any evidence of infection or contamination with any other extraneous pathogen will be referred to the APVMA for consideration.

17. In addition to the requirements specified in this policy, all veterinary vaccines are required to meet all other relevant quarantine policy requirements for vaccines, including the 1997 "Specific quarantine requirements for the importation of inactivated veterinary vaccines" and the 1999 "Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines".

REVIEW

. Biosecurity Australia considers the unmanaged risk associated with the use of SPF eggs of non-Australian origin, especially in live avian vaccines, to be very high. However, possible disruption to the production of SPF eggs within Australia could have serious consequences for animal and human health within Australia. This policy for the importation of SPF eggs and/or veterinary vaccines produced on SPF eggs of non-Australian origin has been developed to address these issues.

. In accordance with the current import policy for live veterinary vaccines, each import application for a live livestock (including avian) vaccine is subject to public consultation.

. Additional testing of the source SPF flock to address quarantine exotic disease concerns with the use of SPF eggs of non-Australian origin in live avian vaccine production is required by this policy. Until a review of extraneous agent testing of live avian vaccines is finalised, an alternative option of using additional extraneous agent tests on live avian vaccines will only be available following case by case assessment.

. The requirement for demonstration of a critical national need in relation to live avian vaccines may be difficult to justify in the long term in relation to Australia's commitment to the WTO. Therefore, producers and end-users of SPF eggs are encouraged to work together on the many commercial issues to develop a mechanism enabling continued supply of SPF eggs to all end users, including the biomedical industry.

. Biosecurity Australia will remove, within a reasonable period of time, the contingency clause from use of SPF eggs of non-Australian origin in live avian vaccine production. A period of 12 months is anticipated as this should provide sufficient time for issues such as additional testing of final live avian vaccines to be resolved.

. The conditions of importation may be reviewed by Biosecurity Australia if there are any significant changes in the international avian health status or at any time at the discretion of the Director.

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Biosecurity Australia

CONDITIONS AND APPENDICES

CONDITION SET A-1

CONDITIONS FOR IMPORTATION INTO AUSTRALIA OF FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN

Scope

This set of conditions (ie Condition Set A-1) is for the importation of SPF eggs into Australia. Imported SPF eggs may be destined for either *in vitro* laboratory use, vaccine production or any other use within Australia. The importer may be a distributor or the end user. Note that additional conditions apply to the end use of the imported SPF eggs (refer Condition Sets B-1, C and D).

1. DOCUMENTATION AND GENERAL REQUIREMENTS FOR IMPORTATION

a. All facilities within Australia used for the holding, handling, using and testing of the imported SPF eggs must be Quarantine Approved Premises for the purpose of using imported SPF eggs.

b. The application to import must be accompanied by copies of the monthly test results for the 4 month period prior to the 21 day pre-collection period.

c. All consignments must be accompanied by the following documents which must be produced to a Quarantine Officer at the port of entry before a "Quarantine Entry" will be issued and must not be modified without the written permission of the Director:

(i) a valid copy of the AQIS import permit (or a method of identifying the permit such as the permit number.

(ii) a declaration by the owner or manager of the source SPF flock (Appendix 1)

(iii) the first certificate from a Government Veterinary Officer of the country of origin - (Appendix 2).

(iv) copies of all relevant test results as detailed in Appendix 2.

2. QUALITY ASSURANCE MANUAL (REQUIRED BY IMPORTER)

Approval as a Quarantine Approved Premises for the purpose of using imported SPF eggs will require adequate quality assurance documentation and standard operating procedures relating to use of the imported SPF eggs (herein called the "QA manual").

The importer must incorporate into their QA manual details of the following:

(i) the procedures and facilities used for the storage, handling and security of the SPF eggs at the importer's premises;

(ii) the standards and procedures for ensuring the imported SPF eggs are not further distributed, except to other Quarantine Approved Premises that have prior AQIS approval to use imported SPF eggs[5];

(iii) the procedures and facilities used for the disposal of all waste associated with the imported SPF eggs (including specifications and validation of disposal methods to ensure effective sterilisation is achieved);

(iv) the procedures used for the transport of the imported SPF eggs from the importer's premises to the end user[5] (including contingency plans for spillages and leakages);

(v) records maintained of all SPF eggs imported and destination/fate.

(vi) internal audit procedures used by the importer to ensure all quarantine concerns are addressed and permits and approvals obtained prior to importation.

3. ELIGIBILITY

a. To be considered for importation, the SPF eggs must be from a country

(i) considered free from clinical Newcastle disease (ND) and avian influenza (AI) as per the Office International des Epizooties (OIE) definition; OR

(ii) in which a stamping-out policy is practised against these diseases and there has been no outbreak within a 25 km radius of the source SPF flock within the last 30 days[6];

b. The country of origin must have an overall acceptable standard of avian health, veterinary services and diagnostic capabilities as assessed by Biosecurity Australia in accordance with OIE guidelines.

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[5] Not applicable if the importer is also the end user.

[6] Additional AI & ND testing may be required on the source SPF flock.

c. The source SPF flock shall meet the requirements specified in Section 4 "Source SPF flock".

4. Source SPF flock

a. The source flock shall be an SPF flock, as specified by and meeting the requirements of the current European Pharmacopoeia 5.2.2 "Chicken flocks free from specified pathogens for the production and quality control of vaccines". The minimum sampling rate and frequency for pathogen testing shall be as specified in the current European Pharmacopoeia Chapter 5.2.2.

Note: It is the end user's responsibility to ensure compliance with any higher rates of sampling and any additional requirements as may be required for some pathogens by the Australian Pesticides and Veterinary Medicines Authority (APVMA) and/or Therapeutic Goods Administration (TGA) for domestic vaccines and/or by foreign authorities for export vaccines.

b. The source SPF flock shall be approved by the relevant veterinary authority in the country of origin or by AQIS as an source SPF flock suitable for the production of SPF eggs for vaccine production as defined by the current European Pharmacopoeia.

c. The source SPF flock must not have been vaccinated against any disease.

d. Each shed/house is considered a separate flock. The source SPF flock shall be housed in secure rodent-proof and bird-proof buildings and shall be isolated by 400 metres from all poultry unless these are also source SPF flocks as defined by the European Pharmacopoeia. Each shed from which SPF eggs are sourced for export to Australia must meet Australian import requirements.

e. Within 21 days before the first day of collection of SPF eggs for export to Australia, the source SPF flock must be tested for:

1) all pathogens listed in and at the rate specified by the current European Pharmacopoeia requirements for source SPF flocks; and

2) if the SPF eggs are destined for veterinary vaccine production or other *in vivo* veterinary use, the source SPF flock shall also be tested for all other pathogens listed in Appendix 5. The rate shall be 5% of the source SPF flock but not less than 10 and need not be more than 200 birds per month[7]; and

3) if the SPF eggs are destined for live avian vaccine production or other *in vivo* avian use where the product is not inactivated[8], additional testing[9, 10] (ie

[7] This rate is consistent with European Pharmacopoeia requirements for SPF flocks. A rate of 1.25% per week will be considered equivalent.

[8] The additional testing specified is not required for the relevant disease if the Director of Quarantine is satisfied that the country of origin is free of the disease.

increased sample size) of the source SPF flock is required for the following pathogens to provide at least a 99% confidence of detection at a 0.5% prevalence level (after taking sensitivity of the diagnostic test into account)

Avian influenza virus
Newcastle disease virus
Avian paramyxovirus-2
Avian paramyxovirus-3
Avian pneumovirus (Turkey viral rhinotracheitis)
Avian adenovirus group 1
Infectious bronchitis virus
Avian reovirus.

Note: Biosecurity Australia will be undertaking a review on the possible use of additional highly sensitive extraneous agent detection tests for the bulk or final vaccine as an alternative to increased sampling of the source SPF flock. Until finalised, this alternative option to increased sampling will only be available on a case by case basis and following rigorous evaluation by Biosecurity Australia.

f. Within 21 days prior to collection of SPF eggs for export to Australia, the source SPF flock must also be tested free of *Salmonella spp* using microbiological culture and isolation from randomly collected shed litter or faecal samples as follows:

1) twenty shed litter samples, each a composite sample of 3 floor and 2 nest litter samples, or

2) faecal samples from 5% of the flock but not less than 10 and need not be more than 200 birds, pooled with up to 10 samples per pool.

g. Within 21 days <u>after</u> egg collection, the source SPF flock must be tested for:

1) all pathogens listed in and at the rate specified by the current European Pharmacopoeia requirements for source SPF flocks, and

2) if the SPF eggs are destined for veterinary vaccine production or other *in vivo* veterinary use AND the source SPF flock size[11] is less than 1800, additional testing is required for Newcastle disease and/or avian influenza to provide at least a 99% confidence of detecting disease at a 5% prevalence

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[9] It is the live avian vaccine manufacturer's responsibility to advise the SPF egg producer and to request the additional testing.

[10] This additional testing should be undertaken within the 21 day period prior to the egg collections. However, subject to case by case assessment and approval by AQIS, this period may be extended to include up to 8 weeks after egg collection but prior to release of the final vaccine. In making this determination, AQIS will need to be confident that the revised sampling regime provides an equivalent or better confidence in detecting each disease. Such permission would also be on the understanding by the manufacturer that any positive test will result in the vaccine being rejected as it may be difficult to determine whether the incursion was before or after egg collection.

[11] Note: The European Pharmacopoeia rate achieves this 99% confidence level for flocks greater than 1800 birds.

level unless the country of origin is free of these diseases or 100% of the source SPF flock has been tested within the previous 12 months.

h. Unless otherwise stated in these conditions or approved by AQIS, applicable test standards as specified in Appendix 5 must be used for the testing.

i. All tests conducted for this protocol using embryonated egg or chick inoculation must use SPF eggs or SPF chicks obtained from flocks other than the source SPF flock.

5. EGG COLLECTION AND TRANSPORT TO AUSTRALIA

a. The SPF eggs shall be collected, indelibly marked and dispatched under the supervision of a Government Veterinary Officer of the country of origin. The SPF eggs shall undergo fumigation by formaldehyde as prescribed or disinfected by an alternative method approved by the Director and then shall be packed and sealed in approved containers for transport to Australia.

b. The SPF eggs shall be packed in such a way to prevent leakage in the event that eggs break during transport.

c. The SPF eggs must be consigned to Australia by air, by a route approved by the Director. They may be accompanied in transit by other eggs or birds only with the approval of the Director. Any trans-shipment requires the prior approval of the Director.

d. The consignment may not be permitted entry into Australia in the event of a consignment arriving in Australia either in an unsealed container, or in a container the seal of which has been broken, or with evidence of contamination en route with risk material, or with inadequate certification.

6. QUARANTINE: IMPORTER

a. The importer's facility shall be a Quarantine Approved Premises for the purpose of holding, and, if appropriate, distributing imported fertile SPF eggs. Storage and other areas holding or handling the imported SPF eggs shall be secure and separate from other biological product including other eggs. The imported SPF eggs will remain subject to quarantine until released by the Director of Quarantine. Any breakages, waste or other products derived directly or indirectly from these eggs shall also remain subject to quarantine until disposed of or released by the Director of Quarantine. Use and/or destruction of all material shall be in accordance with the approved QA manual.

b. The imported SPF eggs may only be distributed to Quarantine Approved Premises for the purpose of using imported SPF eggs. Prior approval must be obtained from AQIS prior to distribution. Such approval will be contingent on the proposed recipient's (ie end user) demonstration of intention and ability to comply with all relevant requirements of this policy.

7. IMPORTER'S / AGENT'S RESPONSIBILITIES

a. The importer or the agent coordinating the importation must be Australian based and must nominate a person who will be accessible to AQIS officers if any problems or emergencies arise.

b. The importer should be aware that if, during the process of quarantine, it is found that the testing or certification requirements have not been fully met, the consignment of eggs may be re-exported or destroyed and any vaccine or other product produced using the imported eggs may also be destroyed at the importer's expense.

c. The importer/agent and the aircraft operator are responsible for the safe transportation of the SPF eggs. The importer is responsible for the safe transportation of the SPF eggs to the end user.

d. All costs associated with the testing, transport, quarantine and veterinary supervision during the importation program must be met by the importer/agent.

e. If any SPF eggs, vaccine or other product derived from the SPF eggs are destroyed or otherwise adversely affected during any period of quarantine control, compensation will not be paid by the Australian Government.

CONDITION SET A-2

CONDITIONS FOR FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN FOR OVERSEAS USE IN VETERINARY VACCINES[12] DESTINED FOR AUSTRALIA

Scope

This set of conditions (ie Condition Set A-2) is for SPF eggs of non-Australian origin used overseas to produce veterinary vaccines and other *in vivo* veterinary products destined for use within Australia. Note that additional conditions apply to the end use of the SPF eggs (refer Condition Set B-2).

1. ELIGIBILITY

a. To be considered eligible for use in Australian veterinary vaccines, the SPF eggs must be from a country

(i) considered free from clinical Newcastle disease (ND) and avian influenza (AI) as per the OIE definition; OR

(ii) in which a stamping-out policy is practised against these diseases and there have been no outbreak within a 25 km radius of the source SPF flock within the last 30 days[13];

b. The country of origin must have an overall acceptable standard of avian health, veterinary services and diagnostic capabilities as assessed by Biosecurity Australia in accordance with OIE guidelines.

c. The source SPF flock shall meet the requirements specified in Section 2 "Source SPF flock".

2. Source SPF flock

a. The source flock shall be an SPF flock, as specified by and meeting the requirements of the current European Pharmacopoeia 5.2.2 "Chicken flocks free from specified pathogens for the production and quality control of vaccines". The minimum sampling rate and frequency for pathogen testing shall be as specified in the current European Pharmacopoeia Chapter 5.2.2.

Note: It is the end user's responsibility to ensure compliance with any higher rates of sampling and any additional requirements as may be required for some pathogens by the Australian Pesticides and Veterinary

[12] Reference within this policy and conditions to veterinary vaccines also refers to other *in vivo* veterinary products.

[13] Additional AI & ND testing may be required on the source SPF flock.

Medicines Authority (APVMA) and/or Therapeutic Goods Administration (TGA) for domestic vaccines and/or by foreign authorities for export vaccines.

b. The source SPF flock shall be approved by the relevant veterinary authority in the country of origin or by AQIS as an source SPF flock suitable for the production of SPF eggs for vaccine production as defined by the current European Pharmacopoeia.

c. The source SPF flock must not have been vaccinated against any disease.

d. Each shed/house is considered a separate flock. The source SPF flock shall be housed in secure rodent-proof and bird-proof buildings and shall be isolated by 400 metres from all poultry unless these are also source SPF flocks as defined by the European Pharmacopoeia. Each shed from which SPF eggs are sourced for export to Australia must meet Australian import requirements.

e. Within 21 days before the first day of collection of SPF eggs for use in Australian veterinary vaccine production, the source SPF flock must be tested for:

1) all pathogens listed in and at the rate specified by the current European Pharmacopoeia requirements for source SPF flocks; and

2) the source SPF flock shall also be tested for all other pathogens listed in Appendix 5. The rate shall be 5% of the source SPF flock but not less than 10 and need not be more than 200 birds per month[14]; and

3) if the SPF eggs are destined for live avian vaccine production or other *in vivo* avian use where the product is not inactivated[15], additional testing[16, 17] (ie increased sample size) of the source SPF flock is required for the following pathogens to provide at least a 99% confidence of detection at a 0.5% prevalence level (after taking sensitivity of the diagnostic test into account)

Avian influenza virus
Newcastle disease virus
Avian paramyxovirus-2
Avian paramyxovirus-3
Avian pneumovirus (Turkey viral rhinotracheitis)

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[14] This rate is consistent with European Pharmacopoeia requirements for SPF flocks. A rate of 1.25% per week will be considered equivalent.

[15] The additional testing specified is not required for the relevant disease if the Director of Quarantine is satisfied that the country of origin is free of the disease.

[16] It is the live avian vaccine manufacturer's responsibility to advise the SPF egg producer and to request the additional testing.

[17] This additional testing should be undertaken within the 21 day period prior to the egg collections. However, subject to case by case assessment and approval by AQIS, this period may be extended to include up to 8 weeks after egg collection but prior to release of the final vaccine. In making this determination, AQIS will need to be confident that the revised sampling regime provides an equivalent or better confidence in detecting each disease. Such permission would also be on the understanding by the manufacturer that any positive test will result in the vaccine being rejected as it may be difficult to determine whether the incursion was before or after egg collection.

Avian adenovirus group 1
Infectious bronchitis virus
Avian reovirus.

Note: Biosecurity Australia will be undertaking a review on the possible use of additional extraneous agent detection tests for the bulk or final vaccine as an alternative to increased sampling of the source SPF flock. Until finalised, this alternative option to increased sampling will only be available on a case by case basis and following rigorous evaluation by Biosecurity Australia.

f. Within 21 days prior to collection of SPF eggs for use in Australian veterinary vaccine production, the source SPF flock must also be tested free of *Salmonella spp* using microbiological culture and isolation from randomly collected shed litter or faecal samples as follows:

1) twenty shed litter samples, each a composite sample of 3 floor and 2 nest litter samples, or

2) faecal samples from 5% of the flock but not less than 10 and need not be more than 200 birds, pooled with up to 10 samples per pool.

g. Within 21 days after egg collection, the source SPF flock must be tested for:

3) all pathogens listed in and at the rate specified by the current European Pharmacopoeia requirements for source SPF flocks, and

4) if the SPF eggs are destined for veterinary vaccine production or other *in vivo* veterinary use AND the source SPF flock size[18] is less than 1800, additional testing is required for Newcastle disease and/or avian influenza to provide at least a 99% confidence of detecting disease at a 5% prevalence level unless the country of origin is free of these diseases or 100% of the source SPF flock has been tested within the previous 12 months.

h. Unless otherwise stated in these conditions or approved by AQIS, applicable test standards as specified in Appendix 5 must be used for the testing.

i. All tests conducted for this protocol using embryonated egg or chick inoculation must use SPF eggs or SPF chicks obtained from flocks other than the source SPF flock.

[18] Note: The European Pharmacopoeia rate achieves this 99% confidence level for flocks greater than 1800 birds.

3. END USER'S RESPONSIBILITIES

a. The end user (eg vaccine manufacturer) of the SPF eggs should be aware that if it is found that the testing or certification requirements have not been fully met, the SPF eggs may be considered unsuitable for use in veterinary vaccines destined for Australia.

b. If any eggs, vaccine or other product are destroyed or otherwise adversely affected during any period of quarantine control, compensation will not be paid by the Australian Government.

CONDITION SET B-1

CONDITIONS FOR THE USE OF FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN FOR VETERINARY VACCINE[19] PRODUCTION WITHIN AUSTRALIA

Scope

This set of conditions (ie Condition Set B-1) is specifically for the use of SPF eggs of non-Australian origin for the manufacture within Australia of veterinary vaccines or other *in vivo* veterinary products.

1. DOCUMENTATION AND GENERAL REQUIREMENTS FOR USE IN VACCINE PRODUCTION

a. All facilities within Australia used for the holding, handling, using and testing of the imported SPF eggs must be Quarantine Approved Premises for the purpose of using imported SPF eggs.

b. The consignment of imported SPF eggs shall either be imported by the vaccine manufacturer in accordance with condition Set A-1 or be obtained from an importer that is a Quarantine Approved Premise for the purpose of importing, storing and distributing SPF eggs in accordance with Condition Set A-1.

c. Because of the inherent risks associated with veterinary vaccines and vaccine substrates, especially embryonated SPF eggs used in live avian vaccine production, a critical national need must be demonstrated[20].

d. *In vivo* approval for use of the SPF eggs in live avian vaccines will be limited to the time necessary to address the critical national need.

e. For live avian vaccines produced on SPF eggs of non-Australian origin, documentation must confirm that the source SPF flock has undergone additional testing for the exotic avian diseases of concern, as described in Condition Set A-1.

- *Note: Refer to the policy for details of the alternative option of using PCR or other highly sensitive tests on the final bulk vaccine.*

f. Copies of the following completed documentation must be presented to AQIS:

Prior to use of the SPF eggs in veterinary vaccine production:

(i) a declaration by the owner or manager of the source SPF flock-(Appendix 1)

[19] Reference within this policy and conditions to veterinary vaccines also refers to other *in vivo* veterinary products.

[20] Refer to the covering policy for detail on how a critical national need is to be demonstrated.

(ii) the first certificate from a Government Veterinary Officer of the country of origin - (Appendix 2).

(iii) copies of all relevant test results as detailed in Appendix 2.

Prior to release of the SPF eggs from quarantine for use within Australia:

(iv) the second certificate from a Government Veterinary Officer of the country of origin - (Appendix 3).

(v) a declaration by the veterinarian/technician supervising the vaccine production at the vaccine facility - (Appendix 4)

2. QUALITY ASSURANCE MANUAL

Approval as a Quarantine Approved Premises for the purpose of using imported SPF eggs will require adequate quality assurance documentation and standard operating procedures relating to use of the imported SPF eggs (herein called the "QA manual").

The veterinary vaccine manufacturer must incorporate into their QA Manual the following:

(i) procedures to verify that only SPF eggs that meet all relevant requirements of this policy are used in the production of veterinary vaccines for use in Australia;

(ii) the standards and procedures for the testing of the SPF eggs of non-Australian origin and subsequent tissue cultures and bulk vaccine in accordance with this policy;

(iii) internal audit procedures used by the vaccine manufacturer to ensure all quarantine concerns are addressed and permits and approvals obtained prior to acquisition and use of the SPF eggs, disposal of waste and release of finished vaccine.

3. ELIGIBILITY

To be considered eligible for *in vivo* approval to use imported SPF eggs in Australia for veterinary vaccine production, the SPF eggs must have been imported specifically for veterinary vaccine production or other *in vivo* veterinary use in accordance with Condition Set A-1 to this policy.

4. QUARANTINE: VETERINARY VACCINE MANUFACTURER

a. Storage, incubation and other areas holding or handling the imported SPF eggs shall be of a standard acceptable to AQIS and be secure and separate from other areas not associated with use of the SPF eggs.

b. The vaccine production shall meet the following requirements:

(i) The exhaust air from areas used for inoculation and harvesting shall be HEPA-filtered.

(ii) The facility shall be an Quarantine Approved Premises for the purpose of holding and using imported fertile SPF eggs.

(iii) The imported SPF eggs will remain subject to quarantine until used in vaccine production or otherwise destroyed. Any tissue culture, substrate or other products derived from these SPF eggs shall also remain subject to quarantine until disposed of or released by the Director of Quarantine. Use and/or destruction of all material shall be in accordance with the approved QA manual.

(iv) The imported SPF eggs shall not be permitted to hatch[21].

5. PRODUCT TESTING

a. Vaccine products using the SPF eggs of non-Australian origin shall be demonstrated free from pathogens of concern as follows:

(i) All veterinary vaccines manufactured using SPF eggs of non-Australian origin must meet all relevant requirements of the 1997 "Specific quarantine requirements for the importation of inactivated veterinary vaccines" or the 1999 "Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines".

(ii) A representative sample of shell debris, membranes, etc[22] from each tray of SPF eggs used in the vaccine production shall be tested for freedom from *Salmonella spp* as per Australian Standard AS1766.2.5 or other AQIS approved method. All embryonic mortalities, prior to inoculation, shall also be sampled and tested.

[21] The hatching and use of chicks from imported SPF eggs at facilities other than in the high security area of AAHL will require an additional risk analysis with biosecurity arrangements expected to be equivalent to that for importation of live birds.

[22] Egg waste after vaccine production may be used.

(iii) Any unexpected signs of infectious diseases in the embryos including high or unexpected embryonic mortalities prior to inoculation must also be investigated and reported immediately to AQIS.

(iv) A representative sample of each batch of bulk vaccine prior to any inactivation step and/or addition of adjuvant must also be demonstrated to be free of all pathogens (excluding the vaccine organism) specified in Appendix 5.

b. Unless otherwise specified, acceptable test standards are detailed in Appendix 5. Additional testing and higher sample rates may be required to meet the requirements of the Therapeutic Goods Administration (TGA) and the Australian Pesticides and Veterinary Medicines Authority (APVMA) and, for export vaccines, the requirements of the relevant regulatory authorities in the importing countries.

c. Where appropriate procedures to prevent cross contamination cannot be demonstrated to the satisfaction of AQIS, all other vaccines for Australian use produced while the non-Australian SPF eggs are held or used at the facility must be tested for all pathogens determined by AQIS to be potential contaminants.

d. The declaration from the veterinarian/technician supervising the vaccine facility (refer Appendix 4) must be submitted to and approved by AQIS prior to release from quarantine of vaccine produced in Australia using the SPF eggs of non-Australian origin.

e. Live avian vaccines: Possible alternative to increased source SPF flock sample size

For live avian vaccines, Biosecurity Australia is currently reviewing the availability, sensitivity and practicality of highly sensitive extraneous agent detection tests as an alternative to tests currently used in vaccine quality control. Once that review is finalised, the following conditions are anticipated as an alternative to the increased source SPF flock sample size required by this policy where the SPF eggs are destined for use in live avian vaccine production:

(i) A representative sample of each batch of bulk vaccine prior to any inactivation or addition of adjuvant shall be tested at AAHL or other AQIS approved independent laboratory for freedom from the following viral pathogens[23] using an appropriate, AQIS approved, highly sensitive test:

Avian influenza virus
Newcastle disease virus
Avian paramyxovirus-2

[23] Infections of overseas SPF flocks with chicken anaemia virus, avian adenovirus, avian leucosis viruses and avian reovirus and some subsequent contamination of vaccines have highlighted the potential risk associated with SPF eggs and short comings of routine surveillance of SPF flocks. Live avian vaccines are considered at greatest risk. Therefore, it is considered necessary that more sensitive detection tests be used on the final bulk live avian vaccine for those exotic viral pathogens which are also potential vaccine contaminants.

Avian paramyxovirus-3
Avian pneumovirus (Turkey viral rhinotracheitis virus)
Avian adenovirus group 1
Infectious bronchitis virus
Avian reovirus.

The test used shall be the most appropriate and sensitive test available for detecting the presence of the pathogen. The presence of any antigen, regardless whether viable or non-viable, is unacceptable as it indicates either a breakdown in biosecurity in the source SPF flock, contamination of the master seed or other substrates used, or cross contamination during the production process.

(ii) The sample volume/size shall be determined by AQIS in consultation with AAHL and/or the testing laboratory.

(iii) Biosecurity Australia recommends that Australian vaccine manufacturers implement similar additional management controls for chicken anaemia virus, avian leucosis viruses and other endemic avian pathogens as there is a significant potential for live avian vaccines to be contaminated with these pathogens. However, Biosecurity Australia and AQIS cannot invoke management controls for endemic pathogens above that applied to domestic source SPF flocks and domestic vaccine production.

7. VACCINE MANUFACTURER'S RESPONSIBILITIES

a. The vaccine manufacturer must nominate a person who will be accessible to Departmental officers if any problems or emergencies arise.

b. The vaccine manufacturer should be aware that if, during the process of quarantine, it is found that the testing or certification requirements have not been fully met, the consignment of eggs may be re-exported or destroyed and any vaccine or other product produced using the imported eggs may also be destroyed at the manufacturer's expense.

c. All costs associated with the testing, transport, quarantine and veterinary supervision must be met by the vaccine manufacturer.

e. If any procedures are not permitted or eggs, vaccine or other product are tested, re-exported or destroyed during any period of quarantine control, compensation will not be paid by the Australian Government.

CONDITION SET B-2

CONDITIONS FOR THE USE OF FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN FOR OVERSEAS VETERINARY VACCINE[24] PRODUCTION

Scope

This set of conditions (ie Condition Set B-2) is specifically for the use of SPF eggs of non-Australian origin for the overseas manufacture of veterinary vaccines or other *in vivo* veterinary products destined for Australia.

1. DOCUMENTATION AND GENERAL REQUIREMENTS FOR USE IN VACCINE PRODUCTION

a. All overseas facilities using SPF eggs of non-Australian origin to produce veterinary vaccines for use within Australia must be approved by AQIS for that purpose.

b. Prior approval must be obtained in writing from the Director of Animal and Plant Quarantine (herein called "the Director") of the vaccine manufacturer's quality assurance documentation and standard operating procedures relating to use of the SPF eggs of non-Australian origin (herein called the "QA manual").

c. All relevant requirements of Condition Set A-2 must be met.

d. Because of the inherent risks associated with veterinary vaccines and vaccine substrates, especially embryonated SPF eggs used in live avian vaccine production, a critical national need must be demonstrated[25].

e. Import approval of live avian vaccines produced using the SPF eggs will be limited to the time necessary to address the critical national need.

f. For live avian vaccines produced on SPF eggs of non-Australian origin, documentation must confirm that the source SPF flock has undergone additional testing for the exotic avian diseases of concern, as described in Condition Set A-2.

- *Note: Refer to the policy for details of the alternative option of using PCR or other highly sensitive tests on the final bulk vaccine.*

[24] Reference within this policy and conditions to veterinary vaccines also refers to other *in vivo* veterinary products.

[25] Refer to the covering policy for detail on how a critical national need is to be demonstrated.

g. Copies of the following completed documentation must be presented to AQIS:

Prior to use of the SPF eggs in veterinary vaccine production:

(i) a declaration by the owner or manager of the source SPF flock-(Appendix 1)

(ii) the first certificate from a Government Veterinary Officer of the country of origin - (Appendix 2).

(iii) copies of all relevant test results as detailed in Appendix 2.

Prior to importation of the veterinary vaccine:

(iv) the second certificate from a Government Veterinary Officer of the country of origin - (Appendix 3).

(v) a declaration by the veterinarian/technician supervising the vaccine production at the vaccine facility - (Appendix 4)

2. QUALITY ASSURANCE MANUAL

The veterinary vaccine manufacturer must incorporate into their QA Manual the following:

(i) procedures to verify that only SPF eggs that meet all relevant requirements of this policy are used in the production of veterinary vaccines for use in Australia;

(ii) the standards and procedures for the testing of the SPF eggs of non-Australian origin and subsequent tissue cultures and bulk vaccine in accordance with this policy;

(iii) internal audit procedures used by the vaccine manufacturer to ensure all quarantine concerns are addressed and permits and approvals obtained prior to export of the vaccine to Australia.

3. ELIGIBILITY

To be considered eligible to use SPF eggs of non-Australian origin in vaccine production overseas, the source SPF flock and SPF eggs must meet Section 1 "Eligibility" and Section 2 " source SPF flock" of Condition Set A-2 to this policy.

4. QUARANTINE: VETERINARY VACCINE MANUFACTURER

The overseas vaccine production facility must be approved by AQIS for the production of veterinary vaccines for Australia

5. PRODUCT TESTING

a. The SPF eggs of non-Australian origin used in production of the veterinary vaccine and the bulk or final veterinary vaccine shall be demonstrated free from pathogens of concern as follows:

(i) All veterinary vaccines manufactured using SPF eggs of non-Australian origin must meet all relevant requirements of the "Specific quarantine requirements for the importation of inactivated veterinary vaccines" or the "Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines".

(ii) A representative sample of shell debris, membranes, etc[26] from each tray of SPF eggs used in the vaccine production shall be tested for freedom from *Salmonella spp* as per Australian Standard AS1766.2.5 or other AQIS approved method. All embryonic mortalities, prior to inoculation, shall also be sampled and tested.

(iii) Any unexpected signs of infectious diseases in the embryos including high or unexpected embryonic mortalities prior to inoculation must also be investigated and reported.

(iv) A representative sample of each batch of bulk vaccine prior to any inactivation step and/or addition of adjuvant must also be demonstrated to be free of all pathogens (excluding the vaccine organism) specified in Appendix 5.

b. Unless otherwise specified, acceptable test standards are detailed in Appendix 5. Additional testing and higher sample rates may be required to meet the requirements of the Therapeutic Goods Administration (TGA) and the Australian Pesticides and Veterinary Medicines Authority (APVMA).

c. Where appropriate procedures to prevent cross contamination cannot be demonstrated to the satisfaction of AQIS, all other vaccines for Australian use produced while the non-Australian SPF eggs are held or used at the facility must be tested for all pathogens determined by AQIS to be potential contaminants.

d. The certificate from the veterinarian/technician supervising the vaccine facility (refer Appendix 4) must be submitted to and approved by AQIS prior to importation of vaccine produced overseas.

[26] Egg waste after vaccine production may be used.

e. Live avian vaccines: Possible alternative to increased source SPF flock sample size

For live avian vaccines, Biosecurity Australia is currently reviewing the availability, sensitivity and practicality of very highly sensitive extraneous agent detection tests as an alternative to tests currently used in vaccine quality control. Once that review is finalised, the following conditions are anticipated as an alternative to the increased source SPF flock sample size required by this policy where the SPF eggs are destined for use in live avian vaccine production:

(i) A representative sample of each batch of bulk vaccine prior to any inactivation or addition of adjuvant shall be tested at AAHL or other AQIS approved independent laboratory for freedom from the following viral pathogens[27] using an appropriate, AQIS approved, highly sensitive test:

Avian influenza virus
Newcastle disease virus
Avian paramyxovirus-2
Avian paramyxovirus-3
Avian pneumovirus (Turkey viral rhinotracheitis virus)
Avian adenovirus group 1
Infectious bronchitis virus
Avian reovirus.

The test used shall be the most appropriate and sensitive test available for detecting the presence of the pathogen. The presence of any antigen, regardless whether viable or non-viable, is unacceptable as it indicates either a breakdown in biosecurity in the source SPF flock, contamination of the master seed or other substrates used, or cross contamination during the production process.

(ii) The sample volume/size shall be determined by AQIS in consultation with AAHL and/or the testing laboratory.

(iii) Biosecurity Australia recommends that Australian vaccine manufacturers implement similar additional management controls for chicken anaemia virus, avian leucosis viruses and other endemic avian pathogens as there is a significant potential for live avian vaccines to be contaminated with these pathogens. However, Biosecurity Australia and AQIS cannot invoke management controls for endemic pathogens above that applied to domestic source SPF flocks and domestic vaccine production.

7. VACCINE MANUFACTURER'S RESPONSIBILITIES

[27] Infections of overseas SPF flocks with chicken anaemia virus, avian adenovirus, avian leucosis viruses and avian reovirus and some subsequent contamination of vaccines have highlighted the potential risk associated with SPF eggs and short comings of routine surveillance of SPF flocks. Live avian vaccines are considered at greatest risk. Therefore, it is considered necessary that more sensitive detection tests be used on the final bulk live avian vaccine for those exotic viral pathogens which are also potential vaccine contaminants.

a. For vaccines manufactured overseas, the vaccine manufacturer should be aware that if the testing or certification requirements have not been fully met, the vaccine or other product produced using the non-Australian SPF eggs may not be imported into Australia.

b. All costs associated with the testing, transport, quarantine and veterinary supervision must be met by the vaccine manufacturer.

e. If any procedures are not permitted or eggs, vaccine or other product are tested, re-exported, destroyed or otherwise damaged during any period of quarantine control, compensation will not be paid by the Australian Government.

CONDITION SET C

CONDITIONS FOR THE *IN VITRO* LABORATORY USE OF FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN

Scope

This set of conditions (ie Condition Set C) is specifically for the use of imported SPF eggs for *in vitro* laboratory purposes only.

1. DOCUMENTATION AND GENERAL REQUIREMENTS FOR IMPORTATION

All facilities within Australia used for the holding, handling, using and testing of the imported SPF eggs must be a Quarantine Approved Premises for the purpose of using imported SPF eggs.

2. QUALITY ASSURANCE MANUAL

Approval as a Quarantine Approved Premises for the purpose of using imported SPF eggs will require adequate quality assurance documentation and standard operating procedures relating to use of the imported SPF eggs (herein called the "QA manual").

The laboratory must incorporate into their QA Manual the following:

(i) the procedures and facilities used for the storage, incubation, handling, security and use of the SPF eggs at the laboratory;

(ii) the procedures and facilities used for the disposal of all waste associated with the imported SPF eggs;

(iii) internal audit procedures used by the laboratory to ensure all quarantine concerns are addressed and permits and approvals obtained prior to acquisition and use of the SPF eggs and disposal of waste.

3. ELIGIBILITY

To be considered eligible for *in vitro* laboratory use in Australia, the imported SPF eggs must comply with Condition Set A-1 to this policy.

4. QUARANTINE

a. The laboratory shall be a Quarantine Approved Premise (QAP) for the purpose of using imported SPF eggs and these eggs shall be held in an approved quarantine area within the QAP. The imported SPF eggs and any material derived from them will remain under quarantine until eventually destroyed. Use and/or destruction shall be in accordance with the approved QA manual.

b. Storage, incubation and other facilities shall be separate from other products and animals including other eggs unless these are also placed under quarantine until autoclaved, incinerated or otherwise effectively sterilised to the satisfaction of the Director.

c. Untoward or unexpected embryonic effects including high or unexpected embryonic mortalities (other than that expected or induced by experimental procedures) must be reported immediately to AQIS and competently investigated to find the cause.

d. Records must be maintained of all SPF eggs obtained, embryonic mortalities, use of the SPF eggs and disposal of waste. These records must be provided to AQIS during QAP audits and at any other time on request.

e. The imported SPF eggs shall not be permitted to hatch. The only exception shall be if the SPF eggs are held, incubated and hatched within the high security area of AAHL with approval from AQIS. The chickens which are hatched from these SPF eggs will remain under quarantine until destroyed and any tissue culture or other products derived from these birds shall also remain under quarantine until disposed of. Any abnormal clinical signs of infectious diseases in the hatched birds (other than those anticipated due to experimental procedures) must also be reported immediately to AQIS and competently investigated to determine the cause.[28]

5. THE LABORATORY'S RESPONSIBILITIES

a. The laboratory must nominate a person who will be accessible to AQIS officers if any problems or emergencies arise.

b. The laboratory should be aware that if, during the process of quarantine, it is found that the pre-export testing or certification requirements have not been fully met, the consignment may be re-exported or destroyed at the importer's expense.

c. All costs associated with the testing, transport, quarantine and veterinary supervision during the importation program must be met by the importer/agent and/or laboratory.

[28] The hatching and use of chicks from imported SPF eggs at facilities other than in the high security area of AAHL will require an additional risk analysis with biosecurity arrangements expected to be equivalent to that for importation of live birds.

d. If any procedures are not permitted or eggs, birds or other product are tested, re-exported or destroyed during any period of quarantine control, compensation will not be paid by the Australian Government.

CONDITION SET D

CONDITIONS FOR THE USE OF FERTILE SPECIFIC PATHOGEN FREE EGGS (*GALLUS GALLUS*) OF NON-AUSTRALIAN ORIGIN FOR HUMAN VACCINE[29] PRODUCTION

Scope

This set of conditions (ie Condition Set D) covers animal biosecurity issues relating to the holding, handling, testing and use of imported SPF eggs for the production of human vaccines within Australia. Human health and safety issues for human vaccines used within Australia, regardless of whether manufactured in Australia or overseas, are regulated by the Therapeutic Goods Administration (TGA). It is the vaccine manufacturer's responsibility to ensure compliance with the requirements of TGA and other regulatory bodies.

1. DOCUMENTATION AND GENERAL REQUIREMENTS FOR IMPORTATION

a. All facilities within Australia used for the holding, handling, using and testing of the imported SPF eggs must be Quarantine Approved Premises for the purpose of using imported SPF eggs.

b. The consignment of imported SPF eggs shall either be imported by the human vaccine manufacturer in accordance with Condition Set A-1 or be obtained from an importer that is a Quarantine Approved Premise for the purpose of importing, storing and distributing SPF eggs also in accordance with Condition Set A-1.

2. QUALITY ASSURANCE MANUAL

Approval as a Quarantine Approved Premises for the purpose of using imported SPF eggs will require adequate quality assurance documentation and standard operating procedures relating to use of the imported SPF eggs (herein called the "QA manual").

The human vaccine manufacturer must incorporate into their QA Manual the following:

(i) the procedures and facilities used for the secure storage, incubation, handling, security and use of the SPF eggs at the vaccine facility;

(ii) the procedures and facilities used for the disposal of all waste associated with the imported SPF eggs;

[29] Reference within this policy and conditions to human vaccines also refers to other therapeutic products for human use only.

(iii) internal audit procedures used by the human vaccine manufacturer to ensure all quarantine concerns are addressed and permits and approvals obtained prior to acquisition and use of the SPF eggs and disposal of waste.

3. ELIGIBILITY

The SPF eggs of non-Australian origin must have been imported in accordance with Condition Set A-1 of this policy.

4. QUARANTINE

a. The facility shall be a Quarantine Approved Premises for the purpose of holding and using imported fertile SPF eggs. The imported SPF eggs will remain subject to quarantine until used in human vaccine production or otherwise destroyed. Any tissue culture or other products, other than the human vaccine, derived from these SPF eggs shall also remain subject to quarantine until disposed of or released by the Director of Quarantine. Use and/or destruction of all material shall be in accordance with the approved QA manual.

b. Storage, incubation and other facilities shall be separate from other products and animals including other eggs unless these are also placed under "quarantine" until autoclaved, incinerated or otherwise effectively sterilised or otherwise handled in accordance with the approved QA Manual. The exhaust air from areas used for inoculation and harvesting shall be HEPA-filtered.

c. Any unexpected signs of infectious diseases in the embryos including high or unexpected embryonic mortalities must also be investigated and reported immediately to AQIS.

d. Records must be maintained of all SPF eggs obtained, embryonic mortalities, use of the SPF eggs and disposal of waste. These records must be provided to AQIS during QAP audits and at any other time on request.

e. The imported SPF eggs shall NOT be permitted to hatch[30].

5. HUMAN VACCINE MANUFACTURER'S RESPONSIBILITIES

a. The human vaccine manufacturer must nominate a person who will be accessible to Departmental officers if any problems or emergencies arise.

b. The human vaccine manufacturer should be aware that if, during the process of quarantine, it is found that the pre-export testing or certification requirements have not been fully met, the consignment may be re-exported or destroyed.

[30] The hatching and use of chicks from imported SPF eggs, except within the high security area of AAHL, will require an additional formal risk analysis with biosecurity arrangements expected to be equivalent to that for importation of live birds.

c. All costs associated with the testing, transport, quarantine and veterinary supervision during the importation program must be met by the importer/agent and/or vaccine manufacturer.

d. If any procedures are not permitted or eggs, birds or other product are tested, re-exported or destroyed during any period of quarantine control, compensation will not be paid by the Australian Government.

APPENDIX 1

DECLARATION BY THE OWNER OR MANAGER OF THE source SPF flock (SPF eggs destined for importation into Australia or for the production of veterinary vaccines destined for use in Australia)

(This declaration to accompany the consignment of SPF eggs)

Details of consignment

a. AQIS Import Permit No[31]: .....…….. .....
b. Importer/Recipient ....
c. Date of consignment ....
d Identification of consignment[32] ....
e. Description of consignment ....

I, ...of
.....
.....,
the owner/manager (delete one) of the source SPF flock from which the specific pathogen free (SPF) eggs were derived either for export to Australia or for the production of veterinary vaccines destined for use in Australia, hereby declare that:

1. No vaccination against any disease has been used in the source SPF flock.

2. The SPF eggs have been laid by a source SPF flock which allowed the introduction of SPF embryos only from another house of equal SPF status on the same site. All introduced birds have been in the source SPF flock and have been kept under SPF conditions for a period of not less than 4 months prior to the egg collection.

3. The source SPF flock is housed in secure rodent-proof and bird-proof buildings and is isolated by at least 400 metres from all poultry other than source SPF flocks as defined by the European Pharmacopoeia. Details of poultry within 400 metres of the source SPF flock are attached.

4. The source SPF flock has maintained its SPF status and has been free from clinical signs of the diseases listed in Appendix 5 within the lifespan of all birds within the flock and has not come into contact with any birds showing evidence of these diseases.

5. The SPF eggs for export to Australia, or for use in veterinary vaccines destined for Australia, were collected over a period of fourteen (14) days or less. The SPF eggs were collected separately to floor and dirty eggs. No floor or dirty eggs are included in this consignment of SPF eggs.
   Dates of collection ……...

[31] Only applicable for shipments of SPF eggs to Australia.
[32] Specific identification markings or coding on the SPF eggs

6. After collection, the SPF eggs referred to in Section 5 above were stacked on new or clean, disinfected egg flats so as to permit air circulation and, within 4 hours of lay, were either:

   (i) fumigated with formaldehyde gas (generated by the addition of 35 cc of commercial formalin [40% solution] to 17.5 grams of potassium permanganate for each 2.38 cubic metres of fumigation space) in a suitable room or cabinet with forced ventilation at a temperature of at least 20^{o}C and a relative humidity of between 80% and 90% for 20 minutes with no free water; or

   (ii) disinfected by an alternative procedure of at least equal efficacy which has prior approval of the Director of Animal and Plant Quarantine (Australia).

7. The SPF eggs referred to in Section 6 above were packed in the room in which they were disinfected. After disinfection, cooling and drying, the SPF eggs were packed and sealed in air tight egg boxes for transport. Only new crates and separators were used. The SPF eggs were handled and packed in a manner to avoid possible re-contamination. The SPF eggs were placed in plastic bags or the approved containers were lined with plastic to prevent any leakage if damage to the SPF eggs occurs during transport. The sealed boxes were held and transported in a manner preventing cross contamination with risk material.

Signature: ..... Date: .....

The contents of this declaration were explained to the Owner and his signature witnessed by

Signature: ..... Date: .....
Official Government Veterinarian
Name: .....
Address: .....
.....

NOTE: All pages are to be endorsed with the Official Stamp of the Government Veterinary Authority of the country of export.

APPENDIX 2

FIRST CERTIFICATE FROM AN OFFICIAL GOVERNMENT VETERINARIAN OF THE COUNTRY OF ORIGIN
(SPF eggs destined for importation into Australia or for the production of veterinary vaccines destined for use in Australia)
(This certificate to accompany the consignment of SPF eggs)

Details of Consignment

a. AQIS Import Permit No[33]: .....
b. Importer/recipient .....
c. Date of consignment .....
d Identification of consignment[34] .....
e. Description of consignment .....

I,....., an Official Government Veterinarian of .... hereby certify that:

1 (a)[#] Clinical Newcastle disease and avian influenza have not been reported in poultry in the country of origin during the previous three years.

OR

(b)[#] The country of origin has a stamping-out policy for clinical Newcastle disease and highly pathogenic avian influenza and neither disease has been reported within a 25 km radius of the source SPF flock in the past 30 days.

[#] DELETE ONE OF (a) OR (b)

2. The source SPF flock, from which the SPF eggs were derived, has not been vaccinated any disease.

3. The source SPF flock has been under my supervision for the previous 90 days and, after due enquiry, I have no reason to doubt the truth of the owner's/manager's declaration (Appendix 1).

4. I am satisfied that the source SPF flock has been clinically free from all diseases listed in Appendix 5 during the period of 90 days prior to the collection of the SPF eggs.

After due enquiry, I am also satisfied that the source SPF flock has been free from clinical signs of all other infectious diseases during the period of 90 days prior to the collection of the SPF eggs.

[33] Only applicable for shipments of SPF eggs to Australia
[34] Specific identification markings or coding on the SPF eggs

5. The source SPF flock is approved by .....(government veterinary authority) as a specific pathogen free flock meeting the standards specified by current European Pharmacopoeia Chapter 5.2.2.

6. The size of the source SPF flock is ……. birds.

7. Within 21 days before the first day of collection of the SPF eggs, a sample of the parent flock was tested for freedom from the following pathogens using an applicable test standard specified in Appendix 5 for the relevant pathogen[35]:

Note 1: The sample size should be at least 5% of the source SPF flock but not less than 10 and need not be more than 200 birds (ie European Pharmacopoeia rate).

*Note 2: If the SPF eggs are destined for live avian vaccine production, a higher sample size may be required for those pathogens marked with a * to provide at least a 99% confidence of detecting the disease at a 0.5% prevalence level after accounting for test sensitivity. Refer to the policy and end user for more information.*

(a) for all SPF eggs destined for export to Australia or for production of veterinary vaccines for use within Australia

Pathogen	Test used	Test sensitivity (%)	Sample size (number of birds tested)	Present in country of origin	100% of birds in flock tested within previous 12 months
* Avian adenovirus group 1				Yes/No	Yes/No
Avian adenovirus group 2				Yes/No	Yes/No
Avian encephalomyelitis virus				Yes/No	Yes/No
* Avian infectious bronchitis virus				Yes/No	Yes/No
Avian infectious laryngotracheitis virus				Yes/No	Yes/No
Avian leucosis virus				Yes/No	Yes/No
Avian nephritis virus				Yes/No	Yes/No
* Avian reoviruses				Yes/No	Yes/No
Avian reticulo-endotheliosis virus				Yes/No	Yes/No
Chick anaemia virus				Yes/No	Yes/No
Haemagglutinating avian adenovirus (Egg drop syndrome-76 virus)				Yes/No	Yes/No
Infectious bursal disease virus				Yes/No	Yes/No
* Influenza virus type A				Yes/No	Yes/No
Marek's disease virus				Yes/No	Yes/No
* Newcastle disease virus				Yes/No	Yes/No
* Turkey viral rhinotracheitis virus (avian pneumovirus)				Yes/No	Yes/No
Mycoplasma gallisepticum				Yes/No	Yes/No
Mycoplasma synoviae				Yes/No	Yes/No
Salmonella Pullorum				Yes/No	Yes/No

[35] It is the vaccine manufacturer's responsibility to ensure the test procedures and sampling rates used also comply with the requirements of the relevant regulatory authorities in the countries in which the final vaccines will be marketed including Australia.

(b)[#] for SPF eggs for production of veterinary vaccines for use within Australia

Pathogen	Test used	Test sensitivity (%)	Sample size (number of birds tested)	Present in country of origin	100% of birds in flock tested within previous 12 months
* Avian paramyxovirus type 2				Yes/No	Yes/No
* Avian paramyxovirus type 3				Yes/No	Yes/No
Fowl pox virus				Yes/No	Yes/No
Turkey herpes virus				Yes/No	Yes/No
Salmonella Gallinarum (Fowl typhoid)				Yes/No	Yes/No
Salmonella Enteritidis				Yes/No	Yes/No

[#] DELETE TABLE (b) IF SPF EGGS NOT DESTINED FOR VETERINARY VACCINE PRODUCTION

8. Where there were positive or suspicious reactors for *Salmonella* Pullorum, *Salmonella* Gallinarum or *Salmonella* Enteritidis, all of the reactors were killed and their organs cultured.

9. Within 21 days before the first day of collection of the SPF eggs, the source SPF flock was determined to be free of infection with *Salmonella spp*

   The absence of *Salmonella spp* was determined by procedures to culture and isolate them from faecal samples or shed litter.

   [#](i) Twenty samples were randomly collected from each shed. Each sample was a composite sample of 3 floor and 2 nest litter samples (ie a total of 60 floor locations and 40 nest boxes per shed).

   [#](ii) Faecal samples were collected at random from ..... birds (ie 5% of the flock but not less than 10 and need not be more than 200 birds). Samples were pooled with up to 10 samples per pool and each pool tested.

   (# DELETE ONE OF (i) OR (ii))

   Tests used: .....
   Total number of composite samples tested: .....

10. All tests for Sections 7, 8, and 9 above were carried out in a government laboratory or a laboratory accredited or approved by the government of the country of origin for such testing purposes. The tests are tests listed in the standards column of Appendix 5 for the relevant pathogen or tests approved by the Director of Quarantine (Australia). The laboratory accreditation or approval is based on proficiency testing and the tests used were appropriately validated. The results of all tests were negative.

11. Copies of the test results specified in Sections 7, 8, 9 and 10 are attached. Copies of results for all other pathogen testing and disease investigations within the 4 month period prior to egg collection and until the date of consignment are also attached.

Signature: ..... Date: .....
Official Government Veterinarian
Name: .....
Address: .....

Note 3: All pages are to be endorsed with an Official Stamp of the Government Veterinary Authority of the country of export.

Note 4: Laboratories conducting the tests on the source SPF flock and must be accredited by the relevant government authority. Accreditation or approval should be based on an appropriate proficiency testing program. All tests undertaken for the purposes of this policy should be appropriately validated on a regular basis

APPENDIX 3

SECOND CERTIFICATE FROM AN OFFICIAL GOVERNMENT VETERINARIAN OF THE COUNTRY OF ORIGIN
(SPF eggs destined for importation into Australia or for the production of veterinary vaccines destined for use in Australia)

Details of consignment

a. AQIS Import Permit No[36]: .....
b. Importer/recipient .....
c. Date of consignment .....
d Identification of consignment[37] .....
e. Description of consignment .....

This certificate relates to the post-collection observation, production records and disease status of the source SPF flock and should be sent to the recipient of the SPF eggs with a copy to the Manager, Biologicals Unit, AQIS, GPO Box 858, Canberra, ACT 2601 as soon as possible after the completion of the 21 day post-collection observation period.

I,....., an Official Government Veterinarian of ..... (country of origin) hereby certify that:

1. The source SPF flock, from which the SPF eggs were derived, has been under my supervision for the 21 days since the SPF eggs were collected.

2 *(a) Clinical Newcastle disease and avian influenza have not been reported in the country of origin during this period and vaccination against these diseases is not permitted.

OR

*(b) Clinical Newcastle disease and avian influenza have not been reported within a 25 km radius of the source SPF flock during this period.

* DELETE ONE OF (a) OR (b)

3. After due enquiry, I am satisfied that the source SPF flock has remained a closed flock and any clinical evidence of disease has been investigated and the results indicated that the diseases listed in Appendix 5 have not occurred during the period since collection of the SPF eggs.

After due enquiry, I am also satisfied that the source SPF flock has been free from clinical signs of all other infectious diseases since collection of the SPF eggs.

[36] Only applicable for shipments of SPF eggs to Australia
[37] Specific identification markings or coding on the SPF eggs

4. Any clinical disease in the source SPF flock or drop in quantity, quality, or fertility/hatchability of the SPF eggs produced by the source SPF flock has been investigated to determine the cause and the laboratory reports are attached.

5. Within the 21 days after collection of the SPF eggs, the source SPF flock has been tested for freedom from pathogens listed in the current European Pharmacopoeia Chapter 5.2.2. The test results are attached.

6. Within 21 days after collection of the SPF eggs, a sample of the source SPF flock was tested for freedom from Newcastle disease and avian influenza. The sample[38] tested was of a sufficient size to give at least a 99% confidence of detecting disease if there was a 5% disease prevalence in the source SPF flock (see Appendix 6).
   Total number of birds in the source SPF flock: .....
   Total number of birds tested: .....

   NOTE: DELETE REFERENCE TO INDIVIDUAL DISEASE OR CLAUSE 6 ENTIRELY AS APPROPRIATE IF AVIAN INFLUENZA AND/OR NEWCASTLE DISEASE ARE NOT PRESENT AND VACCINATION AGAINST THESE DISEASES IS NOT PERMITTED IN THE COUNTRY OF ORIGIN.

Signature: ..... Date: .....
Official Government Veterinarian

Name: .....
Address: .....
.....
NOTE: All pages are to be endorsed with the Official Stamp of the Government Veterinary Authority of the country of export.

[38] Testing performed as part of the routine European Pharmacopoeia testing (ie as per Section 5 above) may be included in the sample size. Sampling above that required by the European Pharmacopoeia should only be necessary if the flock size is less than 1800 birds.

APPENDIX 4

CERTIFICATE FROM THE VETERINARY/TECHNICAL SUPERVISOR OF THE APPROVED VETERINARY VACCINE FACILITY

Details of SPF egg consignment

a. Import Permit No[39] .....
b. Consignor .....
c. Date of Arrival .....
d Identification of consignment[40] .....
e. Description of consignment .....

I, ..., Supervising Veterinarian/Technician, of .....(vaccine manufacturer) certify that:

1. The consignment of SPF eggs described above was carried directly from the SPF facility/aircraft/distributor's premises[#] to the veterinary vaccine facility.
   # DELETE AS APPLICABLE

2. All packing materials consigned with the imported SPF eggs were destroyed by incineration or other AQIS approved method.
   # DELETE 2 IF VACCINE IS NOT MANUFACTURED IN AUSTRALIA.

3. Testing for contamination:
   (a) Appropriate biohazard precautions were taken during collection, preparation and transport of all samples.
   # DELETE (a) IF VACCINE IS NOT MANUFACTURED IN AUSTRALIA

   (b) A representative sample of shell debris, membranes, etc[41] from each tray of SPF eggs used in the vaccine production has been tested and found to be free from *Salmonella spp* as per Australian Standard AS1766.2.5 or other AQIS approved method. All embryonic mortalities, prior to inoculation, were also sampled and tested.

   (c) All abnormalities observed with the SPF eggs including, where applicable, a high embryonic mortality were investigated to determine the cause. A report is attached on the investigations.

   (d) **For inactivated vaccine**[#]
   # DELETE (d) IF NOT APPLICABLE

   A representative sample of each batch of bulk vaccine prior to any inactivation procedure and addition of adjuvant has been tested and found to be free of contamination with extraneous infectious agents. Testing was in accordance with the "Specific Quarantine Requirements

[39] If imported by the Australian vaccine manufacturer. Otherwise, attach batch identifiable details and any copies of relevant AQIS approvals.
[40] Specific identification markings or coding on the SPF eggs
[41] Egg waste after vaccine production may be used.

for the Importation of Inactivated Veterinary Vaccines" (AQIS 1997) Section 3.11 "Final Product Testing – Viral vaccines" and inactivation in accordance with Section 2.5.10 "Inactivation".

(e) **For live mammalian vaccine**[#]

 # DELETE (e) IF NOT APPLICABLE

A representative sample of each batch of bulk vaccine has been tested and found to be free of contamination with extraneous infectious agents. Testing was in accordance with the "Australian Quarantine Policy and Requirements for the Importation of Live and Novel Veterinary Bulk and Finished Vaccines" (AQIS 1999) Section 5.11 "Final Product Testing – Viral vaccines".

(f) **For live avian vaccine**[#]

 # DELETE (f) IF NOT APPLICABLE

A representative sample of each batch of bulk live avian vaccine has been tested for and found to be free of the following pathogens. The sample size, detection test used and testing laboratory for each has been approved by AQIS[42].

Pathogen	Test used
*Avian adenovirus group 1	
Avian adenovirus group 2	
Avian encephalomyelitis virus	
*Avian infectious bronchitis virus	
Avian infectious laryngotracheitis virus	
Avian leucosis virus	
Avian nephritis virus	
*Avian paramyxovirus type 2	
*Avian paramyxovirus type 3	
*Avian reoviruses	
Avian reticulo-endotheliosis virus	
Chick anaemia virus	
Fowl pox virus	
Haemagglutinating avian adenovirus (Egg drop syndrome-76 virus)	
Infectious bursal disease virus	
*Influenza virus type A	
Marek's disease virus	
*Newcastle disease virus	
*Turkey viral rhinotracheitis virus (avian pneumovirus)	
Turkey herpes virus	
Mycoplasma spp	
Salmonella Pullorum	
Ornithobacterium rhinotracheale	
Salmonella Gallinarum (Fowl typhoid)	
Salmonella spp	
Haemophilus paragallinarum	

[42] Unless otherwise approved by AQIS, testing for each pathogen should be in accordance with the procedures detailed in the European Pharmacopoeia section "2.6.6 Test for extraneous agents using chicks".

Testing was preformed at[43] .....
Sampling procedure [44] …….

In addition, a representative sample of each batch of bulk vaccine has been tested and found to be free of contamination with other infectious agents. Testing was in accordance with the "Australian Quarantine Policy and Requirements for the Importation of Live and Novel Veterinary Bulk and Finished Vaccines" (AQIS 1999) Section 5.11 "Final Product Testing – Viral Vaccines".

Note: Those pathogens or certain strains of those pathogens marked with * in the above table are considered exotic to Australia. The policy requires that the source SPF flock undergoes additional sampling and testing for these pathogens. As an alternative to this additional sampling, AQIS may consider the use on the final live avian vaccine of a generic PCR or other highly sensitive test, capable of detecting extremely low levels of the antigen, regardless of pathogen strain. Manufacturers should note that the presence of any antigen, whether viable or non-viable, is unacceptable as it indicates either a breakdown in biosecurity in the source SPF flock, contamination of the master seed or other substrates used, or cross contamination during the production process.

4. All samples and other waste materials held in quarantine pending test results or clearance from AQIS will be sterilised, destroyed or otherwise disposed of in accordance with the approved QA Manual once AQIS approval for release of the final vaccine has been obtained. All other waste and other products that have been in direct or indirect contact with the imported SPF eggs including dead embryos, broken eggs, shells, unused tissue, etc have either been effectively sterilised or destroyed in accordance with the approved QA manual.

 # DELETE 4. IF VACCINE IS NOT MANUFACTURED IN AUSTRALIA

5. During the quarantine and/or vaccine production period, all appropriate security measures with respect to the Quarantine Approved Premises and/or production were taken. This included the SPF eggs, their storage facilities and staff associated with the SPF eggs. To my knowledge at no stage during this period was there a breakdown in security.

6. I attach the reports from the approved testing laboratories which identify the samples tested, establish the validity of all tests undertaken and state the results of all tests.

7. I attach the two certificates which I have received from the Government Veterinary Officer of the country of origin of the SPF eggs and the declaration by the owner/manager of the source SPF flock, which refer to this consignment of SPF eggs. Also attached are copies of the test results of the source SPF flock for the 4 month period prior to egg collection and the 21 day period after.

8. The following veterinary vaccines were manufactured using the SPF eggs of non-Australian origin of this consignment:

---

[43] Testing should be conducted at the Australian Animal Health Laboratory (AAHL). The use of alternative independent laboratories may be possible subject to approval by AQIS.

[44] The sampling rate and/or volume sampled should be detailed.

Vaccines	Production dates	Batch Numbers
.....	.....	.....
.....	.....	.....
.....	.....	.....
.....	.....	.....

Signature: ..... Date: .....
Name: .....
Supervising Veterinarian/Technician
.....(Vaccine company)

For vaccines produced within Australia using imported SPF eggs[45]:

AQIS APPROVAL

After consideration of all relevant information, the above vaccine batches manufactured using the SPF eggs of non-Australian origin of this consignment

ARE / ARE NOT

approved for release from quarantine.

Signature: ..... Date: .....
Name: .....
Authorised Officer of the Director of Quarantine
Australian Quarantine and Inspection Service
Note: All pages are to be endorsed with the Official Stamp

[45] Approval of vaccines manufactured overseas using *SPF eggs of non-Australian origin* will be in the form of an AQIS "Permit to Import Quarantine Material".

APPENDIX 5

STANDARDS/SPECIFICATIONS FOR TESTS

PATHOGEN	source SPF flock		Bulk vaccine	PROCEDURES
	Pre-egg collection	Post-egg collection		
Avian adenoviruses	*Serology*	*Serology*	*Serology*	Serology: ELISA; Gel-precipitin
Avian encephalomyelitis virus	*Serology*	*Serology*	*Serology*	Serology: ELISA; Serum neutralization (SN)
Avian infectious bronchitis virus	*Serology*	*Serology*	*Serology*	Serology: ELISA; SN or Haemagglutination inhibition (HIT)
Avian infectious laryngotracheitis virus	*Serology*	*Serology*	*Serology*	Serology: SN or ELISA
Avian leucosis virus	*Serology*	*Serology*	*Serology*	ELISA for virus (initial testing).SN for antibody (subsequent testing)
Avian nephritis virus	*Serology*	*Serology*		Serology: Florescent antibody (FA)
Avian paramyxovirus type 2 and 3	*Serology*	*Serology*	*Serology*	Serology: HIT
Avian reoviruses	*Serology*	*Serology*	*Serology*	Serology: ELISA (initial testing), FA (subsequent testing); Gel-precipitin or FA
Avian reticulo-endotheliosis virus	*Serology*	*Serology*	*Serology*	Serology: FA
Chick anaemia agent	*Serology*	*Serology*	*Serology*	Serology: FA
Fowl pox virus	*Serology*	*Clinical*	Serology	Clinical: Examination, history and histopathology
Haemorrhagic enteritis virus disease of turkeys	*Clinical*	*Clinical*		Clinical: Examination and history
Haemagglutinating avian adenovirus (Egg drop syndrome-76 virus)	*Serology*	*Serology*	*Serology*	Serology: Haemagglutination inhibition
Infectious bursal disease virus	*Serology*	*Serology*	*Serology*	Serology: SN (initial testing) and immunodiffusion (subsequent testing) against each serotype present in country of origin.; AGID; ELISA
Influenza virus type A	*Serology*	*Serology*	*Serology*	Serology: ELISA; AGID :
Marek's disease virus	*Serology*	*Serology*	*Serology*	Serology: ELISA; FA; AGID
Newcastle disease virus	*Serology*	*Serology*	*Serology*	Serology: Haemagglutination inhibition :
Turkey viral rhinotracheitis virus	*Serology*	*Serology*	*Serology*	Serology: ELISA
Turkey herpes virus	*Serology*		*Serology*	Serology: Gel-precipitin; FA
Mycoplasma gallisepticum	*Serology*	*Serology*	*Culture*	Serology: Agglutination (& haemagglutination inhibition to confirm positives); Rapid slide agglutination Culture: with controls
Mycoplasma synoviae	*Serology*	*Serology*	*Culture*	Serology: Agglutination (& haemagglutination inhibition to confirm positives); Rapid slide agglutination Culture: with controls
Ornithobacterium rhinotracheale	*Clinical*	*Clinical*	*Culture*	Clinical: Examination and history Culture: with controls
Haemophilus paragallinarum	*Clinical*	*Clinical*	*Culture*	Clinical: Examination and history Culture: with controls
Mycoplasma iowae	*Clinical*	*Clinical*		Clinical: Examination and history

PATHOGEN	source SPF flock		Bulk vaccine	PROCEDURES
	Pre-egg collection	Post-egg collection		
Mycoplasma spp			*Culture*	Culture
Salmonella Pullorum	*Serology*	*Serology*	*Serology*	Serology: Agglutination; Rapid slide agglutination; Whole blood tube agglutination test
Salmonella Gallinarum (Fowl typhoid)	*Serology*	*Clinical*	*Serology*	Serology: Rapid serum agglutination test; Whole blood tube agglutination test. Clinical: Examination and history
Salmonella Enteritidis	*Serology*	*Clinical*	*Serology*	Serology: Rapid serum agglutination test; Whole blood tube agglutination test. Clinical: Examination and history
Salmonella spp	*Culture*	*Culture*	*Culture*	Culture
Other infectious agents	*Clinical*	*Clinical*	Routine final product testing.	Clinical: Examination, history and pathology Routine final product testing: for bacterial, fungal, mycoplasma sterility and extraneous viral agents

Note: Subject to prior AQIS approval, more highly sensitive tests would be an acceptable, and in most cases, preferable alternative diagnostic or detection test to the tests listed above. In the context of this policy, a highly sensitive test refers to an appropriate polymerase chain reaction (PCR) test, PCR variant or other highly sensitive test, specifically approved by AQIS, to detect the presence, at extremely low titres, of any and all strains of the extraneous pathogen in the final bulk live avian vaccine.

Clinical: Requires declaration of freedom based on absence of clinical signs and history

APPENDIX 6

SAMPLE SIZE TO DETECT DISEASE

Sample size required to detect disease (assuming 100% test sensitivity)		
Prevalence	**0.5%**	**5.0%**
Confidence level	**99%**	**99%**
Population size	**Sample size**	
10	10	10
20	20	20
30	30	29
40	40	36
50	50	42
60	60	47
70	70	51
80	80	54
90	90	57
100	100	59
120	120	63
140	140	67
160	160	69
180	179	71
200	198	73
250	244	76
300	286	78
400	360	81
450	392	82
500	421	83
600	470	84
700	512	85
800	546	85
900	576	86
1000	601	86
1200	642	87
1400	674	87
1600	699	88
1800	720	88
2000	737	88
3000	792	89
4000	821	89
5000	840	89
6000	852	90
7000	861	90
8000	868	90
9000	874	90
10000	878	90
20000	898	90