



Australian Government

Biosecurity Australia

CONTINGENCY IMPORT POLICY FOR SPECIFIC PATHOGEN FREE (SPF) CHICKEN EGGS

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DEPARTMENT OF AGRICULTURE, FISHERIES AND FORESTRY

CONTINGENCY IMPORT POLICY FOR SPECIFIC PATHOGEN FREE (SPF) CHICKEN EGGS

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.

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.

For the purpose of this policy, an SPF flock is defined as a group of birds sharing a common environment and having their own caretakers who have no contact with non-SPF poultry flocks. This policy contains requirements for sampling and testing of the source flock for at least 12 months prior to egg collection. For the purpose of meeting these requirements, in cases where the production SPF flock is less than 12 months of age or has not been defined by specified testing for at least 12 months, the preceding test results of the parent (progenitor) flock shall be included in the definition of the specified SPF flock to provide a summed 12 months screening period.

Rationale for a policy

Uses of SPF eggs

Availability of SPF eggs is critical to a number of biomedical and veterinary procedures. These include both *in vitro* and *in vivo* uses. *In vitro* uses include

- . disease diagnosis,
- . biomedical research, and
- . quarantine surveillance programs.

While *in vivo* uses include:

- . the hatching of SPF eggs to produce SPF chickens for various purposes,
- . the production of some mammalian and human vaccines,
- . the production of most inactivated avian vaccines, and
- . the production of live avian vaccines.

The various uses of SPF eggs pose different levels of quarantine risk.

Need for continuity of supply

Clearly, the uses of SPF eggs are vital to the ongoing health of Australia's animals and people, being involved in the production of vaccines, and for disease diagnostic and research purposes.

Some years ago, it was recognised that an interruption to domestic supplies of SPF eggs, resulting from a disease “break” in one or more of the then existing SPF flocks could have serious consequences for this country. Therefore, a contingency policy for the importation of SPF eggs was developed and promulgated in 1998. Since that time, factors such as a reduction in the number of local SPF egg producers and an increased demand for live vaccines have prompted a review of the import policy for SPF eggs. This review has been underway for some time. Recently, one of the two SPF flocks maintained by the sole Australian supplier became infected with chicken anaemia virus. If there is a disease outbreak in the other flock, the only option to ensure continued access to address these essential needs will be to import SPF eggs. The need for a policy which facilitates importation yet adequately manages the risk is critical.

Policy review

Biosecurity Australia reviewed the quarantine policy for SPF eggs following requests from three Australian vaccine manufacturers to remove the contingency clause from the current policy on the importation of SPF eggs for vaccine production, and to permit the use of SPF eggs of overseas origin in live avian vaccines. In February 2004, Biosecurity Australia released Animal Biosecurity Policy Memorandum (ABPM) 2004/03¹ for public consultation. APBM 2004/03 included two attachments: a review of the quarantine risks and a draft policy for the importation of non-Australian SPF eggs and the importation of veterinary vaccines manufacturers using non-Australian SPF eggs.

A summary of matters considered in the previously published policy review, and as a result of submissions received in response to that draft policy, follows.

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

Laboratories which are Quarantine Approved Premises (QAP) for the purposes of handling imported SPF eggs have procedures in place to ensure compliance with these control measures.

Risks associated with 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. The use of SPF eggs in the production of live avian vaccines is considered a high animal quarantine risk.

¹ Animal Biosecurity Policy Memorandum ABPM 2004/03 is available at <http://www.daff.gov.au> under Biosecurity Australia - Animal Biosecurity

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.

When there is a need to hatch SPF eggs, there is also the risk that any exotic pathogens contained in the eggs may be present also in the offspring. Australia currently has a policy to manage risks associated with the importation of hatching eggs, which has different testing requirements to those required for SPF flocks. It is therefore considered that no offspring derived from imported SPF eggs should be released from quarantine control except where they have met all the requirements of the existing hatching egg policy.

For these reasons, SPF eggs of non-Australian origin should only be used for vaccine production or other *in vivo* uses, 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 exhausted².

Interaction between Quarantine Act and other legislation

A contaminated veterinary vaccine could result in the introduction, establishment and/or spread of an exotic disease or the further spread of an endemic disease. In addition to protecting Australia from incursion by exotic diseases, the *Quarantine Act 1908* also provides a responsibility to prevent the further spread of endemic disease. 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. However, controls on endemic pathogens would not exceed those applied by the Australian Pesticides and Veterinary Medicines Authority (APVMA) to domestic vaccine production. SPF eggs produced in Australia and used in the Australian manufacture of veterinary vaccines comply with European Pharmacopoeia standards.

Comments on the previous draft policy (ABPM 2004/03)

All submissions received had substantial merit, although their perspectives were divergent. Biosecurity Australia would like to thank contributors for their submissions.

The proposals in the previous draft for additional testing of the non-Australian SPF source flock and the use of more highly sensitive detection methods on the finished vaccine provide a considerable level of quarantine confidence. However, from comments received, these requirements would have been impractical, overly expensive and onerous, thereby limiting the availability of eggs when needed.

A different approach to testing of the SPF source flock has been proposed by a respondent to the previous draft policy. Biosecurity Australia has modelled this approach and found it to be both practical and to provide a level of quarantine confidence at least equivalent or better than previous policies. It has been peer reviewed and confirmed to have scientific merit. The draft policy for

² Refer to the quarantine review of the import policy (February 2004) for the reasons why live avian vaccines are considered higher risk than other products.

importation of SPF eggs has been revised accordingly. A workshop was also held with key stakeholders in September 2005 to discuss this approach and other issues, and the outcomes of that workshop have been incorporated into this policy.

The recent breakdown (September 2005) of one of only two Australian SPF flocks highlights the urgent need for end users to be able to access imported eggs during critical shortages. However, there is a history of disease breakdowns into SPF flocks leading to contaminated vaccines. For this reason, this import policy is released as a contingency policy to be used to facilitate importation of non-Australian SPF eggs or veterinary vaccines manufactured overseas using non-Australian SPF eggs, only when there is insufficient domestic supply to meet critical national needs.

The policy

Basis

Stakeholder submissions to ABPM 2004/03 emphasised that vaccine contamination due to SPF flock breakdowns are more likely to be due to inadequate application of standards or a recent disease incursion prior to egg collection, than to insufficient sampling and testing of the flock or inadequate sensitivity of tests used. A respondent proposed an alternative testing regime that included continued sampling of the source flock as per European Pharmacopoeia³ requirements until several weeks after egg collection. The results would be made available before live vaccines produced from the eggs are released from quarantine. In combination with testing of the bulk vaccine, such a proposal would ensure that disease incursion around the time of egg collection would be detected before products derived from those eggs could be released for use in Australia.

The confidence in detecting a disease in the SPF flock using the respondent's proposed approach has been modeled statistically, and found to be at least as high as the original proposal of 99% confidence in detecting disease at 0.5% prevalence. Details of the mathematical modeling are summarised in Appendix 1 with further details available on request.

Testing of samples from the SPF source flock would depend on the proposed end-use of the SPF eggs.

SPF eggs imported for *in vitro* use or human therapeutic use only

- All SPF eggs imported for *in vitro* or for human therapeutic use (including human vaccine production) should be free of exotic animal pathogens of quarantine concern.
- There is a very low likelihood of exposure of susceptible birds to these eggs or their products. Therefore, Biosecurity Australia considers that compliance with European Pharmacopoeia requirements is sufficient provided that:
 - All importing and other facilities using the imported eggs are AQIS Quarantine Approved Premises (QAP)⁴ with appropriate controls on storage, handling, security and disposal; and
 - The SPF eggs and/or any derivatives do not leave the QAP without prior AQIS approval, unless for disposal in accordance with AQIS requirements; and

³ <http://www.phEur.org/>

⁴ Activities within a QAP remain under quarantine control. QAPs are approved and subject to regular audit by AQIS.

- Imported SPF eggs are not permitted to hatch unless the requirements for hatching eggs are also met (see details below).
- Where used in human therapeutic production, it is the importer's and end user's responsibility to ensure compliance with all relevant requirements of other regulatory authorities such as the Australian Government Department of Health and Ageing, including the Therapeutic Goods Administration (TGA).

SPF eggs imported for hatching

- If SPF eggs are imported for hatching, the eggs should be hatched and the birds held within either a physical containment (PC) level 4 facility⁵; or other secure facility, approved by the Australian Quarantine and Inspection Service (AQIS) as meeting all relevant biosecurity requirements of the policy, "Conditions for the importation from approved countries of fertile eggs (domestic hen)".
- If permitted to hatch, the live birds would only be permitted to leave the facility if the source flock and the hatched birds have met the policy, "Conditions for the importation from approved countries of fertile eggs (domestic hen)"⁶.
- Any products produced using the imported SPF eggs and hatched birds would not be permitted to leave the facility without prior AQIS approval, unless for disposal in accordance with AQIS requirements.

SPF eggs imported for use in veterinary vaccine production or non-Australian SPF eggs used in the overseas production of live avian vaccines destined for Australia

A contaminated veterinary vaccine could result in the introduction, establishment and/or spread of an exotic disease or the further spread of an endemic disease. Quarantine control is justified under the *Quarantine Act 1908* and subordinate legislation if such introduction, establishment or spread is likely to cause significant animal health, environmental or economic impacts. Therefore, quarantine controls on endemic as well as exotic pathogens are considered necessary. Controls on endemic pathogens would not exceed those applied by the Australian Pesticides and Veterinary Medicines Authority (APVMA) to domestic vaccine production. SPF eggs produced in Australia and used in the Australian manufacture of veterinary vaccines comply with European Pharmacopoeia standards. APVMA recognises the European Pharmacopoeia as an acceptable standard for Australian vaccines.

- Assessment in relation to exotic animal pathogens would be undertaken by AQIS.
- Assessment in relation to endemic pathogens would be undertaken by either AQIS or APVMA prior to clearance of the finished vaccine from quarantine.

⁵ Physical Containment (PC) Levels are defined in the Australian/New Zealand Standard for Safety in Laboratories AS/NZS 2243.3:2002. The high security area within the Australian Animal Health Laboratory, Geelong, Victoria is a PC Level 4.

⁶ Available as ABPM2004/14 at <http://www.daff.gov.au> under Biosecurity Australia – Animal Biosecurity. The requirements for hatching eggs, in relation to SPF eggs, will be reviewed when this interim policy is also reviewed.

Live mammalian vaccine and inactivated avian vaccines

- Testing of the source SPF flock would be in accordance with, and for the presence of all diseases listed in Section 5.2.2. "Chicken flocks free from specified pathogens for the production and quality control of vaccines" of the most recent European Pharmacopoeia [i.e. at 5% of flock per month (or 1.25% per week)]⁷ over the 12 month period⁸ prior to egg collection; and
- Testing of live mammalian vaccines would also be in accordance with the "Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines" (1999).
- Testing of inactivated avian vaccines would also be in accordance with Australia's "Specific quarantine requirements for the importation of inactivated veterinary vaccines" (1997).
- Imported SPF eggs are not permitted to hatch unless the above requirements for hatching eggs are also met.

Live avian vaccines

- Testing of the source SPF flock would be in accordance with, and for the presence of all diseases listed in 5.2.2. "Chicken flocks free from specified pathogens for the production and quality control of vaccines" of the most recent European Pharmacopoeia⁹ at 5% of flock per month (or 1.25% per week)
 - over the 12 month period prior to egg collection AND
 - for the following time period after egg collection but prior to the release of the vaccine from quarantine
 - at least 12 weeks for flocks of 8,000 birds or less; or
 - at least 14 weeks for flocks of 8,001 to 16,000 birds; or
 - at least 16 weeks for flocks of 16,001 to 22,000 birds¹⁰
- Testing¹¹ for avian paramyxovirus types 2 and 3 would be:
 - a) Testing of the source SPF flock at 5% of flock per month (or 1.25% per week) for 12 weeks after egg collection and prior to release of the vaccine from quarantine (or greater as per the above mentioned time period, based on flock size)¹², and
 - b) Testing of the bulk vaccine for each pathogen.

⁷ At least 10 but need not be more than 200 birds tested per flock per month.

⁸ Testing history of parent birds will be considered if there is less than 12 months testing history on the source birds. Refer to the definition of flock.

⁹ The most recent version of the Eu.Pharm. now includes avian leucosis subtype J.

¹⁰ The time frame for flocks greater than 22,000 will be determined by BA on request but will be approximately 2 extra weeks for every additional 10,000 birds.

¹¹ Tests used should be approved by AQIS prior to being undertaken. The haemagglutination inhibition test, as described by OIE, is considered an acceptable test.

¹² Tests undertaken for Newcastle disease may be considered as meeting this requirement if the proponent provides valid data substantiating that there is sufficient cross reaction with each of these paramyxoviruses including NDV.

- For *Haemophilus paragallinarum* and *Ornithobacterium rhinotracheale* – Testing of the bulk vaccine for each pathogen.
- Testing of the live avian vaccine would also be in accordance with the “Australian quarantine policy and requirements for the importation of live and novel veterinary bulk and finished vaccines” (1999).

It will be difficult to determine if a positive test on the source SPF flock was due to an incursion before, during or after egg collection. If the incursion is by a disease agent exotic to Australia, vaccines manufactured on eggs from that flock will not be permitted to be used in Australia. If the agent is endemic to Australia, responsibility for determining if and under what circumstances vaccines would be acceptable rests with APVMA.

- Imported SPF eggs are not permitted to hatch unless the above requirements for hatching eggs are also met.

Contingency use

- The importation of non-Australian SPF eggs and the importation of live avian vaccines manufactured overseas using non-Australian SPF eggs remains contingent on demonstration of a critical national need. That is, importation and/or use of non-Australian SPF eggs will only be considered if there is an inadequate supply of Australian SPF eggs to meet the production needs of essential veterinary vaccines, human therapeutic use and *in vitro* uses.
- A disease incursion into all Australian SPF flocks would result in a critical national need as no Australian SPF eggs would be available.
- The policy will be reviewed in the future, in light of its operation and the contingency requirement will be re-examined as part of this review.
- In other cases where there is or is likely to be substantial shortage of SPF eggs, and prior to AQIS issuing an import permit for SPF eggs or for live avian vaccines manufactured overseas using non-Australian SPF eggs, Biosecurity Australia will consult with Animal Health Committee on whether there is a critical national need.
- In providing a recommendation to AQIS on whether there is a legitimate critical national need in cases where SPF egg production in Australia may not meet the demands of vaccine manufacturers or other end users, Biosecurity Australia will consider:
 - the animal and public health risk to Australia arising from the unavailability of SPF eggs for the production of vaccines, or for diagnostic or other purposes; and
 - the animal health risk due to the use of the SPF eggs of non-Australian origin.
- To achieve this, in the first instance, BA will seek advice from:
 - Australian SPF egg producers on whether there are sufficient SPF eggs available to meet vaccine production and other critical needs; and
 - Australian vaccine companies on whether there is sufficient stock of the vaccine(s) to protect the national flock; and

- Peak national poultry associations on impact to health and welfare of the national flock through non-availability of the vaccine(s); and
 - The Department of Health and Ageing on the potential effect to human health of the shortage of SPF eggs; and
 - The APVMA on whether importation is supported and on issues relating to safety and registration of veterinary vaccines; and
 - TGA on the potential effect on availability of human vaccines and on issues relating to safety and registration of human vaccines.
- Biosecurity Australia will provide the above information to, and seek support from Animal Health Committee that there is a critical national need.
 - To further expedite the process, the proponent (e.g. vaccine manufacturer requesting importation) is encouraged to present Biosecurity Australia with verification of the SPF egg shortage and effect on their vaccine production, and support from the key poultry industry associations.
 - The final decision to permit importation of non-Australian SPF eggs or the importation of live avian vaccines manufactured overseas using non-Australian SPF eggs rests with the Director of Animal and Plant Quarantine (or delegate).
 - The import permit, issued by AQIS, would be limited to the period necessary to resolve the critical national need. Any extension may require additional consultation.

MATHEMATICAL MODELLING

Introduction

As a general principle, the longer the interval after disease incursion, the more a disease spreads and therefore the likelihood of detection increases with routine sampling and serological testing. The likelihoods of detecting any disease using the original draft policy (ABPM 2004/03) and using testing regimes based on a respondent's proposal are considered. An extremely conservative test sensitivity of 75% and an incursion just prior to egg collection has been used. Biosecurity Australia also considered the impact of various flock sizes and incursions at different times.

Original draft policy

The original draft policy requires that the SPF flock be sampled and tested for specific diseases of quarantine concern at a rate sufficient to provide a 99% confidence in detecting the disease, taking into consideration test sensitivity, should it exist in the flock at 0.5% prevalence. There is also a 3 week post-egg collection period where routine European Pharmacopoeia test results are also utilised.

Result: Total of 99.5% likelihood of detecting the disease if the disease exists at 0.5% prevalence.

Revised Policy

Routine European Pharmacopoeia testing (at 1.25% of the flock per week) and monitoring, post egg collection, for several weeks post egg collection. A spreadsheet model was made of the disease prevalence as it increases each week, using an extremely conservative initial disease reproductive rate of 1.5 in-contact naive birds becoming infected per infectious bird¹³.

Assuming an incursion 3 weeks prior to egg collection, an infective period of one week, one week to sero-conversion and using routine European Pharmacopoeia testing, the likelihood of the disease being detected within

- a) 8 weeks post egg collection = 98.8%
- b) 10 weeks post egg collection = virtually 100%
- c) 12 weeks post egg collection = virtually 100%

Note:

1. The likelihood of detecting the disease if the incursion occurred later (e.g. one week pre-egg collection), although marginally lower, would still be very high (e.g. 98.8% at 10 weeks and virtually 100% at 12 weeks). Also, the likelihood of any contaminated egg being collected and used in Australian vaccine manufacture would be lower.
2. Because the weekly sample size does not exceed 50 birds, likelihood of detection decreases as flock size increases above approximately 4,000 birds. Assuming an incursion at one week pre-egg collection, at 12 weeks post collection, likelihood of detection is still virtually 100% for 4,000 bird flocks and over 99.8% for flocks less than 8,000 birds. However, 14 to 16

¹³ The reproductive rate refers to the rate of spread of the disease from animal to animal. It was modelled to decrease each week, proportional to the rate that the number of naive birds decrease (and infected and immune birds increase).

weeks post egg monitoring is required to give an equivalent confidence for very large flocks of 16,000 to 22,000 birds.

C o n c l u s i o n

The reproductive rate and test sensitivity used in the model are extremely conservative. In reality, the diseases of quarantine concern are highly infectious and would spread rapidly through a naïve SPF flock. For small flocks (i.e. less than 4,000 birds), monitoring the source flock's routine European Pharmacopoeia test results for 8 weeks post egg collection provides an equivalent confidence with the original proposal, assuming an incursion three weeks prior to egg collection. However, to account for larger flocks or later incursions, monitoring results for 12 or more weeks may be necessary to achieve an equivalent level of confidence.

To address the larger flock sizes, variability between diseases and SPF management practices which may impact on the reproductive rate of the disease, Biosecurity Australia proposes that live avian vaccines produced on non-Australian SPF eggs not be released from quarantine unless the source flock remains free of disease as demonstrated by routine European Pharmacopoeia testing for the previous 12 months prior to egg collection and the subsequent

12 weeks for SPF flocks less than or equal to 8,000 birds, or

14 weeks for SPF flocks with 8,001 to 16,000 birds, or

16 weeks for SPF flocks with 16,001 to 22,000 birds.

The epidemiological model developed by Biosecurity Australia was compared with a Reed-Frost model and the results generated by the two models are very similar.