



**Australian Government**  
**Australian Pesticides and  
Veterinary Medicines Authority**



## **APVMA guideline for autogenous vaccine permit**

May 2020

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## PREFACE

This guideline outlines the different information an applicant can submit to address Australian Pesticides and Veterinary Medicines Authority (APVMA) requirements for autogenous vaccine permits. It also provides guidance on how the information might be presented and assessed. For further information on the safety, efficacy and trade criteria, refer to [our website](#).

An autogenous vaccine is an immunobiological product manufactured from a microorganism(s) isolated from an animal or animals, which the attending veterinarian believes is a causative agent(s) of the disease(s) affecting the flock, herd or aquaculture unit and used for the treatment of animals on the farm or unit in the same locality.

A permit for an autogenous vaccine(s) is generally issued for an inactivated bacterial vaccine(s) for a species, product type or specific location. Applicants are advised to use [pre-application assistance](#) if considering autogenous vaccine applications for microorganisms that are not bacterial and/or not inactivated as there are specific chemistry and safety issues that will need further consideration to ensure they meet the APVMA safety requirements.

An autogenous vaccine can only be used on the herd, flock or aquaculture unit from which the microorganism(s) was isolated. Consideration may be given to other situations where animals may need to be protected prior to the transfer to the holding or unit. It may be useful to use autogenous vaccines in production units that are geographically distinct but part of the same breeding, rearing and/or production chain. For example, pigs on grow-out farms are often best vaccinated while still in the weaner unit. In those exceptional cases, animals may be vaccinated in order to confer immunity to the animals before they encounter the pathogen in the farm they are transferred to.

This type of vaccine is prepared in response to a specific and immediate need, usually when a disease problem arises that where registered vaccines are not available or the attending veterinarian has made an evaluation that the registered vaccines are ineffective in particular situations.

An autogenous vaccine permit may be issued to cover the manufacture of a single vaccine manufactured from single or multiple microorganisms or may cover the manufacture of a range of vaccines with single or multiple microorganisms for multiple target species.

A permit allows a vaccine manufacturer that is the permit holder, to manufacture a vaccine or vaccines for more than one farm, using the permitted microorganism(s). For each farm or unit the microorganism(s) should be isolated from that farm or unit unless justified. For example, a manufacturer who holds a permit for an autogenous *Escherichia coli* vaccine can produce *E. coli* autogenous vaccine for multiple farms. In all cases, the *E. coli* should be isolated from the affected farm and the vaccine should be used in the herd or flock of origin. It would be illegal for the manufacturer to manufacture, for example, an *Actinobacillus pleuropneumoniae* autogenous vaccine, unless it holds a valid permit to produce *Actinobacillus pleuropneumoniae* autogenous vaccine.

A farm in this guideline is defined as a site or facility under a common management and serviced by a common workforce and within a geographic area defined by a common boundary (fence). An exception to this restriction is the vaccination of stock imported into a problem area where there is a high risk of the new stock being infected with a disease endemic on the farm.

The [statutory criteria](#) that the APVMA must be satisfied of to issue an autogenous vaccine permit relate to product quality and safety as well as trade. In addition to these legislative requirements, it is our general policy not to issue a permit for an autogenous vaccine if there is a suitable registered product available for that purpose, unless there is sufficient justification to support the technical advantages of the proposed vaccine or other reasons why the registered product cannot be used.

Justifications based on cost (a cheaper alternative) are generally not acceptable. A suitable or sufficient justification may include a documented assessment of ineffectiveness of the registered product. We may also consider advice from our Compliance section, registrants, state or territory departments, or the Adverse Experience Reporting Program (AERP) on claims of ineffectiveness or adverse reaction of a registered product or in situations where the registered product is unavailable. This policy ensures that the permit system will not circumvent the normal registration processes. Consequently, at the time of renewal of an autogenous vaccine permit, we take into consideration the availability of a registered vaccine with similar claims.

# 1 APPLYING FOR AN AUTOGENOUS VACCINE PERMIT

You can apply for a permit online through the [APVMA Online Services Portal](#).

## 1.1 Types of information that can be submitted to support your application

The APVMA evaluates each application on its merits, and therefore these guidelines should be interpreted flexibly. We may accept valid scientific argument in lieu of data as appropriate.

## 1.2 Information you should provide

You should provide a description of the disease on the farm or unit and the steps taken to isolate and characterise the microorganism(s) used in preparation of the autogenous vaccine(s).

You should provide a description of the vaccine(s), including the diseases and/or conditions that the immunobiological product(s) is designed to control. Information on efficacy claims is not mandatory but the applicant should provide, where possible, evidence of expected efficacy from published literature, unpublished studies or historical data.

You should also provide the clinical particulars of the vaccine(s), including as applicable:

- target species, and indications for use
- net contents of each container
- contraindications
- precautions
- side effects: with reference to frequency and seriousness if known
- dosage and method of administration, in use shelf life
- withholding periods and trade advice if applicable
- safety directions
- first aid warnings
- additional user safety
- environmental statements
- disposal
- storage.

Labels should follow the requirements of the [Veterinary Labelling Code](#) and the label requirements for [veterinary vaccines and antisera](#).

## 2 CHEMISTRY AND MANUFACTURE

### 2.1 GMP status of the manufacturing facility

Evidence that the product will be manufactured in a Category 1 GMP facility (immunobiologicals) licensed by the APVMA. You should provide the APVMA Registration number for the GMP manufacturing site.

### 2.2 Formulation or composition of the product

Full details of the immunobiological product(s) formulation must be provided. This should include the active constituent(s), adjuvants and the excipients of each autogenous vaccine included in the application. Information on the maximum and minimum release titres should be provided on the active constituent.

All adjuvants and excipients should be listed and adequate information provided on their physio-chemical nature and properties and source. The quantity of each constituent in the formulation should be expressed in appropriate units. For example the active constituent quantity should be expressed as CFU/ml. The function of each constituent and the reference to standards should be stated. A sample Certificate Analysis (CoA) for each constituent should be provided.

Any overage should be stated.

### 2.3 Containers

A description of the primary container and closure system, including the composition of the construction materials of each primary packaging component and its specification. The pack size(s) should be provided. You should provide details of the integrity of the container in terms of its compatibility with the product and its performance in protecting the product physically.

The integrity of the container should not be impaired by the product it contains or storage conditions, nor should the product be adversely affected by the packaging material.

CoAs for the primary packaging materials should be proved with reference to the appropriate standard along with the method of sterilisation.

### 2.4 Manufacturing process of the final product

A flow chart of the manufacturing process should be provided.

This should provide a summary of the steps of manufacture and tests conducted on the active and product from Master Seed through to final formulated vaccine.

Adequate description should be provided on the culture of the seed material, harvesting, any purification steps, the inactivation procedure, blending, adjuvanting, bulk antigen storage, filling, as well as in-process and final product control tests during production.

The flow chart should include all critical manufacturing steps and in-process and final product controls. If bulk antigen is subject to storage this should be explained and justified.

## 2.5 Starting materials

Starting materials means all components used in the production of the autogenous vaccine.

The European Pharmacopoeia (Ph.Eur.), British Pharmacopoeia (BP), United States Pharmacopoeia (USP) and Title 9 of the United States Code of Federal Regulations (9CFR) standards, where appropriate monographs exist, should apply to all substances in the product unless justified. Documentation from suppliers, such as certificates of analysis (CoAs) and/or raw material specifications, should be provided.

All starting materials should satisfy the requirements for use in food producing animals including minimising the risk of transmitting animal spongiform encephalopathy agents via veterinary medicinal products, as demonstrated by the provision of relevant In-Vivo Use permits from DAWE.

The specifications and standards of starting materials should be maintained throughout the life of the permit. Records should also be kept on all starting materials in accordance with current APVMA GMP requirements.

Where imported biological raw materials are used in the production of the vaccine, from the initial isolation to the manufacture of the finished product, a copy of a Department of Agriculture and Water Environment (DAWE) current biological In-Vivo Use permit should be provided.

For locally sourced starting materials the specifications should be justified and the tests and methods to ensure freedom from extraneous agents described and justified or CoA provided for the material.

### Starting materials listed in a pharmacopoeia

All starting materials listed in a pharmacopoeia should be presented with an indication as to which pharmacopoeia they are listed under and if they are compliant. The specifications should be in accordance with the Ph.Eur, BP, USP or 9 CFR as relevant and copies of a representative CoA provided.

The function of the material should be described, its method of identification and any particular issues of note, for example storage period/stability.

The name and code identifying the starting material, title of monograph, year of publication, preferably together with a copy of the monograph and certificate(s) of analysis should be submitted.

Controls and tests performed on the starting material, certificates of analysis and a DAWE current biological import permit should be provided where applicable for biological starting materials

### Starting materials of biological and non-biological origin, not listed in a pharmacopoeia

The name of each starting material (trade name, scientific synonyms), description, function, material specifications and purity should be provided.

Controls and tests performed on the starting material, certificates of analysis and a DAWE current biological import permit should be provided where applicable.

### Master and Working Seeds

A record of the origin, date of isolation, storage conditions and passage history of the microorganism(s), including identification, purification and characterisation down to the level of species, subtype, serotype or genotype as appropriate should be provided. Other information that should be submitted is listed below:

- for seed materials include a brief summary of the species of origin, geographical origin (source farm), the procedure for isolation of the suspect pathogen and passage history. Include details of method of preparation of the Pre-Master, Master and Working Seeds, tests for identification, and purity and the method of storage
- for newly isolated seeds for which data may be absent at the time of submission, it is acceptable to provide the methods and tests for a representative seed material of the same species, serotype or strain with a commitment to provide the results of the new seed when available. The applicant should provide the data for the new seed during the assessment of the application or it may form part of the post-permit approval conditions
- for newly isolated seed materials for which there is no defined procedure for manufacture and testing established for the seed material and product, the applicant should provide an outline of production on how they will manufacture and test the vaccine. The applicant should provide the data during the assessment of the application or it may form part of the post-permit approval conditions.

## 2.6 Media

The following information should be provided on the production medium:

- details of the production medium
- method of preparation of the media including any supplements and sterilisation methods
- certificates of analysis of ready-to-use media should be provided as appropriate
- tests for freedom from extraneous agents, as evidenced the submission of the current DAWE In Vivo Use Permits as appropriate
- for Australian sourced materials a CoA and a description of the methods on any in house controls for potential extraneous agents. The range of tests and/or method of inactivation or filtration should be justified.

## 2.7 In-process control tests during production

### Inactivation process

A validated inactivation process and inactivation test is critical for ensuring the safety of an autogenous vaccine and a robust data package will be required at the time of submission or fulfilled as part of the condition of the permit.

The Ph.Eur and BP monograph Vaccines for Veterinary Use, states that data on inactivation kinetics should be obtained using the selected method of inactivation, with the time required for inactivation (which, normally, should not exceed 67 per cent of the duration of the inactivation process).

The APVMA considers that extrapolation of inactivation kinetics results to higher pre-inactivation titres than those used in the corresponding validation studies is not acceptable. The maximum titre of the vaccine microorganism capable to be inactivated by the selected method of inactivation should be established based on the actual data obtained from inactivation kinetics studies. It is permitted to concentrate a representative culture to demonstrate kinetics at the highest titre that may be achieved in routine production.

Inactivation kinetics data should be provided on a representative production batch using the species of microorganism.

A validation report of the in process inactivation test used to verify each batch of inactivated vaccine should be provided with LOD using the inactivated organism.

- for newly isolated seeds for which in process data may be absent at the time of submission, it is acceptable to provide details of the inactivation kinetics and inactivation test for a representative isolate/seed of the same species, serotype or strain with a commitment to provide the results of the new seed when available. The applicant should provide the inactivation data during the assessment of the application
- for newly isolated seeds for which there is no defined inactivation procedure established, the applicant should provide an outline of how you intend to conduct the inactivation kinetics and inactivation test. The applicant should provide the data during the assessment of the application. Where there is an urgent need for the product on the grounds of animal health and welfare the permit may be issued for a short period in the absence of specific inactivation kinetics data.

For both scenarios above inactivation kinetics data is only required for one representative isolate/seed.

## 2.8 Batch release analysis

The final product tests should be described and justified with validation data, where appropriate, provided on each final product test.

In general give the objectives of the test with a reference to the Ph.Eur, BP or 9 CFR if relevant, or the reference to any internal test method or standard. Any deviation from Ph.Eur, BP or 9CFR tests should be justified. As a minimum the following tests should be conducted.

- appearance
- sterility
- safety (condition of the permit for an on farm monitoring)
- free formaldehyde (where formaldehyde is the inactivation agent)
- preservative, if applicable.

Each batch of the product must be monitored for safety in at least two animals of the target species in the most sensitive category (for example, minimum age or stage of gestation), treated by the recommended route of administration, as a single dose and monitored for at least seven days or as recommended by the attending veterinarian.

## 2.9 Stability of the finished product

The APVMA may grant shelf life of the final vaccine up to 24 months from the date filling. A longer shelf life may be granted if appropriate supporting stability data or justification is provided.

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### 3 TOXICOLOGY

You should consider submitting toxicology data and/or valid scientific argument where applicable, for example vaccines containing novel adjuvants.

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## 4 METABOLISM AND KINETICS

You should consider submitting metabolism and kinetics data and/or valid scientific argument where applicable for example vaccines novel adjuvants.

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## 5 RESIDUES AND TRADE

The APVMA may accept valid scientific argument in lieu of data where the autogenous vaccine contains adjuvants and/or excipients that are already approved for other registered vaccines. Applications for vaccines containing novel adjuvants and/or excipients should be accompanied by data.

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## 6 OCCUPATIONAL HEALTH AND SAFETY

You should address potential occupational health and safety risks associated with the manufacture and use of the product in the application. This may include, as appropriate:

- safety instructions, eg if self-injection occurs seek medical advice
- first aid instructions, eg if poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia 131 126
- information for medical practitioners, eg for oil adjuvants the standard APVMA warning should be included.

Labels should follow the requirements of the [Veterinary Labelling Code](#) and the label requirements for [veterinary vaccines and antisera](#).

Adequate information should be provided on the adjuvant to assist the APVMA determine the nature of the chemical and the type of mandatory user safety information that should be on the product label.

Additional information may be requested on accidental self- injection depending on the product antigen/adjuvant combination.

## 7 ENVIRONMENT

Information should be provided on the proposed disposal methods for unused or waste product. The disposal statement should comply with the Veterinary Labelling Code.

An environmental assessment should be considered where the product includes novel components or where exposure to the environment may be a risk, for example aquaculture vaccines used in non-contained natural fresh water or sea water sites.

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## 8 EFFICACY

The association between the disease to be treated and the selection of the agent used for incorporation into the autogenous vaccine need not be demonstrated.

It is the responsibility of the prescribing veterinarian to monitor and evaluate the effectiveness of the vaccine in the target species.

If there is a registered product available, you should provide evidence or justification to support the claim that the currently registered vaccine is not achieving adequate protection against the disease in the flock or herd concerned or is unavailable.

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## 9 SAFETY

No requirement for pre-approval safety studies. Batch safety monitoring requirements are described under chemistry, final product testing and are undertaken as on-farm monitoring tests in non-GMP and non-GLP facilities.

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## 10 LABEL

You should provide a copy of the proposed label that will be attached to the container with your application. The label should contain all of the relevant particulars. The label should have sections for the APVMA permit number, a statement that the product is not registered, the name and address of the farm from which the microorganism(s) was isolated.

Labels should follow the requirements of the [Veterinary Labelling Code](#) and the label requirements for [veterinary vaccines and antisera](#).

### 10.1 Sample label

FOR ANIMAL TREATMENT ONLY

Name of Vaccine

Containing minimum:

This Is Not A Registered Vaccine. Use Only Under Veterinary Supervision.

Approved under APVMA permit no X for use in Species at: Farm

Read The Permit Before Using The Product

DIRECTIONS FOR USE: Mix well before use. Keep mixed during use.

DOSAGE & ADMINISTRATION: Inject Y mL subcutaneously. Initially vaccinate at A weeks of age and again at B weeks, or as directed by your veterinarian.

WITHHOLDING PERIOD: 0 days.

USER SAFETY INFORMATION: *e.g. oil warning*

Take Care to Avoid Self-Injection. This product contains mineral oil. In the event of self-administration, seek prompt medical attention and take this container with you. Accidental self-administration may result in local bruising, pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If pain persists for more than 12 hours after medical examination, seek medical advice again.

FIRST AID: If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia 131126

Manufacturers Address:

Store at 2-8°C. Protect from light. Dispose of empty container by wrapping with paper and putting in garbage.

Batch: xxx/xx

mL

Exp: xx/xx

## 11 RENEWALS

You should provide a suitable Justification at the time the permit renewal is submitted. No additional chemistry data is required if there are no changes to manufacture and testing of the product(s).

A copy of manufacturing details and supply records, including a list of names and addresses of veterinarians supplied with the product and the amount of the product supplied to each veterinarian should be supplied to the APVMA on request and at the time of renewal of the permit.

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## **12 EXAMPLES OF SITUATIONS WHERE APPLICATIONS MAY BE REQUIRED TO CHANGE EXISTING PERMITS FOR AUTOGENOUS VACCINES**

### **12.1 I want to add a new target species to an existing permit**

A new Item 21 application is required to add a new species.

No additional chemistry data is required. The application should include a justification for the vaccine in the new target species. If there is a registered vaccine approved for the species and disease justification why the registered vaccine is not achieving adequate protection at combating the disease in the flock or herd concerned or is unavailable.

A new template label with the relevant label particulars should be provided.

### **12.2 I want to increase the maximum titre of the microorganism pre-inactivation having improved the culture conditions of production**

No change to the existing permit is required. The inactivation kinetics have been assessed during the original application. The condition of the permit requires the holder to validate inactivation kinetics according to the Ph.Eur or BP.

### **12.3 I want to increase the quantity/concentration of antigen in the final product**

No change to the existing permit is required. The label and permit has minimum antigen input. Any increase in antigen content should be monitored during the on farm safety test. The antigen range should be specified in the formulation table and should be within the minimum and maximum specifications stated otherwise a new permit application may be required.

### **12.4 I want to change the media for production**

No change to the existing permit is required. There is no requirement for an Item 21 unless the formulation particulars change.

### **12.5 I want to supply an epidemiologically distinct rearing unit**

No change to the existing permit is required. There is no restriction on supplying rearing units linked epidemiologically if the veterinarian provides a suitable justification to the manufacturer.

## 12.6 I want to change the adjuvant of the vaccine(s)

A new Item 21 application is required to add a new adjuvant. Where necessary the following modules should be addressed:

- chemistry and manufacture
- toxicology
- metabolism and kinetics
- residues and trade
- occupational health and safety
- environment
- efficacy
- safety.

## 12.7 I want to change the site of the manufacture

No change to the existing permit may be required if the permit has not been restricted to a particular site. The new site must have a Schedule 1 GMP approval.

## 12.8 If there is an official name change to the microorganism

No change to the existing permit is required. The name change can be updated at the time of renewal.

## 12.9 I have an existing permit I want to renew

An Item 20 if no changes to the existing permit are required.

## 12.10 I want to combine up to four existing organisms in one permit and to include multiple products (single and multivalent vaccines) and multiple target species under one permit

A new Item 21 application is required to combine the four organisms in one vaccine as previous assessment of the existing permit would not apply to the new application. However, only a minimal technical review should be needed to compile the existing vaccines under one master permit.

## 12.11 I want to change the pack size

No change to the existing permit is required unless the Permit has restricted the pack size.