

SPECIFIC REQUIREMENTS FOR THE PRODUCTION AND CONTROL OF OVINE AND CAPRINE LIVE AND INACTIVATED VIRAL AND BACTERIAL VACCINES

Guideline Title	General Requirements for the Production and Control of Ovine and Caprine Live and Inactivated Viral and Bacterial Vaccines for Veterinary Use
Legislative Basis	Directive 81/852/EEC as amended
Date of First Adoption	prior to September 1994
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Additional Notes	This note for guidance is intended to provide general guidance on the type of data which should be included in applications for marketing authorisations for ovine and caprine vaccines. It is intended to supplement Directive 81/852/EEC as amended, and should be read in conjunction with that Directive. Cross-references to the notes for guidance on <i>General Requirements for the Production and Control of Live Mammalian Bacterial and Viral Vaccines for Veterinary Use</i> and <i>General Requirements for the Production and Control of Inactivated Mammalian Bacterial and Viral Vaccines for Veterinary Use</i> are made.

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SPECIFIC REQUIREMENTS FOR THE PRODUCTION AND CONTROL OF OVINE AND CAPRINE LIVE AND INACTIVATED VIRAL AND BACTERIAL VACCINES

This document is intended to provide guidance on the type of data which should be included in applications for marketing authorisations for ovine and caprine vaccines. It is intended to supplement Directive 81/852/EEC, as amended by Directive 92/18/EEC, and must be read in conjunction with that Directive.

When requirements have been included in the *General Requirements for the Production and Control of Live Mammalian Bacterial and Viral Vaccines for Veterinary Use* or the *General Requirements for the Production and Control of Inactivated Mammalian Bacterial and Viral Vaccines for Veterinary Use*, these requirements have not been repeated here but a cross-reference to these has been given. For brevity, these have been referred to as the “General Requirements for Live Mammalian Vaccines” (GRLMV) or the “General Requirements for Inactivated Mammalian Vaccines” (GRIMV), as appropriate.

I. LIVE VACCINES

PRODUCTION

1. STARTING MATERIAL

1.1 Substances of animal origin

Paragraphs 1.1 to 1.1.4.2 of GRLMV apply except:

1.1.1 Source

The source of substances of animal origin must be chosen following the recommendation of the note for guidance on *Minimising the Risk of Transmitting Agents Causing Spongiform Encephalopathy via Veterinary Medicinal Products*.

The source of ovine material must be considered with regard to the risk from scrapie contamination.

1.1.2 Inactivation

All batches of serum of ruminant origin shall be subjected to a suitable inactivation procedure. The inactivation procedure (GRLMV paragraph 1.1.3) should be validated using indicator bovine viruses such as bovine viral diarrhoea virus. If, exceptionally for vaccine production, it has been shown that only non inactivated serum can be used, the serum batch shall be tested as indicated in paragraph 1.1.3 below.

1.1.3 Freedom from extraneous agents

All batches of serum of ruminant origin shall be shown to be free from contaminants as described in section 1.1.4.1 of GRLMV. Each batch of serum must be tested for freedom from pestiviruses before use. Specific and sensitive tests to detect viruses should be carried out on a representative sample of the batch.

1.2 Cell substrates

1.2.1 General requirements

The requirements of GRLMV paragraphs 1.2.1 and 1.2.2 to 1.2.2.2 apply.

1.2.2 Requirements for cell lines

Tests should be carried out for bovine, ovine and caprine viruses using specific techniques capable of detecting them.

If cell lines are originated from bovine, ovine or caprine species, agents listed in table 1 must be looked for by an appropriate and validated method, using the most sensitive system, as indicated in GRLMV paragraphs 1.2.2.1.4.1 to 1.2.2.1.4.3.

If cell lines are originated from another species than bovine, ovine or caprine, they must be tested for the presence of pestiviruses and for the contaminants listed in table 1.

1.2.3 Requirements for primary cells

The requirements of GRLMV paragraphs 1.2.3 to 1.2.3.2 apply.

If a vaccine has to be produced on primary cells, these cells must be obtained from a specific pathogen free herd maintained and tested as specified in GRLMV paragraph 1.2.3. This herd must be shown to be free of the pathogens listed in table 1.

The cells derived from primary tissues should be tested in accordance with GRLMV paragraph 1.2.3.1 to 1.2.3.2 with the extraneous agents testing carried out with regard to contaminants specific for the species or origin of the cells and for the species for which the product is intended, and as indicated in paragraph 1.2.2 above.

1.3 Virus seed

The requirements of GRLMV paragraphs 1.3 to 1.3.5 apply.

1.3.1 Extraneous agents

The tests for extraneous agents specified in GRLMV paragraph 1.3.5 should be carried out as indicated in paragraph 1.2.2 of this document.

1.4 Bacterial seed

The requirements of GRLMV paragraphs 1.4 to 1.4.3 apply.

2. FINISHED PRODUCT – ASSAY RESULTS REQUIRED IN THE APPLICATION FOR MARKETING AUTHORISATION

2.1 Safety

The requirements of GRLMV paragraphs 2.1 to 2.1.5 apply.

Where the vaccine is intended for use in pregnant animals, the duration of the studies, including the overdosage studies, include observation of the effect of vaccination on the number of live lambs/kids produced.

In the case of appearance of local reactions, the size and the kind of lesions, as well as the duration of local clinical signs, must be recorded.

The types of systemic reaction which may be observed and should be recorded if present include loss of appetite, reluctance to move, drooping of head, standing apart from the rest of the animals.

2.1.1 Field trial

As part of the studies of safety in the field trials, the following should be performed on a sufficient number of target animals, located on more than two farms.

Daily for 3 days before vaccination:

- a) all test animals shall be given a general examination;
- b) the selected injection site shall be carefully examined in all test animals;
- c) temperature shall be recorded in a representative number of test animals.

At vaccination, temperature shall be recorded in the same animals as under c) above.

At a minimum, 4 hours after vaccination: all animals shall be observed for local and/or systemic reactions.

Daily for 4 days after vaccination, temperature shall be recorded in the same animals as under c) above.

Daily for 14 days after vaccination, all animals shall be observed for local and/or systemic reactions.

Note: test animals include both vaccinates and controls.

2.2 Efficacy

Efficacy trials shall be performed on target animals, i.e. ovine and caprine of age, sex, breed, etc. for which the vaccine is intended to be used.

Challenge organisms, including field isolates, should be supported by documentation as to their origin, pathogenicity and purity. Freedom of the challenge strain from extraneous agents must be shown. The strain should be stated, if known, along with the method of preparing the challenge material.

In duration of immunity studies, protection at the end of the period will be assessed by measurement of specific antibodies where correlation with protection is available or by challenge where there is not correlation. The immune status of the vaccinates and/or in

contact sentinel animals must be monitored at intervals to provide evidence that animals have not been exposed to the pathogen since vaccination.

If combination of vaccines or a multivalent vaccine is tested, it is important to perform efficacy trials for each valence in animals vaccinated with the combined vaccines or multivalent vaccine. In combined vaccines or multivalent vaccine, duration of immunity studies must include a challenge where the serological results between mono- and polyvalent or combined vaccines differ.

3. TEST ON FINISHED PRODUCT – BATCH TESTING

The requirements of section 3 of GRLMV apply.

3.1 Safety

To comply with the requirements of GRLMV paragraphs 3.2, the vaccine shall be injected to two susceptible lambs or kids, as appropriate, aged two to five months or the minimum age for vaccination where this is less than 2 months of age. If the product is not to be used in animals younger than 5 months, the safety test may be carried out in two susceptible animals aged 6 to 12 months.

3.2 Extraneous agents

Testing of viral vaccines

To comply with the requirements of GRLMV paragraph 3.4, after neutralisation or removal of the vaccinal strain, the mixture shall be tested for extraneous agents as described in paragraph 1.2.2 of this document on one or several among the most sensitive cellular systems. Observe the cells for 14 days. During this time, carry out the minimum number of passages required to maintain the cultures. The absence of cytopathic effect is checked and an haemadsorption test is also carried out.

II. INACTIVATED VACCINES

PRODUCTION

1. STARTING MATERIAL

1.1 Substances of Animal Origin

1.1.1 Source

See requirements for live ovine and caprine vaccines

1.1.2 Inactivation

See requirements for live ovine and caprine vaccines

1.1.3 Freedom from extraneous viruses

See requirements for live ovine and caprine vaccines

1.2 Cell Substrates and Virus and Bacterial Seed

See requirements for live ovine and caprine vaccines

1.3 Inactivation

The requirements of GRIMV section 1.9 apply.

2. FINISHED PRODUCTS – ASSAY RESULTS REQUIRED IN THE APPLICATION FOR MARKETING AUTHORISATION

See requirements for live ovine and caprine vaccines

2.1 Safety

Local reactions must be particularly looked for. The size and the kind of lesions, as well as the duration of local clinical signs must be recorded.

3. TEST ON FINISHED PRODUCTS – BATCH TESTING

The requirements of section 3 of GRIMV apply.

3.1 Safety

To comply with the requirements of GRIMV paragraph 3.2, the vaccine shall be injected to two susceptible lambs or kids, as appropriate, aged two to five months or the minimum age for vaccination where this is less than two months of age. If the product is not to be used in animals younger than 5 months, the safety test may be carried out in two susceptible animals aged 6 to 12 months.