viraemia or antigenaemia at the time of the test; absence of antibodies and antigen is demonstrated by enzyme-linked immunosorbent assay (2.7.1).

A. Vaccinate, according to the intended schedule, not fewer than ten cats of the minimum age recommended for vaccination. Keep five cats as controls. Record the rectal temperature of each cat on the day before each vaccination, at the time of vaccination, 4 h and 8 h later, and once per day during the four following days. Observe the animals for at least 4 weeks after the last vaccination. No abnormal local or systemic reaction occurs during the test. If the vaccine is not contra-indicated for use in pregnant queens, inject two doses of vaccine into each of not fewer than ten cats at different stages of pregnancy. Observe the cats until parturition and note any effects on gestation and the offspring. The vaccine complies with the test if no abnormal local or systemic reaction occurs during the test.

B. Inject two doses of vaccine by one of the intended routes to not fewer than ten cats of the minimum age recommended for vaccination. At the end of the period of time stated in the instructions for use, inject one dose of vaccine to each animal. Where the instructions for use recommend it, administer a third injection after the period indicated. Observe the animals for 14 days after the last administration. The vaccine complies with the test if no abnormal local or systemic reaction occurs during the test.

C. If the vaccine is not contra-indicated for use in pregnant queens, inject two doses of vaccine into each of not fewer than ten cats at different stages of pregnancy. Observe the cats until parturition and note any effects on gestation and the offspring. The vaccine complies with the test if no abnormal local or systemic reaction occurs during the test.

Immunogenicity. The test described under Potency is suitable to demonstrate immunogenicity of the vaccine.

IN-PROCESS CONTROL TESTS

During production, suitable immunochemical tests are carried out for the evaluation of the quality and purity of the viral antigens included in the vaccine composition. The values found are within the limits approved for the particular vaccine.

BATCH TESTING

Potency. The test described under Potency is not carried out for routine testing of batches of vaccine. It is carried out, for a given vaccine, on one or more occasions, as decided by or with the agreement of the competent authority; where the test is not carried out, a suitable validated alternative method is used, the criteria for acceptance being set with reference to a batch of vaccine that has given satisfactory results in the test described under Potency.

Bacterial endotoxins. For vaccines produced by recombinant DNA technology with a bacterial host cell such as Escherichia coli, a test for bacterial endotoxins (2.6.14) is carried out on each final lot or, where the nature of the adjuvant prevents performance of a satisfactory test, on the antigen immediately before addition of the adjuvant. The value found is within the limit approved for the particular vaccine and which has been shown to be safe for cats.

IDENTIFICATION

When injected into healthy, seronegative cats, the vaccine stimulates the production of specific antibodies against the antigen or antigens stated on the label.

TESTS

Safety. Use two cats of the minimum age recommended for vaccination and that do not have antibodies against feline leukaemia virus. Inject by a recommended route a double dose of vaccine into each animal. Observe the animals for 14 days. The vaccine complies with the test if no abnormal local or systemic reaction is produced.

Inactivation. If the vaccine contains inactivated virus, carry out a test for residual live feline leukaemia virus by making two passages on susceptible cell cultures. No virus is detected. If the vaccine contains an adjuvant, if possible separate the adjuvant from the liquid phase by a method that does not inactivate the virus nor interfere in any other way with the detection of virus.

Sterility. The vaccine complies with the test for sterility prescribed in Vaccines for veterinary use (0062).

POTENCY

Use not fewer than twenty-five susceptible cats of the minimum age recommended for vaccination, free from antibodies against the antigens of feline leukaemia virus and against the feline oncogene membrane antigen (anti-FOCMA antibodies), and showing no viraemia or antigenaemia at the time of the test. Vaccinate not fewer than fifteen cats by a recommended route in accordance with the instructions for use. Keep not fewer than ten cats as controls. Observe the animals for at least 14 days after the last administration of vaccine. Inject by the peritoneal or oronasal route, on one or several occasions, a quantity of a virulent strain of feline leukaemia virus sufficient to induce persistent viraemia or antigenaemia in not fewer than 80 per cent of susceptible animals; use for the challenge an epidemiologically relevant strain consisting predominantly of type A virus. Observe the animals for 15 weeks and, from the third week onwards, test each week for viraemia or antigenaemia (p27 protein) by suitable methods such as immunofluorescence on circulating leucocytes or enzyme-linked immunosorbent assay. A cat is considered persistently infected if it shows positive viraemia or antigenaemia for three consecutive weeks or on five occasions, consecutively or not, between the third and the fifteenth week. The test is not valid if fewer than 80 per cent of the control cats are persistently infected. The vaccine complies with the test if no fewer than 80 per cent of the vaccinated cats show no persistent infection.

LABELLING

The label states the antigen or antigens contained in the vaccine.

FELINE VIRAL RINHOTRACHEITIS VACCINE (INACTIVATED)

Vaccinum rinhotracheitidis viralis felinae inactivatum

DEFINITION

Feline viral rinhotracheitis vaccine (inactivated) is a preparation of a suitable strain of feline rinhotracheitis virus (feline herpesvirus 1) that has been inactivated while maintaining adequate immunogenic properties or of an inactivated fraction of the virus having adequate immunogenic properties.
PRODUCTION
The vaccine strain is grown in suitable cell cultures (5.2.4). The viral suspension is harvested and inactivated. The test for inactivation is carried out using 2 passages in cell cultures of the same type as those used for preparation of the vaccine or in cell cultures shown to be at least as sensitive; the quantity of virus used in the test is equivalent to not less than 25 doses of vaccine. No live virus is detected. The virus may be fragmented and the fragments may be purified and concentrated. The vaccine may be adjuvanted; it may be freeze-dried.

CHOICE OF VACCINE COMPOSITION
The vaccine is shown to be satisfactory with respect to safety and immunogenicity in cats. The following test may be used during demonstration of efficacy (5.2.7).

Immunogenicity. The test described under Potency, carried out using vaccine prepared from the most attenuated virus that will be attained during production, is suitable to demonstrate immunogenicity of the strain.

BATCH TESTING
The test described under Potency is not necessarily carried out for routine testing of batches of vaccine. It is carried out, for a given vaccine, on one or more occasions, as decided by or with the agreement of the competent authority. Where the test is not carried out, a suitable alternative validated test is carried out, the criteria for acceptance being set with reference to a batch of vaccine that has given satisfactory results in the test described under Potency. The following test may be used after a satisfactory correlation with the test described under Potency has been established.

Batch potency test. Use a group of 15 seronegative mice. Administer half a dose of the vaccine to each mouse and 7 days later repeat the administration. 21 days after the first injection, take blood samples and determine the level of antibodies against feline rhinotracheitis virus by a suitable immunochemical method (2.7.1), such as an immunofluorescence technique using pools of serum from groups of 3 mice. The antibody levels are not significantly lower than those obtained with a batch of vaccine that has given satisfactory results in the test described under Potency. The following test is not necessarily carried out using vaccine prepared from the most attenuated virus that will be attained during production, is suitable to demonstrate immunogenicity of the strain.

IDENTIFICATION
When administered to susceptible animals, the vaccine stimulates the production of specific serum antibodies against feline rhinotracheitis virus or against the fraction of the virus used to produce the vaccine.

TESTS
Safety. Use cats 8 to 12 weeks old and preferably having no feline rhinotracheitis virus antibodies or antibodies to a fraction of the virus, or, where justified, use cats with a low level of such antibodies as long as they have not been vaccinated against viral rhinotracheitis and administration of the vaccine does not cause an anamnestic response. Administer a double dose of vaccine by a recommended route to each of 2 cats. Observe the cats for 14 days. No abnormal local or systemic reaction occurs.

Inactivation. Carry out a test for residual infectious feline rhinotracheitis virus using 10 doses of vaccine and 2 passages in cell cultures of the same type as those used for preparation of the vaccine or in other suitably sensitive cell cultures. No live virus is detected. If the vaccine contains an adjuvant that interferes with the test, where possible separate the adjuvant from the liquid phase by a method that does not inactivate or otherwise interfere with detection of live virus.

Sterility. The reconstituted vaccine complies with the test for sterility prescribed under Vaccines for veterinary use (0062).

POTENCY
Use cats 8 to 12 weeks old and which do not have antibodies against feline rhinotracheitis virus or against a fraction of the virus. Vaccinate 10 cats according to the instructions for use and keep 10 cats as controls. 4 weeks after the last administration of vaccine, administer intranasally to each of the 20 cats, a quantity of virulent feline rhinotracheitis virus sufficient to produce in susceptible cats typical signs of disease such as fever, nasal discharge and cough. Observe the cats for 14 days; collect nasal washings daily on days 2 to 14 after challenge to test for virus excretion. Note daily the body temperature and signs of disease using the scoring system shown below. If any sign of disease is observed on more than one day, record the score once only. The vaccine complies with the test if the score for the vaccinated cats is significantly lower than that for the controls.

Sign | Score
--- | ---
Death | 10
Depressed state | 2
Temperature: | 
39.5 °C - 40.0 °C | 1
≥ 40.0 °C | 2
≤ 37.0 °C | 3
Glossitis | 3
Nasal discharge, slight | 1
Nasal discharge, copious | 2
Cough | 2
Sneezing | 1
Sneezing, paroxysmal | 2
Ocular discharge, slight | 1
Ocular discharge, serious | 2
Conjunctivitis | 2
Weight loss ≥ 5.0 per cent | 5
Virus excretion (total number of days): | 
≤ 4 days | 1
5-7 days | 2
> 7 days | 3

FELINE VIRAL RHINOTRACHEITIS VACCINE (LIVE), FREEZE-DRIED
Vaccinum rhinotracheitidis viralis felinae vivum cryodesiccatum

DEFINITION
Freeze-dried feline viral rhinotracheitis vaccine (live) is a preparation of a suitable strain of feline rhinotracheitis virus (feline herpesvirus 1).

PRODUCTION
The vaccine strain is grown in suitable cell cultures (5.2.4). The viral suspension is harvested and mixed with a suitable stabilising solution. The mixture is subsequently freeze-dried.