and then milk to each calf every 6 h or according to the recommended schedule. At 5-7 days after birth, challenge each calf by the oral administration of a suitable quantity of a virulent strain of bovine rotavirus. Observe the calves for 7 days. Note the incidence, severity and duration of diarrhoea and the duration and quantity of virus excretion. The vaccine complies with the test if there is a significant reduction in diarrhoea and virus excretion in calves given colostrum and milk from vaccinated cows compared to those given colostrum and milk from controls.

LABELLING
The label states the recommended schedule for administering colostrum and milk, post-partum.

01/2005:1298

CANINE ADENOVIRUS VACCINE (INACTIVATED)

Vaccinum adenovirosis caninae inactivatum

DEFINITION
Canine adenovirus vaccine (inactivated) is a suspension of one or more suitable strains of canine adenovirus 1 (canine contagious hepatitis virus) and/or canine adenovirus 2, inactivated in such a way that adequate immunogenicity is maintained.

PRODUCTION
The test for inactivation is carried out using a quantity of virus equivalent to at least 10 doses of vaccine with 2 passages in cell cultures of the same type as those used for production or in cell cultures shown to be at least as sensitive. No live virus is detected. The vaccine may contain an adjuvant.

CHOICE OF VACCINE COMPOSITION
The vaccine is shown to be satisfactory with respect to safety (5.2.6) and efficacy (5.2.7). The following tests may be used during demonstration of safety and immunogenicity.

Safety. Carry out the test for each recommended route of administration in animals of the minimum age recommended for vaccination. Use a batch of vaccine of the maximum potency likely to be attained. Use for each test not fewer than 10 dogs that do not have antibodies against canine adenovirus 1 or 2. Administer to each dog a double dose of vaccine. If the recommended schedule requires a second dose, administer one dose after the recommended interval. Observe the dogs for 14 days after the last administration. No abnormal local or systemic reaction occurs.

If the vaccine is intended for use in pregnant bitches, vaccinate bitches at the stage of pregnancy or at different stages of pregnancy according to the recommended schedule. Prolong observation until 1 day after parturition. No abnormal local or systemic reaction occurs. No adverse effects on the pregnancy and offspring are noted.

Immunogenicity. For vaccines intended to protect against hepatitis, the test described under Potency is suitable for demonstration of immunogenicity. If the vaccine is indicated for protection against respiratory signs, a further test to demonstrate immunogenicity for this indication is also necessary.

BATCH TESTING

Batch potency test. 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 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.

IDENTIFICATION
When injected into susceptible animals, the vaccine stimulates the formation of specific antibodies against the type or types of canine adenovirus stated on the label.

TESTS

Safety. Use dogs of the minimum age recommended for vaccination and preferably no canine adenovirus-neutralising antibodies or, where justified, use dogs with a low level of such antibodies as long as they have not been vaccinated against canine adenovirus 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 dogs. Observe the dogs for 14 days. No abnormal local or systemic reaction occurs.

Inactivation. Carry out a test for residual infectious canine adenovirus using 10 doses of vaccine by inoculation into sensitive cell cultures; make a passage after 6-8 days and maintain the cultures for 14 days. No live virus is detected. If the vaccine contains an adjuvant, separate the adjuvant from the liquid phase by a method that does not inactivate or otherwise interfere with the detection of live virus.

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

POTENCY

Use 7 dogs of the minimum age recommended for vaccination and that do not have antibodies against canine adenovirus. Vaccinate 5 of the animals by a recommended route and according to the recommended schedule. Keep the other 2 dogs as controls. 21 days later inject intravenously into each of the 7 animals a quantity of a virulent strain of canine adenovirus sufficient to cause death or typical signs of the disease in a susceptible dog. Observe the animals for a further 21 days. Dogs displaying typical signs of serious infection with canine adenovirus are killed humanely to avoid unnecessary suffering. The test is invalid and must be repeated if one or both of the controls do not die from or display typical signs of serious infection with canine adenovirus. The vaccine complies with the test if the vaccinated animals remain in good health.

LABELLING
The label states the type or types of canine adenovirus present in the vaccine.

01/2005:1951

CANINE ADENOVIRUS VACCINE (LIVE)

Vaccinum adenovirosidis caninae vivum

DEFINITION
Canine adenovirus vaccine (live) is a preparation of 1 or more suitable strains of canine adenovirus. This monograph applies to vaccines intended for active immunisation of dogs against canine contagious hepatitis and/or respiratory disease caused by canine adenovirus.
PRODUCTION

The virus strain is propagated in suitable cell cultures (5.2.4). The viral suspension is harvested, titrated and may be mixed with a suitable stabilising solution. The vaccine may be freeze-dried.

CHOICE OF VACCINE STRAIN

The vaccine is shown to be satisfactory with respect to safety (5.2.6), absence of increase in virulence and immunogenicity (5.2.7). The following tests may be used during demonstration of safety, absence of increase in virulence and immunogenicity.

Safety. The test is carried out for each route of administration to be stated on the label. Use not fewer than 5 puppies of the minimum age recommended for vaccination and that do not have antibodies to canine adenovirus. Administer to each puppy by a recommended route a quantity of virus corresponding to not less than 10 times the maximum titre that may be expected in a dose of vaccine. Observe the dogs for 14 days. The puppies remain in good health and no abnormal local or systemic reaction occurs.

If the vaccine is intended for use or may be used in pregnant bitches, administer the virus to 5 bitches at the recommended stage or at a range of stages of pregnancy according to the recommended schedule. Prolong the observation period until 1 day after parturition. The bitches remain in good health and there is no abnormal local or systemic reaction. No adverse effects on the pregnancy or the offspring are noted.

Increase in virulence. Administer by a recommended route to each of 2 puppies, 5-7 weeks old and which do not have antibodies against canine adenovirus, a quantity of virus that will allow recovery of virus for the passages described below. Kill the puppies 4-6 days later. Remove from each puppy nasal and pharyngeal mucosa, tonsils, lung, spleen and, if they are likely to contain virus, liver and kidney. Pool the samples; administer by a suitable route, for example intranasally, 1 ml of the pooled organ suspension to each of 2 other puppies of the same age and susceptibility; carry out these operations at least 5 times; verify the presence of the virus at each passage by direct or indirect means. If the virus has disappeared, carry out a second series of passages. Inoculate virus from the highest recovered passage level to 5 puppies of the minimum age recommended for vaccination, observe for 14 days and compare the reactions that occur with those seen in the test for safety described above. There is no indication of an increase of virulence as compared with the non-passaged virus.

Immunogenicity. For vaccines intended to protect against hepatitis, test A described under Potency is suitable for demonstration of Immunogenicity. For vaccines intended to protect against respiratory signs, test B described under Potency is suitable for demonstration of immunogenicity.

BATCH TESTING

If the test for Potency has been carried out with satisfactory results on a representative batch of vaccine, this test may be omitted as a routine control on other batches of vaccine prepared from the same seed lot.

IDENTIFICATION

The vaccine mixed with monospecific antiserum against canine adenovirus 2 no longer infects susceptible cell cultures.

TESTS

Safety. Use 2 puppies not older than the minimum age recommended for vaccination and which do not have antibodies against canine adenovirus. Administer 10 doses of the vaccine to each dog by a recommended route. Observe for 14 days. The dogs remain in good health and no abnormal local or systemic reaction occurs.

Extraneous viruses. Mix the vaccine with a suitable monospecific antiserum against canine adenovirus 2 and inoculate into cell cultures known for their susceptibility to viruses pathogenic for the dog. Carry out a passage after 6-8 days and maintain the cultures for a total of 14 days. No cytopathic effect develops and the cells show no evidence of the presence of haemadsorbing agents.

Bacterial and fungal contamination. The vaccine, reconstituted if necessary, complies with the test for sterility prescribed in the monograph on Vaccines for veterinary use (0062).

Mycoplasmas (2.6.7). The vaccine, reconstituted if necessary, complies with the test for mycoplasmas.

Virus titre. Reconstitute the vaccine, if necessary, and titrate in susceptible cell cultures. 1 dose of the vaccine contains not less than the quantity of virus equivalent to the minimum virus titre stated on the label.

POTENCY

Depending on the indications for the vaccine, it complies with test A and/or B for potency.

A. Use 7 puppies of the minimum age recommended for vaccination and that do not have antibodies against canine adenovirus. Vaccinate 5 of the animals by a recommended route and according to the recommended schedule. Keep the other 2 dogs as controls. 21 days later, inject intravenously into each of the 7 animals a quantity of a virulent strain of canine adenovirus 1 (canine contagious hepatitis virus) sufficient to cause death or typical signs of the disease in a susceptible dog. Observe the animals for a further 21 days. Dogs displaying typical signs of serious infection with canine adenovirus are killed humanely to avoid unnecessary suffering. The test is invalid and must be repeated if 1 or both of the controls do not die from or display typical signs of serious infection with canine adenovirus. The vaccine complies with the test if the vaccinated animals remain in good health showing no clinical signs except for a possible transient elevated rectal temperature.

B. Use 20 dogs of the minimum age recommended for vaccination and that do not have antibodies against canine adenovirus. Vaccinate 10 of the dogs by a recommended route and according to the recommended schedule. Keep the other 10 dogs as controls. 21 days later, administer intranasally to each of the 20 animals a quantity of a virulent strain of canine adenovirus 2 sufficient to cause typical signs of respiratory disease in a susceptible dog. Observe the animals daily for a further 10 days. Record the incidence of signs of respiratory and general disease in each dog (for example, sneezing, coughing, nasal and lachrymal discharge, loss of appetite). Collect nasal swabs or washings from each dog daily from days 2 to 10 after challenge and test these samples to determine the presence and titre of excreted virus. The vaccine complies with the test if there is a notable decrease in the incidence and severity of clinical signs and in virus excretion in vaccinated compared to controls.