



Rabbit Haemorrhagic Disease Virus Suspension for Control of Pest Rabbits in Australia

The Rabbit Calicivirus Injection (the ‘injection’) was registered for the first time in Australia in September 1996. Registration allowed for this biological control agent to be manufactured and used via injection to control the European rabbit (*Oryctolagus cuniculus*) in Australia. A further product Rabbit Haemorrhagic Disease Virus Suspension (the ‘suspension’) that is equivalent to the injection has now been registered providing a method of delivering the biological control agent via baits. The virus initiates Rabbit Haemorrhagic Disease (also called Rabbit Calicivirus Disease) (the ‘disease’) which is fatal to susceptible rabbits.

The newly registered product will provide land managers with a new delivery method for the biological control of wild rabbit populations. The Commonwealth Scientific and Industrial Research Organisation (CSIRO) is the registrant for both the injection product and the new suspension.

The wild rabbit as a pest in Australia

The first population of European rabbits that established in the wild on mainland Australia was from a deliberate release in 1859. Since then they have spread and become naturalised over most of Australia south of the Tropic of Capricorn. They have caused extensive environmental impacts to native animals, vegetation and soils and reduced agricultural yields.

Control of rabbits is an ongoing requirement in many parts of Australia. Typical control measures include poisoning, warren ripping, fumigation, trapping, ferreting, shooting, and by two biological control agents, myxoma and the virus. While these measures have been variously effective at different points in time in diverse geographical locations, wild rabbits continue to negatively impact on biodiversity.

While wild rabbits have provided some benefits to Australia in terms of a subsistence food, as pet food, as a source of felt for the hat industry and as a food source for some wildlife species, these benefits have been significantly outweighed by the damage rabbits cause.

What is rabbit haemorrhagic disease virus?

The virus was first reported in China in 1984 and spread through rabbit farms across China and into Europe. Subsequently it has also occurred in northern Africa, North America and on islands in the Indian Ocean. To date it has been reported in over 40 countries world-wide.

Generally, only rabbits older than 12 weeks are susceptible to the virus. A rabbit infected with the virus will develop the disease within one to three days. The virus is lethal in more than 75% of infected susceptible rabbits.

Rabbits younger than 12 weeks that become infected with the virus are less likely to die from it than older rabbits. Young rabbits that survive infection become immune adults.

The virus is the active constituent in the suspension. It is a simple, non-cellular agent comprising an RNA molecule, enclosed within a protein coating. Like all viruses, it reproduces only within the living cells of other organisms as a parasite. After susceptible rabbits are inoculated,

the virus reproduces rapidly, particularly in the liver. This leads to the disease which is fatal due to a combination of effects, including liver failure and blood clotting. Death occurs in as little as 12 hours from the onset of clinical signs.

The suspension is manufactured from an imported Czechoslovakian isolate of the virus, designated strain CAPM V-351. It is manufactured from laboratory rabbits which have been inoculated with the virus.

The CSIRO has conducted testing of the suspension to ensure the product is free of any contaminant which could harm Australian agriculture or the environment. Manufacture and quality control standards for the suspension are similar to those applicable to the manufacture of other biological products, including veterinary vaccines.

Need for an additional method of delivery for the virus?

Since its release in 1996, natural outbreaks of the disease continue to have variable effects on rabbit populations. This variability is due to many factors one of which is that natural outbreaks do not coincide with times when rabbit populations are most susceptible to the disease. The currently available intramuscular injection method for administering the virus has some disadvantages including the limited number of rabbits that can be caught, injected and released in a given area, concern over the effectiveness of the virus at a particular point in time given a range of environmental variables, and poor adoption of the injection method due to cost. An additional method of inoculating rabbit populations that does not share these disadvantages has been sought. The additional method of oral delivery provides landholders with access to correctly prepared baits which can be used to infect relatively larger numbers of rabbits at a lower cost.

Who has been involved in assessing the suspension?

The processes involved in evaluating the suspension have been thorough. It has been assessed under a number of Commonwealth Acts within the regulatory framework. These include the

- *Agricultural and Veterinary Chemicals Code Act 1994*
- *Quarantine Act 1908*
- *Biological Control Act 1984*
- *Environment Protection (Impact of Proposals Act) 1974*

The Biological Control Authority (BCA) previously assessed public submissions and a proposal to release the virus as a rabbit control agent.

The original assessment of the virus by the then National Registration Authority (NRA) in 1996 took account of the BCA's report and added independent evaluation of the proposed product's efficacy, its implications for human health, occupational health and safety, the environment and trade. The most recent assessment by the APVMA builds on and extends the earlier one it conducted.

Four Commonwealth agencies and most of the State and Territory agricultural departments were involved during the NRA's original evaluation. The Commonwealth Department of Health and Ageing undertook specialist human health evaluation; the National Occupational Health and Safety Commission provided an evaluation of occupational health and safety; and the Commonwealth Department of the Environment and Heritage considered environmental implications. The NRA undertook evaluation of residues, assessed implications for trade and coordinated the efficacy evaluation in consultation with State and Territory agricultural departments.

The NRA coordinated its registration process with all the assessments taking place under applicable legislation. NRA registration for the injection product was originally granted only after the requirements of other relevant legislation were also met.

In September 1996, the Agricultural and Resource Ministers' Council of Australia and New Zealand (ARMCANZ) agreed to declare rabbits a 'target organism' and the virus an 'agent organism' under the Biological Control Act 1984.

For the new treated baits expert advice was also sought from the Department of Health and Ageing, National Occupational Health and Safety

Commission, the Department of the Environment and Heritage and an eminent independent reviewer to assess the, occupational health and safety, efficacy and possible additional environmental impacts.

Will the virus adversely affect people and animals other than rabbits?

The virus has been demonstrated in the wild to cause death to only one species, European rabbit (*Oryctolagus cuniculus*).

It has not been known to infect or cause death to any other animal species in the wild. Although data are limited, to date the virus has affected only rabbits in those countries where it has been recorded.

Following discussions in March 1996, the Australian Department of Health and Family Services and the Department of Primary Industries and Energy decided to survey people known to have had contact with the virus in Australia for any evidence of adverse health effects or antibody response.

A survey of people working with, or exposed to, rabbits in South Australia and central Victoria was undertaken. A subsequent study of serum samples from approximately 250 of those people who may have been exposed to the virus in their work was done to measure their level of rabbit calicivirus antibody. In addition, the participants were questioned about their exposure to rabbits and other animals, and about their recent history of clinical illnesses. A comparison of antibody levels and clinical illness was then made between those exposed and those not exposed to the virus.

Results of the study indicated that none of the serum samples obtained contained antibodies to the virus indicating no previous disease infection. In addition, no adverse clinical signs, referable to an infection, were reported. On the basis of this study and an assessment of other relevant data, the Department of Health and Family Services advised the NRA that there were no concerns for public health over the release of the virus.

Laboratory testing has been conducted in Australia and overseas to investigate the ability of the virus to cause disease in a variety of species other than rabbits. In Australia large number of mammal and bird species (over 30) were tested by the CSIRO. No infection or evidence of illness was shown by the methods of detection used.

Antibodies were detected in the blood of two species—kiwi and mice. This evidence, that the immune systems of these test animals were stimulated, is attributed to an immune response without infection as all other tests conducted were negative, including very sensitive tests capable of detecting the presence of viral antigens at very low levels.

Limited additional testing has taken place. No research reported in the scientific literature finds that the disease infects or is pathogenic to any animal other than the European rabbit.

Recent assessments of environmental evaluations concerning the risk of non-target species being affected by the new method of delivery have concluded that there is no undue hazard to other species.

In 1996 the NRA recommended to the CSIRO that any studies conducted on the impacts of the virus on human and non-target species be subject to peer review and published. The APVMA has recommended that this process continue.

Will the virus be an effective biological control agent?

The CSIRO's claims in registering the injection were dependent on the assumption that inoculating a limited number of rabbits with the virus would result in the death of large numbers of rabbits that come into contact with diseased rabbits.

Circumstantial evidence about the spread of the virus under Australian conditions indicates that impact has been unpredictable and patchy. To date, no evidence is available to suggest that spread of the virus will occur under all conditions.

The proponent proposed that this product would be an effective means of infecting wild

European rabbits. Provided susceptible rabbits are inoculated, the APVMA has concluded that the suspension is likely to be effective for the purpose claimed. There can be no guarantee, however, that inoculation of susceptible rabbits and baiting with the virus will result, in all cases, in spread of the disease to other susceptible rabbits. Users of this product should be aware of this limitation.

How is the virus to be used?

The virus is one of a number of measures to control pest rabbit populations. As for all agricultural and veterinary chemicals, State and Territory agencies retain the responsibility for the use of the suspension via baiting and/or injection. The State authorities or persons under their direct control undertake inoculation of captured wild rabbits, prepare baits using the suspension and make baits available to landholders for use in selected sites.

To ensure strict control over the suspension, the APVMA has declared it a restricted chemical product under section 93 of the Agricultural and Veterinary Chemicals Code which tightly controls its preparation and supply.

The suspension constitutes an additional management tool that should be integrated with other rabbit control measures. The suspension is not expected to eradicate rabbits, but is expected to help minimise the impact of pest rabbits, thereby helping primary producers and conservationists in managing the Australian environment.

Conclusion

The APVMA has assessed the CSIRO's application to register the suspension and has granted its registration based on the available evidence and the recommendations of other expert agencies.

The APVMA believes that the product will work and be safe for use when used in strict accordance with the recommendations for its use as incorporated on the approved product label.

If any additional information becomes available which points to a problem with the product, the APVMA could, under the *Agricultural and Veterinary Chemicals Code Act 1994*, take action to suspend or withdraw the registration.

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