

Advice on an application for deliberate release of a GMO for research and development purposes

Advice of the Advisory Committee on Releases to the Environment under section 124 of the Environmental Protection Act 1990 to the Secretary of State for Environment, Food and Rural Affairs and Ministers of the Welsh Assembly Government

Applicant: Defra/APHA.

Application: A veterinary clinical study of a genetically modified (GM) Herpes Virus of Turkeys containing transgenic elements from IBD and HPAI to assess vaccination regiment for HPAI in Turkeys.

Ref: 25/R58/01

Date: February 2026

Summary

ACRE is satisfied that the information provided by the applicant in accordance with the current regulations on the Deliberate Release of genetically modified organisms (GMOs), demonstrates that the 'release' of this GMO under the conditions of the trial has been fully assessed and that the risks of adverse effect on human health or the environment are negligible. ACRE therefore sees no reason for the release not to proceed.

Background

In January 2026 ACRE considered an application from the Defra Exotic Disease policy team and APHA for a veterinary clinical study involving the release of a genetically modified Herpes Virus of Turkeys (HVT) containing antigenic genetic elements from both Infectious Bursal Disease (IBD) and High Pathogenicity Avian Influenza (HPAI), in accordance with the Genetically Modified Organisms (Deliberate Release) Regulations 2002 (as amended). Members assessed the environmental risks (including risks to humans coming into contact with the GM virus) associated with the release of this GMO under the conditions of the clinical study set out in the application.

To give context to how severe the diseases protected against by this GMO are: Marek's disease (MD) in unvaccinated birds can cause mortalities of 10-90%; Infectious Bursal Disease Virus (IBDV) is a cause of significant but generally unquantified economic losses in the poultry industry, (with estimates of flock revenue reductions by up to 15%); whilst HPAI

causes severe symptoms in, and is of high risk to, both wild and domesticated birds, with an estimated 1.8 million birds having been culled since winter 2024 in the UK alone.

The planned release is to conduct a poultry trial assessing the vaccination regimen for high pathogenicity avian influenza in turkeys. The trial aims to replicate the size of a small-scale commercial turkey business and will involve 1000 turkeys. The trial will compare three recombinant vaccines along with a further booster vaccine, an inactivated subunit antigen derived from the GMO described in this application. A small subset of each vaccine group will be challenged with HPAI in biosafety level three laboratories by APHA. This is the first application for deliberate release within the UK of this GMO.

The GMO

The GMO as described in the application, contains serotype 3 turkey herpesvirus (FC-126 strain of Maleagrid Herpesvirus 1) as the parental organism, which expresses both the VP2 gene of the Infectious Bursal Disease Virus (IBDV) strain Faragher 52/70 and a synthetic Haemagglutinin A (HA) gene based on a consensus of high pathogenicity avian influenza (HPAI) virus H5N1 strains. The two genes were inserted into the US2 gene of the HVT genome as one large expression cassette.

The wild-type organism HVT strain FC-126 is a fully non-pathogenic virus with a host range limited to avian species, and although able to spread (by release of dust particles from feather follicles) in turkeys, no spreading is observed when vaccinated into other poultry. Strain HVT FC-126 has been used for more than 45 years to vaccinate against Marek's disease (MD). The recombinant strain considered here, rHVT/IBDVP2/H5 was genetically modified by the insertion of both the VP2 gene of infectious bursal disease and the HA gene from HPAI. The HA gene is a synthetic construct based on a consensus of HPAI virus H5N1 strains, modified to possess a monobasic amino acid cleavage site with the same properties seen in HA0 of low pathogenic Avian Influenza (LPAI). This is because the polybasic cleavage site seen in HA3 of HPAI allows HPAI viruses to cause systemic infections with severe disease outcomes, including sudden mortality. Therefore, this alteration in the HA gene of the GM vaccine raises an antigenic response to HPAI (and both IBD and MD) without altering the tissue tropism of the wild type, parental HVT strain.

The HA gene in this recombinant vaccine is a bioinformatically optimized sequence (Computationally Optimized Broadly Reactive Antigen, COBRA) based on known HPAI HA-3. This synthetic construct has been modified at the cleavage site by replacing several basic amino acids, creating a monobasic amino acid cleavage site with the same properties seen in HA0 of low pathogenic Avian influenza (LPAI). Both the VP2 and HA genes are separated by an internal ribosome entry site (IRES) and are equipped with a CMV (murine cytomegalovirus) promoter and simian virus (SV) 40 polyadenylation signal.

The finished product is presented as a live, frozen, cell-associated vaccine for injection with the brand name Vaxxitek HVT-IBD-H5. This itself is an extension of the vaccine "Vaxxitek HVT-IBD," which was authorized for the European market in 2002; and renewed for continued use in GB during 2025.

Phenotypic characterisation

In the vaccine to be tested in this study, and as described above, a monobasic cleavage site is present in the HA gene, which is a distinguishing difference between high and low pathogenic influenza viruses. The monobasic cleavage site in LPAI can only be cleaved by trypsin-like proteases in the respiratory tract and intestines, while the polybasic cleavage site in HPAI can be cleaved by intracellular proteases expressed throughout the body. This allows HPAI viruses to cause systemic infections with severe disease outcomes, including rapid morbidity and ultimately, mortality.

Safety study data on rHVT-IBD-H5 was submitted as part of a previous trial application to the Netherlands GM competent authority in 2023. These safety studies examined, among other things, the tissue tropism of the GM-HVT vaccine and safety at a 10-fold overdose in both chicken and turkey. The studies demonstrated that the tissue tropism of the GM-HVT vaccine was comparable to that of the parental virus and that no replication occurred in mammalian cells. The overdose did not lead to health problems, clinical symptoms, or macroscopic lesions in either chickens or turkeys. No apparent qualitative differences between the GMOs and HVT FC-126 in terms of virus localization and chronology of virus appearance in tissues tested except for slightly reduced replication were seen. Therefore, the dissemination rate of the GMO from vaccinated poultry is the same or decreased compared to the recipient virus. ACRE had noted that this marginal reduction in fitness was observed in other rHVT vaccines, previously advised on by the committee.

The applicant states that no mutations were found in 5 *in vitro* passages of the master seed virus (MSV) on chicken embryonic fibroblast (CEF) cells and that 100% sequence identity is guaranteed in the production method. Phenotypic stability of the rHVT vaccine after passage was confirmed with specific mono- and polyclonal antibodies against the expressed proteins in an immunofluorescence assay.

The Veterinary Clinical Trial

The proposed veterinary trial will be field based, involving 1000 turkeys, and conducted over an approximately 168-day period. The trial will compare three recombinant vaccines in total; two of these were previously considered by ACRE in relation to applications for marketing authorisations within GB, (Innovax-ND-H5 and Vectormune rHVT-HA5). These are therefore not part of the present GM release application under consideration by ACRE. There is also a further booster vaccine, which is an inactivated subunit antigen, derived from the GMO described in this application.

One day old poults will be vaccinated: 300 in total for each of the three viable recombinant vaccines, with 100 serving as unvaccinated controls, and all birds then transported to a brooding site. Following this at 42 days old 150 birds from each vaccine group will receive the booster vaccine. All the birds (except the sample numbers to be challenge tested as described below) will then move to the rearing /finishing sites to complete a regular production period of 168 days.

There will be two challenge studies conducted with a subset (20 per group) of each treatment (vaccine +/- booster) at 106 days and a further subset at 148 days to evaluate the impact of age on infection and vaccination status. Challenge tests will be conducted in containment animal facilities at APHA with a contemporary UK isolate of H5N1 clade 2.4.4.4b HPAI virus.

ACRE duly noted that enhanced biosecurity measures will be applied at the hatchery, brooding and rearing/finishing sites in line with those that are required in an avian influenza prevention zone (AIPZ) (a zone declared by government, where strict biosecurity and hygiene measures are mandatory for all bird keepers to prevent the spread of avian influenza). Measures include only essential movements of people, vehicles and equipment to and from the areas where the poultry are kept; cleansing and disinfection of equipment, vehicles and footwear; and, storing feed, water and bedding under cover.

ACRE concluded that the trial conditions could be considered close to contained use, due to the applicant stating the trial birds will be kept under climate-controlled indoor conditions at all times, including when “in the field”, the laboratory or when in transit.

The trial birds will be housed in five different groups at the brooding and rearing / finishing sites. No other poultry will be kept at the premises during the trial. ACRE observed that this and the imposition of enhanced biosecurity measures at the site(s) during the trial will ensure no further post-release treatment is required. The applicant noted that this measure was due to it being imperative that the field trial birds do not get naturally infected with HPAI from the environment. If this was to happen, the standard response procedure to a confirmed infected premises would be stood up, disease control zones put in place and all birds on the infected premises will be humanely culled. In addition, all sites will undergo cleansing and disinfection post-trial.

Comment

Following a detailed consideration of the application, ACRE was content that the environmental risk assessment provided by the applicant was thorough and included sufficient consideration of the risks to human health and the environment as well as a good description of appropriate measures employed to minimise these risks.

ACRE were content to advise that this GM construct can reasonably be assumed to be non-pathogenic with only turkey as the natural host. Therefore, the GMO has little opportunity to spread or persist in the environment. Furthermore, ACRE noted that their deliberations on a number of similar rHVT vaccines concluded that they represented negligible environmental risk, and the committee could not see anything in the current proposal that would increase this risk.

ACRE noted that the enhanced biosecurity measures for HPAI prevention zones will be strictly enforced at all sites. These measures include keeping birds indoors, ensuring feed, bedding & water are inaccessible to wildlife, cleaning & disinfection of equipment, vehicles, housing & entry/exit points, vermin control, detailed record keeping of birds & movements,

eggs & deaths and the use of bird scarers to keep wild birds away. These measures will ensure any environmental risk is negligible.