Advisory Committee on Releases to the Environment

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

Applicant: Imperial College London

Application: A Phase I Single-Blind randomised trial investigating immunisation strategies using Ad4-EnvCN54, MVA-CN54 and CN54rgp140 combinations in order to maximise antibody responses to Human Immunodeficiency Virus

Ref: 16/R49/01

Date: February 2017

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.

ACRE is satisfied that the information provided by the applicant in accordance with the current regulations on the Deliberate Release of GMOs, demonstrates that the 'release' of this GMO under the conditions of the trial will not have an adverse effect on human health or the environment. ACRE therefore sees no reason for the release not to proceed.

Background

In February 2017 ACRE considered an application from Imperial College London for a clinical trial involving the release of this GMO in accordance with Directive 2001/18/EC. Members assessed the environmental risks (including risks to humans who have not been administered this GM vaccine) associated with the release of this GMO under the conditions of the trial set out in the application. No public representations were received on this trial.

The application was for a Phase I Single-Blind randomised trial using fully competent adenovirus type 4 as a vector carrying a truncated HIV1 envelope glycoprotein (CN54gp150). The vaccine will be delivered orally, alone or in

combination with either a non-replicative modified vaccinia ankara (MVA) (also carrying the truncated CN54gp150) or the CN54gp150 protein (or both) in order to maximise antibody responses to Human Immunodeficiency Virus. The environmental risk assessment provided by the applicant does not concern the recombinant MVA vector since this is non-replicative.

Adenovirus serotype 4 is classified as a hazard group 2 biological agent according to the European Economic Community classification (Directive 2000/54/EC). It has no known natural animal reservoirs and exclusively replicates in human cells.

The GMO

The Ad4-EnvCN54 vaccine is a live, replication-competent recombinant adenovirus serotype 4 (Ad4) vaccine vector expressing an HIV-1 clade C truncated (gp150) envelope protein. The construct was derived from the wild type adenovirus serotype 4 (Ad4) used by the US military as a vaccine and originally developed by Wyeth. Oral administration confers attenuated pathogenicity.

The clinical trial

The GM vaccine will be administered orally to optimize immune responses to the HIV-1 envelope glycoprotein, the primary target for protective antibodies. Following initial screening of responses, patients will be selected from the best dosage regime for additional vaccine administration.

The vaccinations of clinical trial volunteers will take place at a purpose-built facility dedicated to clinical research comprising clinic rooms, wards, laboratories and support facilities. The facility workforce includes doctors, nurses, laboratory and operational staff who have substantial clinical research training and experience. The facility will have restricted access.

All clinical site personnel involved in the handling or administration of study vaccine will be trained according to the study protocol, and all supportive documentation, including study specific laboratory and clinical trial material manuals.

A thorough study-specific training session will occur prior to the initiation of the study via a formal investigator meeting and/or on-site study initiation visit. Volunteers will be vaccinated, observed and then released to return to their normal residencies, mostly in Greater London until the next study visit 7 and 28 days later.

Comment

The data provided by the applicant demonstrated that the GM vaccine is genetically stable and that the detection methods for identifying the GMO were appropriate and easily able to distinguish between the GMO and wild type Ad4 strain. Whilst the GM vaccine is fully replicative, administration via the oral route offers a degree of attenuation. Importantly, a proportion of recipients of the vaccine will be expected to shed live vaccine in faeces.

ACRE considers that the applicants have thoroughly described the risks associated with this shedding, including the potential for transmission to non-participants via the faecal-oral route. Appropriate mitigation measures such as the participant exclusion regime and teaching participants correct hand washing technique were described. In addition the applicants have described the biological fate of the GM vaccine once it has entered the sewerage system and thoroughly considered the level of risk associated with this. ACRE agrees with the conclusion that whilst it is theoretically possible for small quantities of vaccine to escape inactivation by sewage treatment it is highly unlikely that it would be present in quantities sufficient to result in harm to human health or the environment.

The potential for environmental exposure within the area of administration was also appropriately described by the applicant including appropriate risk mitigation measures associated with staff training and treatment of clinical waste.

ACRE considered that overall the applicant had provided a good quality dossier, which provided sufficient evidence for an assessment of potential risks. ACRE concluded that this assessment demonstrated that the risks posed to human health and the environment, by the proposed releases in this trial, are negligible.