CT BRASIL, MINISTÉRIO DA CIÊNCIA E TECNOLOGIA
[Ministry of Science and Technology] and
CTNBio, Comissão Técnica Nacional de Biossegurança
[National Technical Biosafety Committee – CTNBio]

MINISTRY OF SCIENCE AND TECHNOLOGY
NATIONAL TECHNICAL BIOSAFETY COMMITTEE – CTNBio
EXECUTIVE SECRETARIAT

PRELIMINARY CONCLUSIVE TECHNICAL APPROACH
No. 099/2004

Process No: º: 01200.005090/2003-92

Applicant: Merial Saúde Animal Ltda.

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CNPJ [National Register of Legal Entities]: 57.600.249/0017-12

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Subject: Application of Preliminary Conclusive Technical Approach for the production, marketing, and export of the product named VAXXITEK MD/IBD.

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Previous Abstract: 069/2003 published in D.O.U [Federal Official Gazette] No. 241 of December 11, 2003.

Meeting: 77 Ordinary Meeting held on May 12, 2004

069/2003 published in D.O.U [Federal Official Gazette] No. 241 of December 11, 2003.77 Ordinary Meeting held on May 12, 2004

Decision: GRANTED

CTNBio, after assessing the process concerning the application of Conclusive Technical Approach for the production, marketing, and export of the product named VAXXITEK MD/IBD, has concluded by the GRANT.

At the extent of the provided for in Article 1 D, Law 8974/95, the Committee has concluded that the application meets the CTNBio guidelines as well as the relevant

legislation that seeks to assure the biosafety of environment, agriculture, and human and animal health.

PRELIMINARY CONCLUSIVE TECHNICAL APPROACH OF CTNBio

NOTE: This Approach has confidential items

1) Technical Background:

The institution has requested Preliminary Conclusive Technical Approach concerning the production, marketing, and export of the product named VAXXITEK MD/IBD, a vaccine against Marek's disease and Gumboro's disease, that is prepared from a Marek's disease recombinant virus as a vector of Gumboro's disease.

This GMO, subject of the present application of the marketing release, is a recombinant virus named vHTV013-69. This virus is originating from a non- pathogenic serotype of Peruvian herpesvirus routinely used as live vaccine against Marek's disease, an avian illness that affects economically several countries. A Gumboro's disease-virus gene was added to this herpesvirus. The added gene cannot cause the disease and it can promote protection against Gumboro's disease virus.

According to a favorable approach from Ministry of Agriculture and Fishing (General Food Management) and French Ministry of Interior and Environment (Management of Pollution and Risk Prevention), the recombinant virus is originating from a parental strain FC126 of Peruvian herpesvirus (HVT) used in the United States and France for producing live vaccines against Marek's disease, without undesirable effects. The virus HVT belongs to the risk classification Ea1, for confinement category L1. The expression strand, which integrates the gene encoding protein of interest, is inserted in an uncoded intergenic region. Also according this approach, this recombinant virus does not show tropism change and nor spread from chicken to chicken. Mammals are refractory to HVT infection, not constituting, therefore, risks for public health.

The vaccine will be supplied frozen in glass ampoules with a suspension of tissue culture medium from cells infected with recombinant virus.

Characterization of GMO:

Receiver microorganism - *Meleagrid herpesvirus* 1 or Peruvian herpesvirus (HVT), strain FC-126, the vHVT-013 will be the vector virus. This strain has been widely used since 1971 as a vaccine against Marek's disease;

Donor Microorganism - Birnavirus or Gumboro's Disease Virus (IBDV), strain 52/70 Faragher. The gene, which is not capable of causing diseases, inserted into vector genome is the VP 2, whose toxic effect not has been still identified (the gene is encoded for one of the IBDV capsid proteins).

The applicant company has considered both receiver and donor as belonging to Group I.

The process includes the properly answered items of Instruction Normative No. 03 from CTNBio.

2) Biosafety measures described in the process.

The applicant institution has presented the safety characteristics of the product under consideration regarding the human and animal health and environmental safety, such as:

For animal health: The virus did not show any virulent property when inoculated in 1-day chicks in a 10-fold higher the field dose recommended; no adverse immune interaction is expected with this vaccine use; retro-transport studies has shown that the vHVT-013-69 virus does not revert to virulence when administered to chicks; the HVT FC-126 strain is avirulent for chickens; the inserted gene, and its products, do not have known pathogenic or toxic properties; there is no evidence showing that vaccine recombinant strain is different from HVT; studies of viral proliferation have detected no viral recovery in mice tissue samples inoculated with recombinant virus; it is not expected that the recombinant virus will be a safety problem for non-target species.

For human health: Risks for public health are not expected; there are no reports of HVT productive infection in any species other than the avian as well as there no report of human infection; the human exposure will be limited to the personnel who administer the vaccine and conduct field studies; the parental HVT vaccine has been used in Europe, as marketed vaccine for chickens, without any report of adverse effects or danger for public health; once the man never has been inoculated with recombinant virus, the effective result of an accidental inoculation is unknown; the experts on human and poultry cancer believe that Marek's disease and respective vaccines do not represent any risk for human health.

For the environment: The risks for environmental safety are low; the recombinant vaccine-shedding/diffusion capacity is limited; the specificity of the host/band of the experimental vaccine does not show changes in relation to wild-type HVT that is restricted to the avian species; the in vivo potential recombination with field virus and other vaccine viruses is unknown; the Marek's disease virus has worldwide distribution; it is expected that the potential recombinant virus transmission will be minimum, even occurring transmission, the attenuated properties of vHVT-013-69 should not be changed.

3) There are no restrictions to the OGM Derivatives use in question and the project does not require considerations of ethical nature involving genetic manipulations.

Once met the biosafety recommendations and measures included in the process, this activity does not cause a potentially significant environmental degradation nor it is harmful to the human health.

Jorge Almeida Guimarães
President of CTNBio