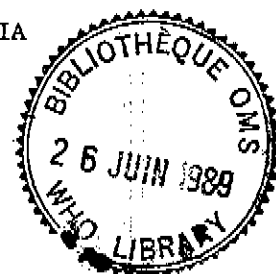




REPORT OF WHO CONSULTATION ON REQUIREMENTS AND CRITERIA
FOR FIELD TRIALS ON ORAL RABIES VACCINATION
OF DOGS AND WILD CARNIVORES

Geneva, 1-2 March 1989



INTRODUCTION

Parenteral vaccination has for years been the basis for the control and prevention of rabies in domestic animals, especially dogs. This technique, while still useful in the developed world, has not been successful as regards unowned or uncontrolled dogs or for vaccination of wild animals. In recent years, attempts have been made to reduce the dog and wild animal populations in the hope that this would break the chain of natural transmission of rabies. Experience has shown that this does not work. The important species have reproductive capacities that exceed our ability to remove animals from the standing population. Further, the mass killing of animals on the scale required to control rabies is no longer tolerable in modern society.

The only technique available today for control of rabies in those animals that remain out of physical reach is oral rabies vaccination (ORV). While ORV has proven successful in the laboratory, and is proving so in the field environment, this technique is subject to new safety and public acceptance problems.

In order to provide guidance for the use of the ORV technique with specific regard to safety and field application requirements, a WHO consultation was held in Geneva from 1 to 2 March 1989. (The list of participants is included in Annex 1). The following report of this consultation is necessarily incomplete in areas still in the process of definition, but its guidelines should help to organize control and research efforts in a safe and productive direction for the next several years.

It should be noted that the guidelines must represent a compromise between unattainable absolute safety and complete freedom for research and development with no regard for safety. The guidelines should permit continued development of new technology in a knowledgeable and responsible fashion.

These guidelines are divided into four parts: the first part deals with planning and organization of an ORV project; part two addresses the issue of vaccines to be used; part three deals with bait configuration and application; and part four contains research recommendations.

This document is not issued to the general public, and all rights are reserved by the World Health Organization (WHO). The document may not be reviewed, abstracted, quoted, reproduced or translated, in part or in whole, without the prior written permission of WHO. No part of this document may be stored in a retrieval system or transmitted in any form or by any means - electronic, mechanical or other without the prior written permission of WHO.

The views expressed in documents by named authors are solely the responsibility of those authors.

Ce document n'est pas destiné à être distribué au grand public et tous les droits y afférents sont réservés par l'Organisation mondiale de la Santé (OMS). Il ne peut être commenté, résumé, cité, reproduit ou traduit, partiellement ou en totalité, sans une autorisation préalable écrite de l'OMS. Aucune partie ne doit être chargée dans un système de recherche documentaire ou diffusée sous quelque forme ou par quelque moyen que ce soit - électronique, mécanique, ou autre - sans une autorisation préalable écrite de l'OMS.

Les opinions exprimées dans les documents par des auteurs cités nommément n'engagent que lesdits auteurs.

1. RECOMMENDATIONS FOR PROJECT PLANNING AND ORGANIZATION

1.1 Introduction

Project planning must precede actual field application of baits, and related administrative activities will vary in structure and detail depending upon political and other variables. Planning and organization are vital to the success of the programme.

1.2 Preparation of field trials

A project proposal must include background information on the area to be treated using the ORV technique, estimated costs and benefits of the project, dates of sequential events, safety considerations, methods for post-baiting evaluation, and relevant data on target population. The proposal should be distributed to concerned institutions well in advance for consideration. A scientific committee should evaluate the project. Upon request, WHO may help in providing the necessary expertise.

Epidemiological data based on reliable surveillance and laboratory studies must be available before field trials can be initiated.

1.3 Implementation of field trials

1.3.1 Selection of field trial areas

(a) Geographical location

If several areas could be selected, priority should be given to those surrounded by natural barriers and/or where one can rely upon community cooperation and logistic support. The rabies situation in neighbouring areas should also be taken into account. The selected areas should be readily accessible to central government veterinary/medical services.

(b) Epidemiological considerations

Areas should be selected according to the frequency of wildlife rabies or the number of dog cases and human exposures. Dog vaccination campaigns can be initiated at any time; fox rabies vaccination campaigns starting during the decreasing phase of an epizootic are more successful and less expensive.

(c) Size of the area

In the case of dog rabies, the area should be based upon dog population, dog ecology and the human-dog bond. In the case of wild carnivores, the size of the area to be covered by the ORV technique should not be less than 2000 km².

1.3.2 Project implementation

The field application of oral immunization against rabies should be based on a comprehensive plan which describes the objectives, justification, technical and organizational details and budgetary requirements of the project and defines the responsibilities of the collaborating institutions.

(a) Responsibilities

Responsibilities for project implementation should rely upon the existing agencies, preferably inter-ministerial commissions or an Advisory Committee. Their responsibilities will be to provide guidance and coordination for field programmes within a state or country; to assume responsibility for programme activities; to act as liaison between other activities; and to interact with news media and the public on issues relating to the project.

(b) Budget

Adequate funds should be ensured before initiation of any field projects. These must also include funds for post-baiting evaluation and surveillance during a minimum of three years.

(c) Legal aspects

Legal requirements and regulations of local, national, and supranational jurisdictions should be fulfilled.

(d) Time schedule for oral vaccinations

See Annex 2.

1.3.3 Vaccine application strategies

In the case of dog rabies, vaccine strategies should be decided upon according to results obtained after a study of efficacy of the methods used. The present fox rabies epidemiological situation in western Europe requires two vaccinations per year over a period of two years. Spot vaccination may be necessary to finally eliminate rabies from some areas. Establishment of immune belts should be considered for protection of a rabies-free area.

1.3.4 Infrastructure requirements

(a) Community participation

Community participation requires information, promotion and, in some instances, training for baiting and disease surveillance.

(b) Field services

Medical and veterinary practitioners should be aware of the campaign so as to take appropriate measures in case of accidental exposure to the vaccine. An advisory group should also be established at central level.

(c) Laboratory services

Sampling of specimens should be carried out under appropriate conditions. Laboratory facilities should be readily accessible in order to monitor vaccine safety. Laboratories must be able to carry out the tests for evaluation of the bait uptake, and seroconversion rates and to diagnose rabies.

(d) Epidemiological investigation group

Specialists should be assigned to the campaign to investigate the epidemiological situation both in man and animals before, during, and after the implementation of the project, and should report to the responsible authorities on a regular basis.

1.4 International cooperation

As rabies does not recognize national borders, it is necessary for governments to cooperate at all levels to achieve effective vaccination programmes. Adjacent countries should carefully coordinate their activities along common borders. If field trials reach a country border, local administrative staffs from both countries should coordinate their efforts at the national level. WHO may be particularly helpful in assisting in coordination of rabies vaccination programmes involving borders between countries.

Oral rabies vaccination generates new epidemiological concerns. For this reason, research should be coordinated by the inclusion of at least two independent WHO Collaborating Centres in the planning and execution of field trials and post-baiting evaluation.

The establishment under WHO auspices of a group of consultants for assisting countries in the preparation and submission to funding agencies of their project proposals for ORV should be considered later on. This group should also collaborate with countries during the subsequent implementation and evaluation phases.

1.5 Evaluation of the project

After each campaign, evaluation of the results is of the utmost importance in order to define the future strategy. Methods of evaluation should be used as described in section 3.4 of this document.

2. RECOMMENDATIONS FOR VACCINES

2.1 Introduction

Two types of oral rabies vaccines have been used in experimental and field studies, namely modified live vaccines and recombinant vaccines. Extensive field experience has been acquired with the use of modified live vaccines in European foxes.

Oral vaccination is now contemplated for other species such as dogs, skunks, raccoons, mongoose, jackals, raccoon dogs, and other wild carnivores. A variety of rabies vaccines, both attenuated and recombinant, are being developed for use in these species. Safety considerations for non-target species and humans are basic to the field use of these vaccines.

Those recombinant vaccines for which innocuity in the intended species is established (as by genetic modification) may be considered of reduced virulence in other species. This in no way implies that further studies in other species should be curtailed. In addition, special studies (in the case of recombinant vaccines) are indicated in species which are known to be particularly susceptible or sensitive to the parent carrier virus.

Carefully planned field trials should be strongly encouraged only when the efficacy and safety of newly developed vaccines have been laboratory in the laboratory.

2.2 Modified live vaccines (MLV)

2.2.1 Efficacy and safety of orally administered MLV

Many MLV have been used in attempts to immunize foxes orally. They include two which are not effective at high concentrations of virus, namely CVS and HEP Flury. (1) The one strain which has consistently been shown to be an effective oral immunogen for foxes is the SAD strain or its derivatives. (2,3,4) The first field trial with SAD was carried out in Switzerland, beginning in 1978, and its use (in chicken head baits) has since then resulted in the virtual elimination of rabies from that country. In Switzerland, continual surveillance detected three animal cases of vaccine-induced rabies (one cat, one stone marten and one baby fox). (5) No other vaccine deaths were noted in over 900 rabid animals examined. So far, approximately 1 000 000 baits have been distributed in this country.

In the Federal Republic of Germany, a SAD derivative called SADB19 was developed by selection in cloned BHK cells. The vaccine is an effective immunogen in foxes at the 1×10^6 TCID₅₀/ml level, and its use (in Tübingen fox baits since 1983) has resulted in a 60% reduction of fox rabies in that country. No case of vaccine-induced rabies has been found in approximately 10 000 rabid animals examined, after the placement of over 8 000 000 baits in nine European countries. A laboratory experiment on raccoon dogs has shown 100% seroconversion and protection after oral application of 10^8 TCID₅₀/ml of SADB19 vaccine in fox baits. After field vaccinations with a dose of 5×10^7 TCID₅₀/ml, 80% of 80 raccoon dogs showed seroconversion. In limited experiments this vaccine also effectively immunized 75% of raccoons at $10^{8.8}$ TCID₅₀/ml, and gave approximately 50% protection at $10^{7.5}$ TCID₅₀/ml. The raccoons did not develop antibodies and were not protected after oral administration of the ERA strain.

Only limited studies have been carried out on the efficacy of SAD and SAD derivatives in dogs. ERA (BHK) has only limited efficacy when administered orally to young adult dogs at a level of 10^8 MICLD₅₀/ml (approximately 30%); in contrast, SADB19 has been administered orally to 40 dogs in the Tübingen laboratory (with Tübingen baits) and found to be effective at doses of $10^{7.5}$ TCID₅₀/ml. All dogs developed serum neutralizing antibodies (range at levels of 2-20 I.U./ml). One puppy (4-5 weeks old) inadvertently took the bait and was immunized - no disease developed.

2.2.2 Safety requirements of modified live vaccines

The candidate vaccine strain should be characterized according to classical procedures.

A. Innocuity testing

Dogs

(a) The vaccine chosen should not produce any disease in 10 young dogs (3-6 months old) when administered orally at a 10-fold concentration of the quantity recommended for field use.

(b) To trace the possible excretion of vaccine virus in saliva of orally vaccinated dogs, 10 dogs administered 10 times the field concentration of vaccine should be swabbed daily for three days and no virus should be present after three days. Any virus recovered should be characterized by monoclonal antibodies.

(c) To test for possible latency, 10 dogs given 10 times the field concentration orally should be sacrificed and brain and salivary gland examined at 6 months. Any vaccine strain leading to latency should be rejected.

Other target species

Analogous procedures for other target species should be applied as described under the section on Dogs, above.

Non-target species

(a) Wild rodents. Where feasible, at least 10, and if possible, 50 of each of the most common local rodent species should be administered 0.05 ml of the recommended field dose of vaccine by two routes: oral and intramuscular. No more than 10% of the animals so vaccinated should develop sickness or death attributable to vaccine (in Europe the rodents tested have included Rattus and Apodemus).

(b) Wild or domestic animals (other than rodents). Five of the most relevant local wild or domestic animals that may take baits should be administered the field concentration of vaccine orally in the volume indicated in Table 1. (For example, in Europe, the common species are wild boars, stone martens, badgers and cats.) No animal given that dose should show signs of vaccine rabies.

Table 1 - Volume of Vaccine/Animal

<u>Weight</u>	<u>Volume</u>
< 500 g.	0.05 ml.
500 g. - 1 kg.	0.10 ml.
1 - 4 kg.	1.00 ml.
4 - 20 kg	2.00 ml.
> 20 kg	5.00 ml.

Any results obtained by the production laboratory or a WHO Collaborating Centre on Rabies (regarding oral vaccination of dogs or other wild carnivores) should always be corroborated by another WHO Collaborating Centre on Rabies.

B. Risk assessment

(a) Humans

An intense surveillance system should be established to detect any possible human exposure to vaccine. Humans accidentally in contact with the vaccine (by mouth, nose, eye or wound) should receive rabies postexposure prophylaxis. Similarly, persons working with the vaccine and at risk of exposure to it should receive pre-exposure immunization.

(b) Domestic or wild animals

Any rabies virus isolated from animals in vaccination areas should be examined by monoclonal antibodies to ensure that no vaccine-induced rabies has occurred.

2.3 Recombinant live virus vaccines (RLV)

2.3.1 Innocuity testing

This section deals with the intrinsic safety aspects, i.e. the innocuity of a RLV preparation for the vaccinee. A first evaluation of residual virulence of the candidate strain should be performed by standard laboratory methods, e.g. oral and parenteral inoculation of laboratory animals. Subsequently, oral vaccination of the target species should be performed (e.g. fox, raccoon, dog). The same general guidelines should be followed as have been indicated for Modified Live Vaccines (section 2.2.2). Appropriate laboratory tests (e.g. pock markers, epitopes recognizable by monoclonal antibodies, genetic probes) can be useful for periodic monitoring of virulence, once its genetic basis has been defined.

Innocuity can be expected from vaccine strains where either genomic deletions or insertional mutagenesis has led to the inactivation of virulence-relevant gene(s). It has been shown, for instance, that inactivation of the thymidine kinase gene leads to vaccinia virus mutants of reduced virulence; the same approach should be followed for other candidate vector viruses.

2.3.2. Risk assessment of non-target species

Here, other safety aspects are considered, i.e. the innocuity of a vaccine for non-target species and for man. Where possible, the transmission of vaccine virus to humans should be tested.

Real and hypothetical risks must be differentiated. The real risk for non-target species can be definitely established by innocuity testing of non-target species in the laboratory. Aspects of pathogenicity of the candidate vaccine strain can and should be studied in appropriate laboratory animals, the non-target species, the most relevant wild vertebrates and in man, if possible. Thus the course of infection by the RLV must be known, such as its spread from the site of entry, excretion, transmission, contagiousness, and virus persistence. Where approved human vaccines against the carrier virus exist, their use should be considered for those persons involved in vaccine production or distribution.

In the case of vaccinia vectored rabies glycoprotein vaccine (as now developed) where the rabies glycoprotein gene is inserted at the thymidine kinase position in the vaccinia DNA, this vaccine may be considered non-infectious for rabies, and pre-exposure or postexposure rabies vaccination is not recommended for persons exposed to this vaccine. Rabies risks from other recombinant vaccines must be evaluated on an individual basis as such vaccines are developed.

A hypothetical risk is the recombination of the RLV vaccine viral genome with that of another virus, with the resulting recombinant possessing higher virulence and greater epidemiological potential. The realization of this hazard has not been borne out for poxviruses either in the laboratory or in nature. Nevertheless, the possibility of other RLV's to recombine, to cause persistent infections, or to become oncogenic should be kept in mind and investigated. This applies especially to other potential vector viruses whose DNA replication is in the nucleus.

2.3.3. General considerations on risk

In summary, a safe vaccine virus candidate should:

- (a) not acquire virulence during replication in the vaccinee;
- (b) not be oncogenic in the vaccinee;
- (c) be apathogenic for non-target species (including humans) and not cause persistent infections;
- (d) not recombine with viruses occurring in nature to result in viable progeny.
- (e) demonstrate that its possible excretion has not been shown to be hazardous;
- (f) bear at least one genetic marker for identification (for instance, the B-galactosidase gene).

3. RECOMMENDATIONS FOR BAIT CONFIGURATION AND APPLICATION

3.1 General recommendations for baiting systems

Major carnivores for which oral vaccination techniques are desired include: dog, red fox, arctic fox, skunk, raccoon, raccoon dog, mongoose and jackal species.

An oral vaccination technique for the dog is clearly the most important of these.

Baiting system guidelines will vary widely depending upon climate, target species ethology, target and non-target species characteristics, and urban versus rural environments.

Within one animal type, the dog, several variables have been identified which might alter the type of bait delivery system recommended, e.g. presence or absence of an effective parenteral vaccination programme, accessible or inaccessible dog population.

Whereas specific recommendations can be issued for rabies vaccination of dogs, this is not possible for wildlife which is composed of many different animal species.

If an adequate parenteral rabies vaccination programme exists in the area, oral rabies vaccination may not be necessary and may actually be detrimental to comprehensive dog vaccination.

3.2. Recommendations for bait composition (dogs and wildlife)

3.2.1 General considerations:

The ideal bait should:

- not interfere with vaccine efficacy;
- immediately attract the target species;
- not attract non-target species, including humans;
- deliver the vaccine into the oral cavity;
- be free from adventitious agents;
- protect the vaccine under field conditions;
- be producible in standard form under local conditions;
- contain a biomarker;
- withstand environmental and storage conditions;
- be safe for target and non-target species if many baits are consumed;
- retain physical integrity when applied by aerial baiting;
- be economical to produce.

3.2.2 Attractants

A proper attractant should:

- present optimal stimuli (e.g. visual, tactile, olfactory/gustatory) for target species while minimally attractive to non-target species;
- be compatible with bait and vaccine and adherent to the bait;
- remain palatable for a defined period;
- withstand temperature extremes;
- be economical and producible under local conditions.

3.2.3 Biomarkers

In general, markers in current use can be grouped as follows:

- (a) surface markers (rhodamine B, other dyes);
- (b) tissue markers (iophenoxic acid, etc);
- (c) calciphilic markers (tetracycline).

Biomarkers should be:

- compatible with other bait components;
- safe for target and non-target species;
- detectable using technically simple, economical and locally available assay methods in target species for a defined period;
- absent or minimally present in subject population;
- economical to produce;

3.3 Bait distribution techniques

There are several bait delivery systems. Each has different efficacy and safety implications. More than one technique may be necessary to ensure optimal cost-effectiveness. The number of baits distributed will depend on several factors such as the estimated density and habitat characteristics of the target species, competition for baits between target and non-target species, etc.

3.3.1 Techniques for dogs

(a) Aerial baiting

Large-scale bait broadcasting is not generally recommended except when dogs are not otherwise accessible.

(b) Terrestrial baiting techniques include:

- non-specific distribution (e.g. from a moving vehicle such as a bicycle, automobile);
- specific, manual placement without recovery of baits at selected sites to maximise target and minimize non-target (especially humans) uptake;
- specific manual placement with recovery of baits at selected sites is labour intensive but further improves target species exposure and minimizes human exposure;
- hand-feeding of individuals facilitates identification of vaccinated animals but may increase risk to human handlers.

3.3.2 Techniques for wildlife

The basic techniques are the same as for the dog, but there may be greater emphasis on aerial bait distribution and non-specific bait distribution, whereas hand-feeding is not applicable.

3.4 Baiting evaluation

3.4.1 Pre-baiting evaluation

Prior to bait application the following data should be obtained in target and non-target species:

- (a) background biomarker levels;
- (b) results of several placebo bait trials;
- (c) antibody prevalence to relevant antigens (e.g. rabies and vaccine vectors).

3.4.2 Post-baiting evaluation

After baiting application, the following should be investigated:

- (a) proportion of target/non-target animals ingesting baits by biomarker analysis;
- (b) proportion of target animals vaccinated;
- (c) antibody prevalence to relevant vaccine antigens in non-target species;
- (d) disappearance or disturbance of baits, especially if species responsible can be determined;

- (e) identification of virus type, inclusive of vaccine strain, when relevant in a rabid animal;
- (f) morbidity or mortality in target or non-target species which may be caused by a vector agent or potential natural viral recombinants;
- (g) impact of oral vaccination on the natural occurrence of rabies.

4. RESEARCH RECOMMENDATIONS

Much progress has been made in the development of the oral rabies vaccination technique, and its application is resulting in the elimination of rabies from a growing number of areas. Nevertheless, much research remains to be done, particularly with new vaccine types which offer hope for more effective immunization. Areas identified as important for research include:

4.1 Programmatic research

Research projects should be initiated on:

- (a) Improving epidemiological surveillance techniques, including use of computer-based data systems.
- (b) Techniques for relevant information dissemination to the public.

4.2 Vaccine research

Additional studies should be carried out in order to:

- (a) Identify new MLV vaccines which effectively immunize other target species (in addition to the fox) and are as safe as the present fox vaccines.
- (b) Develop inactivated vaccines for oral administration.
- (c) Obtain more information on the distribution of orthopoxvirus or other vector viruses in wild fauna and the pathogenesis of oral and parenteral infection in these species.
- (d) Attenuate further the virulence of vector viruses without impairing their immunogenicity; also, insertion of foreign genes (e.g. lymphokines) to reduce pathogenicity for immune-compromised individuals.
- (e) Assess pre-existing immunity to the vector virus and its potential impact on (re)vaccination efficiency by the RLV?
- (f) Investigate recombination between poxviruses (or other potential vectors).
- (g) Select other potential vectors for recombinant virus vaccines, especially for oral immunization of dogs.
- (h) Test the feasibility of including multiple gene insertions in virus vectors to immunize against other diseases in addition to rabies.
- (i) Experiment techniques for slow release of viral vaccine within the animal, especially within the intestinal tract.

4.3 Bait and field application research

- (a) Improve economical biomarkers and assays for live animals and post-mortem use in target and non-target species.
- (b) Develop and evaluate improved attractants and baits for all target species.
- (c) Develop and implement improved techniques for determining population parameters for all target species.
- (d) Establish most effective target species/bait ratios, especially for dogs, in different environments.
- (e) Determine the risk to humans from oral vaccination of dogs under different cultural settings.
- (f) Assess influence of oral rabies vaccination upon vaccine coverage by conventional parenteral methods.
- (g) Evaluate cost-effectiveness of different vaccination techniques and distribution methods.

LIST OF REFERENCES

1. Baer, G.M., Abelseth, M.K., Debbie, J.G. (1971) Oral vaccination of foxes against rabies, Am.J.Epidemiol., 93, 487-490.
2. Debbie, J.G., Abelseth, M.K., Baer, G.M. (1972) The use of commercially available vaccines for the oral vaccination of foxes against rabies, Am.J.Epidemiol., 96, 231-235.
3. Debbie, J.G. (1974) Use of inoculated eggs as a vehicle for the oral rabies vaccination of red foxes (Vulpes fulva), Infection and Immunity, 9, 681-683.
4. Steck, F., Wandeler, A., Bichsel, P., Capt. S. Hafliger, U., Schneider, L.G. (1982) Oral immunization of foxes against rabies: Laboratory and field studies, Comparative immunology, Microbiol. and Infectious Diseases, 5, 165-171.
5. Rupprecht, C.E., Pietzschold, B., Cox, J.H., Schneider, L.G. (1989) Oral efficacy of a SAD-B19 vaccine for raccoons (Procyon lotor), J. Wildl. Dis. (submitted for publication).

ANNEX 1

LIST OF PARTICIPANTS

- Dr G. Baer, WHO Collaborating Centre for Reference and Research on Rabies, Rabies Laboratory, Centers for Disease Control, POB 363, Lawrenceville, GA 30246, USA
- Dr J. Blancou, WHO Collaborating Centre for Research and Management in Zoonoses Control, C.N.E.V.A., Laboratoire d'Etudes sur la Rage et la Pathologie des Animaux sauvages, B.P. No 9, F-54220 Malzéville, France
- Dr C. Foggin, Veterinary Research Laboratory, P.O. Box 8101, Causeway/Harare, Zimbabwe
- Dr Nadia Haddad, Directeur, Institut de Recherche vétérinaire de Tunisie, La Rabta, Tunis 1006, Tunisia
- Dr M.C. Horzinek, Virology Department, Veterinary Faculty, Rijksuniversiteit, P.O. Box 80 175, 3508 TD Utrecht, Netherlands
- Dr E. Istanbuluoglu, Director General, General Directorate of Protection and Control, Ministry of Agriculture, Forestry and Rural Affairs, Ankara, Turkey
- Dr D.O. Johnsen, Health and Science Attaché, United States Mission to International Organizations, Geneva, Switzerland
- Dr Florence Lafay, Laboratoire de Génétique des Virus, Centre National de la Recherche scientifique (CNRS), F-91190 Gif-sur-Yvette, France
- Dr D. Luchsinger, Animal Health Adviser, Science and Technology Bureau, US Agency for International Development, Washington D.C. 20523, USA
- Dr P.-F. Pastoret, Department of Virology and Immunology, Faculty of Veterinary Medicine, University of Liège, 45 rue des Vétérinaires, 1070 Brussels, Belgium
- Dr B. Perry, International Laboratory for Research on Animal Diseases (ILRAD), P.O. Box 30709, Nairobi, Kenya
- Dr C.E. Rupprecht, WHO Collaborating Centre for Reference and Research on Rabies, The Wistar Institute, 36th Street at Spruce, Philadelphia, PA 19104, USA
- Dr L.G. Schneider, WHO Collaborating Centre for Rabies Surveillance and Research, Federal Research Institute for Animal Virus Diseases, Postfach 1149, D-74 Tübingen, Federal Republic of Germany
- Dr G. Tang, Vice-Director, National Control Institute of Veterinary Bio-Products and Pharmaceuticals, Beijing, People's Republic of China

Dr A. Wandeler, WHO Collaborating Centre for Reference and Research on Viral Zoonoses, Virology Department, Institute of Veterinary Virology, 122 Langgass strasse, 3012 Berne, Switzerland

Dr T.D. Yilma, Department of Veterinary Microbiology and Immunology, School of Veterinary Medicine, University of California, Davis, CA 95616, USA

Other Organizations

International Office of Epizootics (OIE) - Dr Y. Ozawa

Secretariat

Dr K. Bögel, Chief, Veterinary Public Health, Division of Communicable Diseases WHO, Geneva

Dr F.-X. Meslin, Scientist, Veterinary Public Health, Division of Communicable Diseases, WHO, Geneva

Dr D.D. Joshi, General Manager, Dairy Development Corporation, P.O. Box 838 Lainchaur, Kathmandu, Nepal (Consultant)

Dr M. Kaplan, PUCWASH Conferences on Science and World Affairs, 11A Avenue de la Paix, 1202 Geneva (Consultant)

Dr V. Houba, Microbiology and Immunology Support Services, Division of Communicable Diseases, WHO, Geneva

Dr P. Sizaret, Biologicals, Division of Drug Management and Policies, WHO, Geneva

Dr William G. Winkler, 5472 Hugh Howell Road, Stone Mountain, GA 30087, USA (Consultant)

ANNEX 2

TIME SCHEDULE FOR ORAL VACCINATIONS
(A typical fox vaccination programme)

<u>Days prior to and after vaccination</u>	<u>Activities</u>
Immediately	- General planning; responsibilities - Budget
-12 to -6 (months)	- Information of governmental authorities (health, agriculture, hunting and forestry, police)
-60 to -14 (days)	- information of hunters and game wardens: assignment of duties of all persons concerned (e.g. staff responsible for aerial distribution of baits)
-30 to -10	- Transportation of baits to place of storage (-20°C)
-7	- Information of schools
-4	- Information to news media
-1	- Preparation of baits for distribution (storage at +4°C)
0/00	- Issue of baits and maps to distributing teams - Distribution of baits
+4, +8, +14	- Control of baits for uptake in special control areas (hand placement of baits)
+1 to +200	- Virological, serological and tetracycline testing (see handouts) - Evaluation of information - Inclusion of experience into future trials

= = =