EUROPEAN COMMISSION FOR THE CONTROL OF FOOT-AND-MOUTH DISEASE

Research Group Consultation

Lyons, France, 4 and 7 October 1976

On the occasion of the International Symposium on Foot-and-Mouth Disease organized by the Institut Français de la Fièvre Aphteuse (IFFA) at Lyons, the Research Group of the European Commission for the Control of Foot-and-Mouth Disease held a consultation on items which had been referred to the Group.

The consultation was attended by Dr. J.G. van Bekkum (Netherlands) Chairman of the Research Group, Dr. J. Brooksby (U.K.), Dr. M. Jensen, representing Dr. E. Michelsen (Denmark), Dr. L. Nardelli, accompanied by Dr. G. Panina (Italy), Dr. G. Eissner representing Dr. M. Mussgay (Federal Republic of Germany), Dr. J. Leunen, accompanied by Dr. R.P. Strobbe (Belgium), and Dr. J. Fontaine, who attended in an observer capacity on behalf of the host Institute, IFFA, Mérieux. Dr. G. Kubin was unable to attend. Dr. G.M. Boldrini, assisted by Dr. H. Girard, formed the secretariat.

This consultation substituted the regular meeting of the Research Group which could not be convened as previously planned, for protocol reasons. As the Research Group members were attending the IFFA Symposium, it was a good opportunity for the Chairman of the Group to call a consultation for the purpose of having an exchange of views and thus obviate the necessity for calling a regular meeting of the Group before the Twenty-Second Session of the European Commission.

The Mérieux Foundation and IFFA provided a site for the consultation as well as secretarial assistance.

The following points were discussed by the Group:-

1. The carrier state as seen by an administrator

As suggested by the Executive Committee at its 38th Session (Oslo 15-19 June 1976) the conclusions reached by the Research Group when discussing this item at the meeting held by the Group at Brescia/Padua in September 1975 were re-examined. It was felt that clarification of conclusion (3) of the Research Group's document when applied to trade of potential carriers was required especially as a guidance to those European member countries which are able to maintain disease freedom in the absence of vaccination.

The definition of 'exotic' as understood by the Group for the purpose of this document was also given. The new text agreed to by the Research Group is as follows:-

"(3) The possible existence of carriers in a population was not considered a valid reason for the restriction of animal movements between countries

once the disease has been eradicated and the usual quarantine restrictions have been lifted. These measures were considered acceptable for European countries where the cattle are vaccinated annually and when dealing with European virus types.

However, the virus carrier is felt to constitute a small but definite risk.

Therefore, before admitting potential virus carriers into countries which have been free from the disease in recent years, and when disease control is based on the application of veterinary police measures only, quarantine and probang testing should be considered for breeding stock.

Potential carriers of exotic FMD virus should not be admitted into any European country.

Footnote For the purpose of this document the Group considers any virus strain 'exotic' that is new to the region and against which the available vaccines do not show the accepted standards of potency; even if the cattle population had an appreciable immunity due to repeated vaccination, there might still be an extensive outbreak in pigs against which no suitable vaccine might be available."

... The full text of the revised document on the carrier state is attached hereto.

2. PD50 content of FMD vaccines

The previous conclusions reached by the Research Group on the occasion of the meetings held at Brescia (September 1969), at Lelystad (October 1974) and at Brescia/Padova (September 1975) on the PD_{50} content of FMD vaccines were reviewed.

The outcome of the meeting held at Alfort, 16/17 March 1976, by the European Pharmacopoeia Commission, with the participation of delegates from FAO and OIE, to discuss problems connected with the elaboration of a monograph on FMD vaccine was then examined.

Dr. van Bekkum and Dr. Leunen explained the stand taken by the Research Group members present at the meeting and the positive results achieved in a two-day discussion especially with regard to the difficult subject of vaccine potency and the way to measure it.

The following conclusions of the Pharmacopoeia meeting, as shown on pages 9 and 10 of Document PA/PH/Exp. 15V(76)3 of 31 March 1976, were considered by the Group.

"1. Foot-and-mouth disease vaccine should, at the dose prescribed, protect 70 percent (lower fiducial limit, having P = 0.95) of animals in the conditions of the test against an inoculation with 10,000 ID_{50} doses given in 2 sites) of the type or sub-types of virus used for the preparation of the vaccine.

2. The potency test in the monograph shall be by the determination of the PD_{50} in cattle by challenge with virulent virus, administered three weeks after vaccination, the observation time before reading the results being eight days. Two animals shown to be free of foot-and-mouth disease and having no anti-bodies against the strain of virus used to prepare the vaccine shall be used as controls.

3. The vaccine shall contain not less than 3 (lower fiducial limit) PD_{50} per vaccinating dose.

4. A footnote shall recognise that national control officers may authorise alternative methods for routine assays provided that:

   - the method used is sufficiently widely known

   - a thorough statistical evaluation has established a satisfactory correlation between the method used and the PD_{50} established for the vaccine by the officially prescribed method.

5. If desired the K-index method and the determination of the PD_{50} by serum neutralisation could be described in an annex as examples of methods which satisfy the above requirements.

6. The period of observation in the safety test shall be 10 days (4 days in the first stage and 6 days in the second stage).

7. The safety test in cell cultures shall be transferred from "tests" to "preparation" and treated as an in-process control."

While admitting that the new standards were higher than those proposed at the 1974 meeting at Lelystad, the Group accepted the conclusions of the Alfort meeting, with the understanding that:

a) The statement under item 3 of the conclusions i.e. "The vaccine shall not contain less than 3 (lower fiducial limit) PD_{50} per vaccinating dose" means that not more than one in twenty vaccines will contain less than 3 PD_{50}.*

b) The potency test will be carried out using bicarbonate buffer as diluent and as specified in the report of the meeting, the results will have to be analyzed by the probit method.

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* The average number of PD_{50} per dose should be six to nine.

Note by the secretary

The existence of some contradiction between conclusion (1) where reference is made to the minimal requirement of 70% protection in vaccinated animals, and conclusion (3) where a minimum of 3 PD_{50} is recommended (according to available information this would correspond to about 85% protection) was noted by the Research Group. It was remarked that 70% protection would have very little meaning in the absence of an indication of age of the animals and time of challenge. At the International Symposium, on the other hand, it was pointed out that 70% protection had been proposed at a time when FMD was endemic in Europe, with the objective of stopping epizootic waves of the disease throughout the continent. The new 85% protection limit was then accepted in this meeting which was also attended by representatives of OIE and the industry.

3. Inter-laboratory evaluation of methods for virus and antibody assays

Dr. Brooksby informed the Group that the Animal Virus Research Institute (AVRI) Pirbright, was ready to start the programme proposed by the Research Group for a study on techniques for the evaluation of virus for the preparation of FMD vaccine. This study would be carried out in collaboration with a number of FMD laboratories concerned with the manufacture or official testing of FMD vaccine. AVRI would prepare and distribute to the various laboratories a reference virus and the corresponding antiserum, and the secretariat of the European Commission would collect the results of the tests with a view to evaluating them at the next meeting of the Research Group. Dr. Brooksby submitted also to the Group the draft protocol for the basic biological tests (virus titrations and serum neutralization by different methods - quantitative complement fixation - radial immunodiffusion) to be carried out as a first stage of the joint study. The Group approved the protocols and expressed appreciation for the substantial collaboration offered by AVRI to the Research Group's activities. It was suggested that the programme should commence as soon as possible in order to have at least part of the work completed by the end of 1976.

A list of twenty laboratories was drawn up for participation in the study; the Plum Island Center (USA) and the Pan American Center for FMD, Rio de Janeiro, were included.

The Secretary undertook to contact all selected laboratories just after his return to headquarters in order to ascertain their willingness to participate in the study. It was hoped to have the virus despatched soon after 20 November.

Acknowledgements

The assistance and hospitality given to the Group by IFFA, Mérieux, was highly appreciated.

Rome, 15 November 1976

THE CARRIER STATE

The conclusions reached by the Research Group when discussing Dr. Werdelin's paper "The views of an administrator on the virus carrier" at Brescia in September 1975, were revised by the Group at the Lyons consultation. The revised text is given hereunder.

(1) The Group considered that only ruminants which continued to produce and excrete viruses either continuously or intermittently over periods beginning 3 - 4 weeks after exposure to the virus, should be considered to be virus carriers.

(2) The Group was unanimous in feeling that in a primary outbreak all animals, whether vaccinated or not, should be eliminated. However, this view was not based on the possible creation of carrier animals among the protected animals, but rather on the advisability to deal drastically with a virus which might be new for the country.

The possible existence of carrier animals in a herd was not considered sufficient argument for stamping out the herd in question in countries where the population is routinely vaccinated. The policy followed in Denmark consisting in the elimination of the whole herd involved in the primary outbreak and the application of ring vaccination, was considered acceptable because, the population not being routinely vaccinated, the chance of the creation of carriers in the susceptible population was considered to be reduced. Secondary outbreaks should also be dealt with by stamping out.

(3) The possible existence of carriers in a population was not considered a valid reason for the restriction of animal movements between countries once the disease has been eradicated and the usual quarantine restrictions have been lifted. These measures were considered acceptable for European countries where the cattle are vaccinated annually and when dealing with European virus types.

However, the virus carrier is felt to constitute a small but definite risk.

Therefore, before admitting potential virus carriers into countries which have been free from the disease in recent years, and when disease control is based on the application of veterinary police measures only, quarantine and probang testing should be considered for breeding stock.

Potential carriers of exotic FMD virus should not be admitted into any European country.

(4) The risk involved in the trade within Europe of meat derived from carrier animals is not considered to be of any importance. The trade in offal of carrier animals may have to be considered to constitute a risk in case of exotic viruses.

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