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

AN/58

Standing Technical Committee

Minutes

of the Meeting held at Pirbright on 24 and 25 June 1958

A meeting of the Standing Technical Committee of the Commission was held at the Virus Research Institute, Pirbright, on 24 and 25 June 1958. The following members were present:- Dr. H.S. Frenkel, Dr. I.A. Galloway, Dr. E. Michelsen, Prof. B. Ubertini together with the Secretariat:- Sir Thomas Dalling and Dr. Erik Fogedby.

An apology for absence was received from Dr. J.M. van den Born (Chairman of the Commission).

In addition, Prof. L. Nardelli (Italy) and Dr. J.B. Brooksby (United Kingdom) attended the meeting.

Dr. I.A. Galloway was appointed Chairman and extended a warm welcome to all present.

The Agenda, as circulated, was adopted.

The subjects for discussion were: (1) Future Work of the World Reference Laboratory for Foot-and-Mouth Disease, Pirbright, for Europe; (2) Supplies of virus instead of vaccine; (3) Inspection of carcases for detection of lesions of foot-and-mouth disease; (4) Variants of the virus of foot-and-mouth disease in Argentina and (5) Supplies of vaccine.

FOOT-AND-MOUTH DISEASE REFERENCE LABORATORY

The need for designating a laboratory as a Reference Laboratory for the Commission and its Member countries has been discussed on several occasions and at its Third Session the Commission decided "that a formal approach be made to the appropriate authorities in the United Kingdom with a view to the designation of the Virus Research Institute, Pirbright, as a reference laboratory for virus types, to maintain all strains of virus and type-specific anti-sera, to label variant strains within types and to confirm typing of viruses, on request from countries". The Food and Agriculture Organization has expressed its interest in the designation of the Pirbright Institute as a World Foot-and-Mouth Disease Reference Laboratory and negotiations on the subject between the Organization and the Government of Great Britain were recently completed. It was agreed at the Fifth Session of the Commission that the contract in course of preparation between the Government of Great Britain and FAO should include the interests of the Commission, already discussed by the Executive Committee, and that the future work of the Refernce Laboratory, as far as European countries are concerned, should be further discussed by the Commission's Technical Committee.

A memorandum, prepared by Dr. Galloway, was considered at the present meeting and, following some amendments now included, the text of the memorandum was agreed and reads as follows:

The Function of the World Reference Laboratory for Foot-and-Mouth Disease in Respect of European Countries

1. The World Reference Laboratory will be responsible for the examination and identification of strains of virus which are suspected to be types other than O, A and C.

This work will be given high priority.

(a) It is particularly appropriate that the World Reference Laboratory should be asked to accept this responsibility because of its experience in examination of samples of virus from all over the world, and because it has all the necessary facilities for the full examination of suspect material.

(b) The virus material submitted for examination will be treated by the World Reference Laboratory in the same way as field samples submitted by countries other than those in Europe.

(c) Information should be submitted with the virus samples, similar to that requested in the instructional leaflet of the World Reference Laboratory for countries in other areas than Europe in respect of place of origin of the sample, number and species of the animal involved in the outbreak. It should included also supplementary information on the number of animals at risk of infection in the area, and on any circumstances which might indicate the source of infection.

(d) The basis of the suspicion that the virus strains submitted for examination may belong to a type other than O, A or C should be given.

(e) The rapidity with which an answer can be expected will depend on a number of factors. The Laboratory will make reports by telegraph or telephone of the progress of the examination. The greatest delay to be expected will be when the virus sample proves to be infective in animal tests but cannot be classified in any of the seven recognised immunological types.

(f) As soon as there is sufficient confirmatory evidence that the outbreak is associated with a virus type other than O, A and C, this information will be transmitted to the country concerned and to the European Commission for Foot-and-Mouth Disease, and the Secretariat of the Commission will then inform FAO and OIE.

(g) It is to be expected that the World Reference Laboratory will request a collection for exmination of further field samples from the area involved in the outbreak.

2. The World Reference Laboratory will be responsible for the maintenance of a collection of sub-type strains which have been found in Europe, and of their corresponding anti-sera.

It seems clear that there is justification for continued investigation of the sub-type problem since the evidence available points to the significance and usefulness of detailed immunological comparison of strains in relation to epidemiological studies and vaccination. The examination of strains by the World Reference Laboratory will depend mainly on complement fixation and other serological tests.

(a) This will involve in the first place a review of the present position with regard to sub-types. It does not seem appropriate, for example, that samples of virus labelled A_5 from all laboratories should be compared. Any attempt to compare all the numbered strains from all the laboratories would be a major task which would not be justified and would not lead to early progress on the work in connection with the strains in current outbreaks. It would be preferable to make a start by selecting one set of A type strains, and after check tests, to use these standard sub-types for further comparison. This will necessitate the preparation and storage of the corresponding stock anti-sera for these strains, and the preparation and storage of guinea-pig virus and perhaps also mouse virus. A similar procedure would be followed in respect of O and C type strains. This part of the work would take some time. In the meantime, it is desirable that the collection of new sub-types should proceed.

(b) The ultimate aim is that the World Reference Laboratory will establish a collection of all confirmed sub-types, and at least guinea-pig strains with their corresponding anti-sera.

(c) The World Reference Laboratory collection of sub-type strains, of which a catalogue will be made, will be increased as time goes on by the addition of strains sent in from the various laboratories, and perhaps also by the occasional sampling of virus from current field outbreaks. The main development of this will, of course, rest with the laboratories of the countries concerned.

3. Suspicion of the existence of a new sub-type will be confirmed wherever possible by the laboratory in the country concerned. Duplicate samples of the original field material will, at the same time, be sent to the World Reference Laboratory. On request from the country concerned, based on evidence of sub-type difference, the World Reference Laboratory will then carry out investigations and number the sub-type strain. It will not be the responsibility of the World Reference Laboratory to carry out the initial examination of virus samples for strain differences, unless it is impossible for such work to be done in the country of origin.

(a) It is not intended that the World Reference Laboratory should perform the initial examination of strains as a routine. This recommendation is necessary because examination of each strain to determine whether it is a sub-type or not, involves a considerable amount of work, and this would place too great a strain on the World Reference Laboratory organization.

(b) The individual laboratories in the countries concerned should make their own investigations to determine whether the strains under consideration are sub-types or not. It is necessary to make the proviso that duplicate samples of original virus material, which is being studied by the individual laboratories for this purpose, should be sent to the World Reference Laboratory as a precaution against the possible accidental contamination of the strain under examination with another strain. That such accidental contamination can occur has been confirmed as a result of examination of materials submitted to the Pirbright Institute in the past.

(c) It is clear that the role of the World Reference Laboratory is to confirm the results of the investigations made by individual laboratories, and that by accepting this responsibility the World Reference Laboratory will overcome the difficulty created by different laboratories separately numbering strains whenever they have evidence indicative of a new sub-type.

4. Standard strain specific anti-sera for the established sub-types in the World Reference Laboratory collection will be supplied to the laboratories requiring them.

Laboratories wishing to investigate strains of virus occurring in their territories will be supplied with stock sub-type anti-sera from the World Reference Laboratory collection. These sera will be supplied free of charge for small quantities, say 4 mls. and at production cost for larger quantities.

5. New sub-types will be numbered only after checking against earlier established sub-types, and these numbers will be allocated by the World Reference Laboratory.

(a) A procedure for interim numbering of new sub-type strains should be adopted, namely to start numbering at an arbitrary level, for example O_6, A_{10}, C_6, to avoid confusion with earlier established strains.

(b) The collection and numbering of new sub-type strains will of necessity be somewhat delayed, but the World Reference Laboratory will issue a bulletin at intervals in which new sub-types with information relating to them will be listed.

In the control of foot-and-mouth disease in Europe, it is of importance that, in addition to information being available on types and strains of virus present in European countries, the Commission should also have knowledge of types and strains causing infection in countries in close proximity to Europe. Information on this subject will be made available to the Commission as far as possible through reports from the World Reference Laboratory to FAO. The Commission is particularly interested in the position in Turkey which, although a Member of the Commission, extends largely into Asia. The Reference Laboratory agreed to treat the whole of Turkey as a country outside Europe, so that the arrangements made between the Laboratory and FAO would apply. These include the regular typing of samples from outbreaks in the whole country by the World

Reference Laboratory, irrespective of the extent or severity of the outbreaks and the supplying of the laboratory with full particulars on the location of the outbreaks in the country (longitude and latitude particulars would be convenient) from which samples were sent, together with epizootological information. It was agreed that the Commission would inform the Turkish authorities of this arrangement and the details of the requirements, such as the technique of collecting and despatching samples.

The Turkish authorities would be informed that the World Reference Laboratory, Pirbright, sends the results of typing of samples as soon as possible and that, when lengthy examinations are involved, progress reports would be made to them from time to time.

SUPPLIES OF VIRUS INSTEAD OF VACCINE

This question was discussed fully. Then the chairman suggested that the Secretariat with Dr. Frenkel should prepare a memorandum on this question for record purposes and so that any points could be commented on further by members of the Committee later.

What follows records the results of the deliberations at the meeting at Pirbright on 24 June 1958 and after studying the memorandum:-

At the Fifth Session of the Commission, during the discussions on supplies of vaccine to countries through the Commission, Dr. Frenkel raised the question of supplying culture virus instead of vaccine, the preparation of the finished vaccine to be completed in the countries concerned. The Commission referred the suggestion to the Standing Technical Committee.

The present position is that, in order to put into effect the Commission's overall plan for the control and eradication of foot-and-mouth disease, supplies of vaccine are required by some countries in Europe, in which production is not so far possible. In addition, although laboratories have been or are being constructed and equipped for vaccine production, using culture virus, in some European and Asian countries, some difficulties are certain to arise, at least temporarily, because of lack of well-trained and experienced personnel and, in some countries, local conditions. Assistance might, therefore, be given to such countries in the control of foot-and-mouth disease, if cattle or culture virus, produced in European laboratories could be supplied and the final vaccine prepared in the countries concerned.

It was considered that there would be difficulties and a number of disadvantages and risks if arrangements were made for the supply of cattle culture virus to such countries.

Consideration was given to the suggestion of supplying formalin inactivated virus instead of fully infective virus for vaccine production.

Reference was made to the fact that there appeared to be indications from early experiments made in Denmark and more recent experiments reported at the meeting by Dr. Ubertini that it is possible to prepare as effective a vaccine by inactivating the virus with formalin before adding the adsorbant and adjuvant aluminium hydroxide as by treatment of the mixture of virus and aluminium

hydroxide with formalin, which is the usual method of making the Schmidt-Waldmann type of vaccine. There was some indication (Ubertini) also that concentrated formalin inactivated virus which has been stored for 6 to 8 months can be used for making vaccine. Reference was made also to the advantage which would be gained if it were found possible to prepare fully antigenic dried formalin inactivated virus for vaccine production.

It was agreed that further work would be required to confirm all these points and to establish the feasibility and reliability of such procedures. Many more experiments would have to be done and attention would have to be given to tests of innocuity, in fully susceptible cattle, of the formalin treated virus supplied. Decisions would have to be made also on the procedures to be adopted for the determining of the antigenic potency of formalin inactivated virus or on the other hand vaccines prepared therefrom and on where this testing should be done.

The Committee considered that attention should be given to this problem and that experiments along the lines discussed were well worth pursuing.

INSPECTION OF CARCASES FOR DETECTION OF LESIONS OF FOOT-AND-MOUTH DISEASE

The discussion referred chiefly to the inspection before shipment of carcases imported into Europe from South American countries. Dr. Fronkel had suggested at the 5th Session of the European Commission that it might be possible for more rigid inspection of carcases to be carried out. It seemed highly probable that unless specially trained inspectors were examining the carcases and special attention was being given to the parts of the carcases where it would be suspected that lesions might be found, such lesions might escape detection.

It was felt that the Committee was not in a position to consider the question fully or make any recommendation until they had had an opportunity of studying a copy of the report which presumably would be made available to them, of the FAO mission to South America which was looking into the question. The problem of minutely inspecting carcases for signs of foot-and-mouth disease infection was different from the routine inspection usually carried out in abattoirs or in "frigorificos".

VARIANTS OF THE VIRUS OF FOOT-AND-MOUTH DISEASE IN ARGENTINA

Reference was made by Dr. Fogedby to the fact that there had been reports that there were strains of the virus of foot-and-mouth disease (O, A and C types) which differed antigenically from the strains of virus associated with outbreaks in Europe.

The evidence on which these reports were based were not available to the Committee. It seemed, however, that the antigenic differences suggested were of the order which would bring them within the class of variant or sub-type differences. The validity of the conclusions on which these reports were based would have to be investigated and this would be a major task. The problem was not dissociated from that for which the World Reference Laboratory had now

accepted responsibility in respect of European countries (vide supra) and sub-type strains. The significance and usefulness of detailed immunological comparison of strains in relation to epidemiological studies and vaccination had already been agreed in the earlier discussions on this subject. It was not possible for the Committee to discuss the matter of virus strains from the Argentine further until they had the evidence on which the reports were based.

SUPPLIES OF VACCINE

The Secretariat pointed out that some discussions had taken place at the meeting of the Committee in Paris in May 1957 on tests for the innocuity and potency of vaccines but no conclusions had been reached. The matter was raised again at the present meeting. The members felt that it would be difficult at the present juncture to agree upon recommendations for standard tests for innocuity and potency of inactivated vaccines which would be universally acceptable. All agreed that stringent tests for innocuity of inactivated vaccines are essential and that cattle of full susceptibility should be used for vaccines to be administered to cattle. It was not easy for all countries to make arrangements for such tests and in some cases unweaned mice were used instead while relying on their high grade of susceptibility to infection with most cattle virus strains. There was no evidence from accumulated results of comparative tests, with different strains in cattle, mice and tissue culture for non-infectivity of vaccines, that reliance could be placed on employing mice and/or tissue cultures instead of cattle. One of the difficulties encountered by some countries was in making arrangements for such tests on cattle of known susceptibility. Now that more techniques are available for checking antibody levels in cattle of doubtful susceptibility this difficulty should in part be overcome. Everyone realizes that the more stringent are the tests for non-infectivity of virus vaccines, the "safer" are the vaccines likely to be, whether they be foot-and-mouth disease or poliomyelitis or any other other vaccines; i.e. the less chance will there be that inoculation of the vaccine may lead to the development of the disease in some more highly susceptible hosts. The problem of testing vaccines more stringently was originally raised in relation to the question of supply of vaccines from a vaccine producing country to a non-vaccine producing country and it was particularly in relation to such supplies that renewed interest had arisen in the desirability of reviewing the question of testing of vaccines for innocuity and potency.

The greatest concern was felt in respect of the possibility of an inadequately tested vaccine being supplied to a country which had been previously always free of the disease or free at least for a considerable number of years and which had become invaded by e.g. an A type virus and wished to carry out vaccination to limit spread. The worst circumstances would arise if perchance the imported vaccine was a bivalent or trivalent vaccine O, A or O, A, C and if the vaccine had been inadequately tested and was not "safe" in respect of the O or C components.

It would be equally unsatisfactory if the vaccines supplied had not been recently tested for potency on cattle of unknown susceptibility. In this connection the value of supplementing virus challenge tests with determination of antibody levels was stressed.

In the time available it was not possible to go further into the question of testing of vaccines at this meeting but it was considered important that it should be kept under constant review.

It seemed clear that there are undue hazards associated with the indiscriminate supply of vaccines and that some procedure should be adopted for ensuring that they are adequately tested.

FUTURE WORK OF THE STANDING TECHNICAL COMMITTEE

A short discussion took place on the future work of the Standing Technical Committee and the opinion was expressed that more use should be made of it by the Commission. Since the meeting, the Chairman (Dr. I.A. Galloway) has given some thought to the subject and has prepared the note given in the Appendix to these minutes.

A P P E N D I X

Draft Note on the Future Activities of the Standing Technical Committee

The feeling was expressed that if the intended functions of the Commission were to be fulfilled more use should be made of the research members of the expert committee of panel. It seemed that although the panel had been in being for some time and there had been several meetings, little progress had been made in giving consideration to important problems. It seemed to be desirable that the research people should have the opportunity of meeting for free informal discussions. It would be appreciated that there are many problems which laboratory workers wish to discuss freely among themselves and which they could not suitably do in the type of meeting of the expert panel which has been held so far. Ideas that emerged from this were that it would seem to be a suitable arrangement that a meeting should be held at least at each of the four institutes (Frenkel - Holland, Ubertini - Italy, Michelsen - Denmark, Galloway - Great Britain) in turn once a year, and that the chairman at each meeting would be the director of the institute at which the meeting is held. Such meetings of say, two days' duration would provide the means also of arranging for members of the staff of the respective institutes to present short reports of current activities and be co-opted when necessary. There should also be opportunities provided for the members to visit individually, in pairs or as a group, other institutes from time to time say as a minimum, one visit of two days per person per year (i.e. institutes in other countries in Europe, not necessarily members of the European Commission e.g. Germany, France, Portugal, Spain, etc. working on foot-and-mouth disease and/or other virus diseases). More rarely it would be very useful if it were possible, should any new method for preparing vaccines or new technique be developed in an institute outside Europe, that a visit could be made by one or preferably two of the panel to get all essential details.

Full reports would be prepared of the matters discussed at each meeting held in Holland, Italy, Denmark and Great Britain for circulation only among the research panel members. Reports of visits to other institutes would be submitted to the research panel for consideration.

During the meetings or visits opportunity should be taken to get first hand information on disease incidence and problems related to field control including vaccination as the laboratory workers must be fully conversant with practical issues and epidemiological aspects.

The arrangements for the meetings and visits suggested would place the research members of the expert panel in a much better position to make recommendations to the Executive Committee and the Commission on lines of action and to make suggestions for the support of certain projects.

Since the research panel would not only keep detailed minutes of their meetings and a collection of their reports of visits and all information on foot-and-mouth disease available, it would also be in a better position to advise on any points which may be submitted for its consideration.

It would be an improvement if the research panel group were asked to prepare, after exchange of ideas and consultations, an agenda for the main meeting of the expert panel which it is understood will now be held annually before the meeting of the Commission.

If these proposals are accepted there would have to be appropriate funds available to the Commission for the travel and subsistence of panel members. It should be possible to make a rough assessment of the total sum required for the meetings and short visits in Europe and much rarer visits to countries outside Europe, but the impression was that the sum should be of the order of at least £2,000.

The feeling was that much could be achieved if the activities of the research group were increased and the procedures for organizing a more coordinated effort were developed. There appeared to be no justification or satisfaction to anyone in perpetuating an expert panel which had no programme and little influence.
