



Argentine—United States
Joint Commission on
Foot -and-Mouth Disease

Final Report

National Academy of Sciences

FINAL REPORT

U. S. COMPONENT OF ARGENTINE - UNITED STATES
JOINT COMMISSION ON FOOT-AND-MOUTH DISEASE

AND

THE U. S. ADVISORY COMMITTEE
ON FOOT-AND-MOUTH DISEASE

30 June 1974

Contract AID/1a-4
Argentina

The United States Agency for International Development
and
The National Academy of Sciences
The National Research Council
2101 Constitution Avenue
Washington, D.C. 20418

1974
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ARGENTINE - U.S. JOINT COMMISSION ON
FOOT-AND-MOUTH DISEASE

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Dr. William R. Hinshaw, Executive Secretary
National Academy of Sciences

REPORT SUMMARY

1. **Project Title:** To provide certain assistance to Argentina in its livestock improvement program, at the request of the Argentine government.
2. **Contract Number:** AID/1a-4 - Argentina.
3. **Purpose:** The purpose as stated in the original contract (1962) was as follows:
"To provide advice and consultations on the design and conduct of a program of investigation to assess the current situation on Foot-and-Mouth Disease (FMD) and to determine whether the application of science and technology can free certain forms of processed meat from viable virus."

In 1965, following the expressed wishes of the governments of the United States and Argentina, the National Academy of Sciences Division of Biology and Agriculture proposed an expanded program for the U. S. Advisory Committee on FMD to include subcommittees on meat technology, animal virology, and epidemiology, and to give particular attention to training of Argentine scientists and technicians. Since 1968 the emphasis has been on evaluation of newly developed FMD vaccines in Argentine cattle.
4. **Contractor:** National Academy of Sciences - National Research Council, 2101 Constitution Avenue, Washington, D. C. 20418.
5. **Contract Period:** 15 June 1962 - 30 June 1974. Final extension No. 18, 1 January 1974 - 30 June 1974.
6. **Period covered by this report:** 1 January 1970 - 30 June 1974, with summary of information for 1962-1969, covered in detail in previous reports.
7. **Total AID Funding of Contract:**

AID/1a-4, through Amendment 18,	\$698,000.00
AID/csd-2273 (1969) 1 yr supplement	\$ 49,000.00
TOTAL	\$747,000.00

It should be noted also that large monetary contributions to this project were also made by the U.S. Department of Agriculture, Plum Island Animal Disease Center (PIADC),* Argentina (INTA and SELSA) and Pan American Health Organization, Foot and Mouth Disease Center, Rio de Janeiro, Brazil (PAHO, FMDC). The support of these agencies included laboratory support, animals used in laboratory and field trials, personnel and holding facilities (such as those furnished by Argentina on the Valdes Peninsula in the Chubut Province of Argentina).

* Formally the Plum Island Animal Disease Laboratory (PIADL).

FINAL REPORT
AID/1a-4
ARGENTINA

1 January 1970 - 30 June 1974

This report covers the period supported by contract AID/1a-4 - Supplements 17 and 18. Reports for period 1962-70 (Amendments 1-16) have been previously submitted. A historical summary of the 1962-69 period is included below.

BACKGROUND

The following excerpt from a "Status Report - Contract AID/1a-4" by W. R. Hinshaw, 15 April 1973 summarizes the historical background:

"Previous to 1959 the U. S. Department of Agriculture permitted salt-cured beef to be imported from countries where Foot-and-Mouth Disease (FMD) was known to exist. The reasons for this were that until then it was not known that FMD virus would remain alive following the salt-curing process and that no outbreaks in the United States had been traced to this product. In 1959, USDA prohibited the further import of salt-cured meat products from countries infected with FMD, based on research at Plum Island Animal Disease Center (PIADC) which proved that the FMD virus could survive in lymph nodes in salt-cured beef.

The announcement of this regulation by USDA acted as a 'bombshell' to the many countries affected. Unsuccessful attempts were made by a number of countries to have the decision reversed. President Arturo Frondizi of Argentina, during a visit to the United States in September 1961, requested President John F. Kennedy's assistance in the solution of the FMD problem which was adversely affecting importation of beef into the U.S. President Kennedy requested NAS/NRC to assume responsibility for appointing a special mission to go to Argentina. Such a mission, headed by Dr. George Harrar, The Rockefeller Foundation, went to Argentina in January 1962. The mission's findings, including recommendations for short-term as well as long-term corrective programs, were reviewed by a U.S. - Argentine conference sponsored by NAS in March 1962.

Following the March 1962 Argentine - U.S. conference, which led to the formation of the Argentine - U.S. Joint Commission on Foot-and-Mouth Disease, President Kennedy asked the National Academy of Sciences to activate and manage the

United States' participation in the joint program. To finance the U.S. Component of the Joint Commission and the NAS U.S. Advisory Committee on Foot-and-Mouth Disease, a contract (AID/la-4) was signed by the U.S. Agency for International Development and the National Academy of Sciences. The Argentine Component was financed by the Argentine Government. AID has continued to support NAS by periodic renewals of contract AID/la-4. In 1969, a supplemental AID contract (AID/csd-2273) for one year gave additional support. Mention should also be made of the substantial support given to the Project by USDA, Pan American Health Organization (PAHO), and Argentina.

A ten-man Joint Commission was organized to carry out the program. The five Argentine members were appointed by the Argentine President while the U.S. members were appointed by the President of NAS under the agreement between President Kennedy and NAS. NAS also appointed 13 members to a U.S. Advisory Committee on FMD to work with the Joint Commission.

George C. Poppensiek, Dean, Veterinary Medicine, Cornell University, served as Chairman of both the U.S. Component of the Joint Commission and the Advisory Committee from 1962 to 1967. Stewart H. Madin, University of California, has served as Chairman of both groups since July 1967. James H. Gillespie, Cornell University, served as Staff Officer from 1962 to June 30, 1967. William R. Hinshaw has served as Staff Officer since July 1, 1967. On January 1, 1972, the size of the U.S. Advisory Committee on FMD was reduced to five members. The five members were appointed to serve jointly as members of the U.S. Advisory Committee and the U.S. Component of the Argentine - U.S. Joint Commission on FMD. They are as follows:

Stewart H. Madin, Berkeley, California (Chairman)
Carl A. Brandly, Champaign, Illinois (Co-Chairman)
Victor Conquest, Chicago, Illinois
Robert P. Hanson, Madison, Wisconsin
Maurice S. Shahan, Greenport, L.I., New York

The members of the Argentine Component of the Joint Commission are as follows:

Dr. Venancio Deulofeu (Chairman)
Dr. Constantino Brendariz
Dr. Luis F. Leloir
Dr. Enrique Garcia Mata
Dr. Augusto L. Durlach (Executive Secretary)
Dr. A. Parodi (former member, is deceased.)

The problem of FMD has been under surveillance by the Argentine - U.S. Joint Commission on FMD since it was established in 1962 by action of the governments of the two countries. Studies on the persistence of virus in vaccinated animals as it relates to the meat packing industry and a serologic survey of animals on Tierra del Fuego, were completed in 1964. The results of these studies, supported by NAS/AID contract AID/la-4, involving scientific collaboration between laboratory and field personnel in Buenos Aires, Tierra del Fuego, the Pan American Health Organization Foot-and-Mouth Disease Center (PAHO, FMDC) in Rio de Janeiro and USDA have been published in the National Academy of Sciences (NAS) Publication 1343, 1966.

In 1965, following the expressed wishes of the governments of the U.S. and Argentina, the NRC Division of Biology and Agriculture proposed an expanded program for the U.S. Advisory Committee on FMD to include sub-committees on meat technology, animal virology, and epidemiology, and to give particular attention to training of Argentine scientists and technicians.

An early accomplishment (1962-63) of the Meat Technology Committee of the Argentine - U.S. Joint Commission was to recommend development of a cooked meat roll which could be frozen for meat export without danger of transmitting FMD. This product has met USDA requirements and has replaced the salt-cured beef formerly shipped to the U.S. Recent reports from Argentina indicate that exports of this product to the U.S. now exceed the volume of salt-cured products formerly exported to the U.S.

Meat technology was kept active by Victor Conquest, the Chairman of the NAS Subcommittee on Meat Technology. He kept in close contact with the meat situation in Argentina and gave consultation aid on a number of occasions. He also gave help and advice on the Meats Research Laboratory being built at Castelar (the "Beltsville of Argentina"). This laboratory and another at Castelar for animal disease research including FMD, was partially funded by USAID. Both laboratories are now ready for occupancy.

Aid in improving the technical knowledge of the professional staff in both meat technology and animal disease control has been one of the priority missions of the Joint Commission. The U.S. Group has cooperated in this training program by aiding the Argentines in locating available candidates in U.S. universities and to a minor extent in furnishing funds from the AID/la-4 contract budget. At least ten persons have been aided by the U.S. Group in getting training of some type in the U.S. since 1962.

At a meeting of the Argentine - U.S. Joint Commission held in Buenos Aires, 2-6 March 1970, it was agreed that the Joint Commission will have completed its mission when the current 'vaccines' project is completed. The Joint Commission has gone on record to this effect, and has recommended that it be dissolved as soon as feasible after completion of this project. At the same meeting, the Argentine - U.S. Joint Commission recommended that an Interamerican FMD Commission similar to the European FMD Commission be established."

At a meeting of the Argentine Component of the Joint Commission, held in February 1974, the following recommendation was made in a report of the meeting to the Argentine Minister of Agriculture:

"The Argentine Group of the Joint Commission feels that the Commission has achieved the objectives of its mission and at the same time has been instrumental in the integration of the main research groups in the Americas concerned with foot-and-mouth disease. Each of the members of the Argentine Group individually, and all of them jointly, agree that the mission of the Group can be terminated. Nevertheless, they remain ready to help any officer or institution involved in the problem of foot-and-mouth disease, if it is considered that the experience they have acquired should be used." (See Appendix 2)

The final report (February 1974) of the Argentine Component received from Dr. V. Deulofeu in February 1974 was first discussed at the 5-6 March meeting of the U.S. Component and again reviewed at the final meeting on June 25, 1974. The U.S. Members agreed to concur with the Argentine Members that the mission of the Joint Commission has been accomplished and should be terminated on 30 June 1974 - the final date of NAS Contract AID/1a-4. (See Appendix 3)

At the final meeting of the U.S. Component of the Joint Commission held on 25 June 1974, at PIADC, the following recommendation was made:

"Even though the mission of the Joint Commission has been accomplished, there is a need by NAS/NRC for a continued participation in an advisory capacity on foreign animal diseases including FMD. An indication of this is the fact that several government agencies have repeatedly emphasized this continued need to members of this group. This function could be assigned to the newly organized Committee on Animal Health in the Board on Agriculture and Renewable Resources (BARR)."

SUMMARY OF RESULTS OF 1972 - 1974 FIELD TRIALS

At the third official meeting of the Argentine - United States Joint Commission on Foot-and-Mouth Disease in Buenos Aires, Argentina, 30 November - 2 December 1965, its Committee on Vaccines recommended that a project on "Comparative antigenic evaluation of oil-adjuvant and aluminum hydroxide vaccines" be initiated.

Such a project was started in 1968 in cooperation with the PAHO Foot-and-Mouth Disease Center (PAHO, FMDC) in Rio de Janeiro. In 1969, cooperative field trials were started in Argentina. Both phases of this project were partially supported through contract AID/la-4 and a supplemental contract AID/csd-2273 with the cooperation of USDA, PAHO and Argentina. The results of the 1968 and 1969 trials were reported in the Final Report for contract AID/csd-2273 on 25 September 1970.

At a meeting of the Joint Commission held in Buenos Aires, 2-6 March 1970 to evaluate the results of the 1968-1970 vaccine evaluation trials it was decided to repeat the 1969-1970 Argentine trials. Tentative plans for these trials made at this meeting were finalized at a meeting held in February 1971 between the Argentine (INTA) and the U.S. Department of Agriculture (PIADC). During the interim, laboratory preparation of the FMD vaccines, and plans for the field trials in Argentina were in progress. A summary of the results of the field trials which were finally started in June 1972 is given below.

A tentative report of these field trials prepared by USDA, Plum Island Animal Disease Center staff is included in the Appendix. Since the laboratory tests on blood samples and tissues collected from the cattle will not be available for several weeks, a complete technical report prepared jointly by PIADC and INTA staff members is planned for publication by NAS/NRC at a later date.

A total of 371 cattle purchased by the Argentine Government from the FMD-free area in Patagonia (Chubut Province) were used. These were finally transferred to the Argentine Cattle Holding Stations in Valdes Peninsula in the Chubut Province.

The cattle were vaccinated for the first time in June 1972 using a trivalent vaccine prepared from South American FMD virus strains. A-24 Cruzeiro, C-Resende, and O₁ Caseros viruses were propagated at PIADC, and hand-carried to Buenos Aires for preparation of the three different vaccines. Three groups of 16 cattle, plus 4 spares, were vaccinated with each vaccine. An equal number of cattle were left unvaccinated to act as controls. The three vaccines were all prepared from viruses grown in baby hamster kidney (BHK) cells, inactivated with acetyleneimine (AEI) and emulsified with an oil-adjuvant used by INTA. The vaccines were designated according to preparation as follows:

Vaccine #1 Crude

Vaccine #2 1 x concentrated

Vaccine #3 20 x concentrated

At the end of six months in December 1972 one group was revaccinated to be challenged for immunity after an additional year. A second group, vaccinated once, was challenged at six months and a third group, vaccinated once, was vaccinated at one year. Thus, two groups were vaccinated once, and one group had been vaccinated twice. The results of these three tests follows:

Results of Challenge for Immunity with A-24 FMD Virus				
Date of Challenge	Controls (Not Vaccinated)	Vaccine		
		1	2	3
December 1972 - 6 mos	0/16	*13/16	12/16	15/16
June 1973 - 12 mos	1/16	11/16	10/16	13/16
January 1974 - 19 mos (2nd vaccination at 6 mos)	0/16	9/15	13/16	11/16

* 13 out of 16 protected.

These results are considered satisfactory and better than could be expected from any commercial vaccine now available in Argentina.

The results reported above do not begin to indicate the extent of laboratory work and number of animals which have been necessary to accomplish them. Preparation of the vaccines at the PIADC, and INTA laboratories; the cattle and other animals used in testing the vaccines, and their care; the collecting of blood samples at periodic intervals and the laboratory testing of these are examples. It is estimated that it will take about several weeks to complete the laboratory tests. When these are completed, a technical report will be jointly prepared for publication by the cooperating staff members of INTA and PIADC. As has been stated above, this scientific report will be published by NAS/NRC.

REFERENCES *

- Argentine - United States Joint Commission of Foot-and-Mouth Disease. 1966. Studies on Foot-and-Mouth Disease (Estudios sobre Fiebra Aftosa). I. Survival of the virus in cured meat prepared from vaccinated and unvaccinated cattle. II. Epizootiologic survey of the Island of Tierra del Fuego. National Academy of Sciences - National Research Council Pub. 1343:1-90 (plus Spanish translation 1-90).
- Argentine - United States Joint Commission of Foot-and-Mouth Disease. 1966. Minutes of Third Meeting of the Joint Commission, held in Buenos Aires, 30 November - 1 December 1966. (Mimeo)
- Argentine - United States Joint Commission on Foot-and-Mouth Disease. 1969. Minutes, Technical Meeting on Foot-and-Mouth Disease held in Buenos Aires, 27 January - 1 February 1969. (Mimeo)
- Argentine - United States Joint Commission on Foot-and-Mouth Disease. 1970. Minutes, Technical Meeting held in Buenos Aires during week of 2 March 1970 to evaluate results of past year field trials on evaluation of FMD vaccines. (Mimeo)
- Argentine - United States Joint Commission on Foot-and-Mouth Disease. 1970. Minutes, Official Meeting of Joint Commission held in Buenos Aires during week of 2 March 1970. (Mimeo)
- NAS/NRC - U.S. Advisory Committee on Foot-and-Mouth Disease. 1970. Laboratory and Field Testing of a Foot-and-Mouth Disease Vaccine, for Potency, Viability and Immunity Duration. Final Report, Contract AID/csd-2273. (Mimeo)
- NAS/NRC - U.S. Advisory Committee on Foot-and-Mouth Disease and U.S. Component of Argentine - U.S. Joint Commission on FMD. 1966-1974. Minutes of meetings held in this interim. (Mimeo)

* The above references are included for record purposes. Copies of each report were furnished to AID/W/LA/RD as completed. They are also on file in NAS/NRC Archives, and in the Library of the USDA Plum Island Animal Disease Center.

APPENDIX 1

COOPERATIVE FMD VACCINE STUDY* (June 1972 - January 1974)

A meeting was held in February 1971, between the Argentine (Instituto Nacional de Tecnologia Agropecuaria [INTA] and United States (Plum Island Animal Disease Center [PIADC]) representatives to plan a Foot-and-Mouth Disease (FMD) vaccine study in Argentina. It was contemplated that the experiment would be primarily a duration of immunity study without revaccination; however, the desirability of revaccination would be determined by serological results and response to challenge of immunity.

The discussion involved the use of a number of trivalent FMD vaccines. It was agreed that three vaccines would be prepared for the trial, prepared as follows:

1. Virus grown in baby hamster kidney (BHK) cells, inactivated with acetyleneimine (AEI) and emulsified with oil-adjuvant.
2. BHK virus concentrated 100 fold by the polyethylene glycol method and adjusted to contain approximately the same antigenic mass as vaccine number 1.
3. BHK virus concentrated 100 fold by polyethylene glycol method and adjusted to contain 20X the antigenic mass of vaccine number 1.

Initially, the oil-adjuvants as prepared by the PIADC and INTA formulation were to be compared; however, it was agreed that the INTA formulation only would be used. INTA formulation involved the use of Arlcel 83 in lieu of Arlcel A and the inclusion of Tween 40.

The following types of FMD virus used for vaccine preparation in Argentina were used in the vaccine preparation: type A, subtype 24, strain Cruzeiro; type O, subtype 1, strain Caseros; type C subtype 3, strain Resende.

All cattle for the project were selected from Chubut Province in the FMD-free area in Patagonia. Serums from the selected cattle were examined for antibodies by the mouse protection test as prescribed by the Pan American Foot-and-Mouth Disease Center. This screening test was done by the INTA personnel and a portion of each sample sent to Plum Island for reference purposes. Three hundred and seventy-one cattle between 1 and 2 years of age, were selected for the experiment. Fifty-two cattle were vaccinated for each vaccine test - 48 to have their immunity challenged in groups of 16 and 4 spares, and an equivalent number retained as controls.

* Report by Dr. P. D. McKercher, USDA, Plum Island Animal Disease Center, given on 5 March 1974, at a meeting of the U.S. Component of the Argentine U.S. Joint Commission on FMD, Washington, D. C.

Serum samples were collected at 0, 30, 60, 120, 180, 240, 300, 365, 455, and 545 days postinoculation. Serums were analyzed at PIADC by a variety of serological techniques such as examination for virus infection-associated (VIA) antibodies, radial immunodiffusion, microneutralization, plaque reduction test, mouse PD₅₀ and serum protection tests. Sixteen cattle from each of the vaccine groups along with 16 controls had their immunity challenged by the IDL inoculation with 10,000 bovine ID₅₀ at four sites at times indicated by their serological response. Groups numbering 52 animals were selected from the 371 animals by pseudo random number selection on a computer. Each group was given a tag color and animals were randomly tagged as they came through the control gate with their respective color groupings in numbers 1-52. Red was designated the color for vaccine #1 (referred to crude); blue for the control group; green for the 20X; and yellow for the 1X group.

The viruses were grown in BHK-21 cell layers in roller bottles (2-liter Baxter bottles). The harvested material was inactivated at 25 C with 0.05% AEI for 72 hours. A portion of the inactivated material was stored at 4 C for preparation of vaccine #1, the remainder concentrated 100-fold by the polyethylene glycol technique as described by Wagner et al., 1970*. Samples were collected at 0, 30, 60 and 90 minutes for inactivation kinetics and the final innocuity test performed in steers. Six inactivations were pooled by mixing 40 ml from each virus lot and then removing a 50-ml sample from the pool as the test sample - 2 ml of which was inoculated IDL into each of six steers.

The activity of the viral antigens used in the vaccines was determined by plaque-forming units (PFU) and complement fixation (CF) before inactivation, by CF after inactivation and after 100-fold concentration. Some problems were encountered with vaccine production and two complete sets of vaccines were made and tested. The first lot of vaccine was discarded because of some apprehension that the larger than normal reactions obtained at the sites of inoculation may in some way have been related to some residual toxins remaining in the virus harvests after filtration - although sterility tests of the virus harvests after filtration were negative.

The second lot of vaccine was prepared, safety tested and potency tested in guinea pigs, steers, and swine. Reactions at sites of inoculation were of considerable concern and testing of the various ingredients continued without specific results. However, the PD₅₀ levels obtained from the serums of the potency test animals appeared reasonably good. There was considerable apprehension on the use of the product because of the reactions at the sites of inoculation. It was determined after the vaccine was prepared that the BHK cell line obtained from Germany might possibly contain other than BHK cells; however, at the urging of

* Immunochemical Studies of Foot-and-Mouth Disease. VII. Characterization of Foot-and-Mouth Disease Virus Concentrated by Polyethylene Glycol Precipitation, by G. G. Wagner, J. L. Card and K. M. Cowan. Arch. Ges. Virusforsch. 30:343-352, 1970.

the Argentine investigators it was decided to proceed to Argentina and test the vaccines in a limited number of animals and have the Argentines decide whether the test should be conducted with these products. The vaccine was tested in 19 cattle - 9 of which had previously been vaccinated (30) days with INTA oil adjuvanted vaccine, and 10 which had not. There were only 3 reactions that might be considered larger than normal and the Argentines considered these reactions more or less normal so it was decided to proceed with the test. The vaccination of the animals was completed and reactions were within acceptable limitations. Complement-fixation titers of the inactivated viruses were, in the crude vaccine: A-24 Cruzeiro, 1:80; C-Resende, 1:64; and O₁ Caseros, 1:48; in the 1:1 concentrate, 1:48; and in the 20X concentrate vaccine, 1:1200.

As determined by ultracentrifugation the mass antigen per ml was approximately nine micrograms for each virus type. However, by radial assays using hyperimmune serum absorbed with 12S antigen, the antigen mass was greater, varying from 11 to 19 micrograms/ml.

It was anticipated that following the results of the serological assays, the first challenge of immunity would be undertaken at 6 months or 180 days postvaccination. Serums were examined for VIA and the radial immunodiffusion and mouse PD₅₀ tests were completed on all serums to 120 days postvaccination. It had been planned to conduct the challenge of immunity with O₁ Caseros virus and consequently at this time PD₅₀ values were not obtained against the A-24 and C-Resende antigens.

A 50% protective dose evaluation was conducted with vaccine #1-Crude and vaccine #2 - 1:1 concentrated for the O₁ antigen. Vaccine #2 was estimated to have 16 bovine protective doses and the crude to have 5. A 50% protective dose was not completed for vaccine #3 - 20X but it was considered to be greater than 16 protective doses. Mouse PD₅₀ values against O₁ Caseros virus were disappointing in the serums from all of the vaccinated groups and thus consideration was given as to whether one of the other virus types in the trivalent product should be used as the virus in the challenge of immunity.

The initial potency test had proved satisfactory and further testing of the aqueous stored products again indicated adequate potency. However, in the emulsified product there appeared to be some antigenic deterioration of all 3 virus types, particularly the O₁ type.

By random number selection on a computer, each vaccinated group was divided into 3 groups of 16 animals each. The groups were classified as follows: one group to have its immunity challenged at 6 months; one group to remain as it was; and the remaining group to be revaccinated at 6 months. From the antibody titers obtained with the serums of the 120-day sampling, it was determined that the best response had been with C-Resende antigen, then A-24 Cruzeiro and the poorest with O₁ Caseros. It was the opinion of the Plum Island investigators that nothing could be achieved by challenging the vaccinated groups with O₁ Caseros virus.

After some discussion between the Argentine and Plum Island groups, it was decided to challenge the immunity of the selected groups with A-24 Cruzeiro virus and to revaccinate the selected groups at six months, leaving one group from each test vaccine with only the initial vaccination. The revaccination was carried out with vaccine #1 referred to as "crude vaccine" because there was more of this product available. When the groups were revaccinated, large reactions at the sites of revaccination occurred in almost all animals. The virus used for challenge of immunity was prepared and tested at Plum Island and then transported to Buenos Aires. The results obtained when the groups were challenged with A-24 virus were as follows:

	<u>Protected</u>
Vaccine #1 Crude	13/16
Vaccine #2 1X	12/16
Vaccine #3 20X	15/16
Controls	0/16

To confirm opinions on the predicted lack of protection afforded to O₁ Caseros virus, two of the spare animals were selected from each vaccine group and the control group. These animals were challenged with O₁ Caseros virus and all 8 animals including the 2 control animals became infected.

Blood samples were collected at 60-day intervals and the group of animals receiving only the initial vaccination were challenged with A-24 Cruzeiro at 12 months from the initial vaccination. Results were as follows:

	<u>Protected</u>
Vaccine #1 Crude	11/16
Vaccine #2 1X	10/16
Vaccine #3 20X	13/16
Controls	1/16

In January 1974, the remaining animals which had been revaccinated 12 months previously were exposed to A-24 Cruzeiro. Results were as follows:

	<u>Protected</u>
Vaccine #1 Crude	9/15
Vaccine #2 1X	13/16
Vaccine #3 20X	11/16
Controls	0/16

Tests for VIA have been completed on all serums as well as the radial immunodiffusion assays. All serums have been assayed by the mouse PD₅₀ test. An agreement has been reached, acceptable to both investigational groups, that the remaining assays will be completed only on serum samples prior to the challenge of immunity at 6 months, 12 months, and 18 months (12 months post-revaccination). These assays include the plaque reduction, microneutralization, and the serum protection tests in mice. Because of the number of serums involved, it will be approximately 6 months before the tests are completed, data assembled and analyzed.

DISCUSSION

Despite the problems with this product, the results obtained were superior to any obtained with present-day commercial products. One might say that the test could be considered successful with 2 of the 3 virus types involved.

A shelf-life study of vaccines prepared at Plum Island with similar FMD types and strains is expected to at least partially resolve some of the problems occurring with this product.

At present, Tween 40 would appear to be the product detrimental to the antigens in the INTA emulsion. It will be some time before all the data on this 12-month shelf-life study is completed.

CONCLUSIONS

One can conclude that (1) the trial was worthwhile as despite the drawbacks of the product, it produced better results than could be expected with any commercial product; (2) that the INTA adjuvant must be examined in greater depth and possibly some other emulsifier other than Tween 40 used; (3) results as indicated in the laboratory experiment probably would have been improved by use of the Plum Island adjuvant; (4) the INTA emulsion is more stable than the incomplete Freund's (Plum Island); (5) from the results of the trial, from the results of the laboratory trial, and from the results obtained in the field trial conducted at the Pan American Center, 6 months would not appear to be the ideal time to revaccinate with an oil-adjuvanted vaccine. Perhaps 12 months would be more suitable; however, this is something that must be determined. From the results obtained in Argentina, vaccine #2-1X which had the lowest antibody mean at the time of revaccination appeared to obtain the best response; (6) the holding area on the Valdes Peninsula is perhaps one of the better areas in South America for keeping a limited number of animals (750-800) for an indefinite period for this type of study; (7) however, when the immunity of these animals is to be challenged, the animals must be transported some 1500 miles to Buenos Aires by truck. The barns at Castelar where this work is done are far from satisfactory and because of possible contamination of the animals with other FMD types and strains, the challenge of immunity must be done no later than 24 hours after their arrival.

The cooperation between the Argentine investigators and those of Plum Island has been very good. As might be expected in such trials, in going from a laboratory level to a limited field trial everything did not work as planned. Hopefully, however, a great deal of useful information will be obtained when all data is assembled and analyzed.*

* To be published in a scientific report to be prepared by PIADC and INTA staff members.

APPENDIX 2

ARGENTINE - UNITED STATES JOINT COMMISSION ON FOOT AND MOUTH DISEASE*

The origin of the Joint Commission can be traced to a ruling of the U.S. Government, banning the import of so-called "cured" beef from countries with endemic foot-and-mouth disease (FMD). Shortly before, in 1959, the Plum Island Animal Disease Laboratory (PIADL) proved that if cured beef were prepared from the carcasses of non-vaccinated susceptible cattle, experimentally infected with FMD virus, the virus would survive for a relatively long time in the lymph nodes included in the pieces of beef so prepared.

The ban covered the type of cured beef which, up to that time, was imported in increasing amounts from Argentina.

When, in 1961, President Frondizi met with President Kennedy, they discussed the problem posed to the Argentina meat industry. The Presidents agreed on having the problem looked into by a special Commission of scientists from both countries who were not to be associated with either administration, so that they would be in a position to use independent judgement free from any political influence and on a purely scientific level.

As a first step, in January 1962, a mission headed by Dr. George J. Harrar, Chairman of the Rockefeller Foundation, arrived in Buenos Aires. The mission held several technical meetings with a comparable Argentine group, headed by Dr. Bernardo A. Houssay (Commissioned by Presidential Decree No. 107/62).

At the meetings, the Argentine delegation pointed out several of the main barriers to the increase of meat exports from Argentina to the U.S., the latest of which being the ruling on cured beef. Another important obstacle was a ban on mutton and mutton products from the island of Tierra del Fuego (shared by Chile and Argentina), in spite of the island being free of FMD, and the preliminary agreements included in the Sanitary Convention between the U.S. and Argentina, signed by Cordell Hull and Felipe Espil in 1935. The Argentine Delegation also mentioned the fact that cooked beef, imported from Argentina, had to be "recooked" in the U.S., a process which decreased the quality of the product and increased its cost.

The possibilities of a research and development program aimed at the elimination of the obstacles mentioned was discussed, as well as an outline of means which would make sure that no active FMD virus was carried in cured or cooked beef. At the same time the members of the Harrar Mission suggested several other projects which, they thought, would help the meat industry in Argentina.

* Translation of "Comision Conjunta Argentino - North Americana para El Estudio de Fiebre Aftosa" (In Forme Final), referred to in attached letter of 23 March 1974, V. Deulofeu to W. R. Hinshaw.

The report of the meeting, written from the point of view of the Argentine Delegation, was submitted by Dr. Houssay to President Frondizi. The report is one of the documents which make up the compilation of information about the activities of the Joint Commission.

Two months later (March 1962) the U.S. National Academy of Sciences assembled in Washington, D.C., an "Ad Hoc Scientific Conference on FMD and Food Technology in Relation to the Meat Industry in Argentina," to implement the recommendations of the meeting held in Buenos Aires, and invited the participation of the Argentine Government. The Argentine Delegation was commissioned by Presidential Decree No. 2082/62.

The meeting worked out a preliminary protocol for an experiment involving the survival of FMD virus in the cured meat of vaccinated and non-vaccinated cattle, and recommended an epidemiological survey throughout the Island of Tierra del Fuego, to establish if any traces of FMD infection could be found in susceptible animals on the island. At a meeting in Montevideo, Uruguay, (February 1962) convened by the Pan American FMD Center, Argentine and Chilean delegates had agreed that such a survey should cover the entire island, and had offered complete support to the project.

Several recommendations were also made, in connection with the re-cooking of beef exported from Argentina to the U.S.

Long range experiments were discussed and proposed including the exchange between Veterinary Schools and other scientific institutions of both countries, as well as a cooperative program in food science and technology.

The Conference recommended a Joint Committee, with five members from each country, to take over the operating responsibility for the projects, to propose other experiments, to implement them and to evaluate the results obtained.

Each of the two groups was to nominate a project leader, as coordinator of the work to be done in his own country. As the Pan American FMD Center was to participate in some of the experiments, the Director of the Center was invited to nominate his own project leader.

Both Governments accepted the proposals and the Argentine Group was commissioned in June 1962 by Presidential Decree No. 6941/62. Its five members were Drs. Constantino Brandariz, Venancio Deulofeu, Enrique Garcia Mata, Luis F. Leloir and Armando Parodi, (the last named died in 1969 and has not been replaced). The Argentine Group selected Dr. Augusto L. Durlach, a member of INTA, for secretary, and Dr. Hector G. Aramburu for project leader.

The President of the U.S. Academy of Sciences nominated the following members of the U.S. Group: Drs. George C. Poppensiek (Chairman), Samuel G. Goldblith, Stewart H. Madin, Maurice Shahan and Richard E. Shope. Dr. Shope, due to illness, resigned in August 1963 and his place was taken by Dr. Carl A. Brandly. Dr. James H. Gillespie acted as secretary to the U.S. Group and one of its members, Dr. Shahan, as project leader.

At the time the two groups were being formed, a mission nominated by the President of the U.S. Academy of Sciences visited Argentina under the Chairmanship of Dr. James H. Gillespie. The members of the mission discussed with their Argentine counterparts means and ways to initiate the activities of the U.S.-Argentine Joint Commission of FMD.

The first meeting of the U.S.-Argentine Joint Commission was held in Buenos Aires on November 6, 7 and 8, 1962. The Joint Commission took notice of the documents produced in previous meetings and reports of the several missions and the two national groups.

The Joint Commission was informed, through a letter from Mr. M. R. Clarkson, Associate Administrator of the USDA, to Dr. J. H. Gillespie, dated November 1st, 1962, that as an outcome of these meetings, good progress had been made to establish under what conditions Argentine cooked beef could be introduced in to the U.S., without being "recooked" in that country. This particular problem was favorably solved: the table in Appendix 1 shows the effect on the export of cooked beef from Argentine to the U.S. (See Appendix 4.)

The Joint Commission approved the detailed protocol for an experiment on the survival of FMD virus in cured beef from vaccinated and non-vaccinated cattle, on the basis of the suggestions made in March of the same year, at the Ad Hoc Conference in Washington.

The experiment involved work in both countries as well as at the Pan American FMD Center. It was, therefore, suggested that representatives of the countries and the Center would work together at the different locations. Dr. Emilio Gimeno represented the Argentine Group at PIADL.

At the Ad Hoc meeting in Washington, March 1962, while discussing the cured beef experiment, differences of opinion appeared on the possibility of stating a priori what type of results of the experiment would enable the U.S. to readmit cured beef from Argentina. The U.S. Delegation held the opinion that, due to U.S. sanitary regulations, no a priori statement could be acceptable to the regulatory authorities. Dr. L. F. Leloir, member of the Argentine Group, presented a document which suggested the calculations which could be made to know the probability of introducing FMD virus into the U.S. with cured beef, and that a sufficiently low probability should be acceptable to the U.S. Government.

The Commission also studied the report submitted by the Pan American FMD Center, on a methodology for the epizootiological survey on the Island of Tierra del Fuego, designed to find out if the island is free, or not, of FMD. The Commission found it convenient that the survey should be coordinated by the Pan American Center.

Finally, the Commission studied several other proposals, concerning such matters as the development of methods for the inactivation of FMD virus in meat; the implementation of long-range research on problems related to the disease, and the exchange of university personnel, and of similar institutions, so as to train Argentine scientists in food technology (particularly in meat technology) in the U.S.

The two main experiments (Survival of FMD virus in cured beef and survey on the Island of Tierra del Fuego) were implemented at a rate dependent on the organizations which had to be created.

In May 1963, the program directors approved the detailed protocol for the cured beef experiment. The survey on the Island of Tierra del Fuego, planned and supervised by the Pan American FMD Center, started at the beginning of 1963, with the collection of serum samples, which were later studied by the Center.

The reports on the results of both experiments were approved by the program directors in a meeting at Rio de Janeiro on April 7-13, 1964.

The reports mentioned, together with other items, were discussed by the Joint Commission at its second meeting in Washington, D.C., on May 19-21, 1964.

Dr. William M. Henderson, Director of the Pan American FMD Center, summarized the Tierra del Fuego survey and pointed out that enough information was available for discussion and interpretation of the results, even if information on some of the samples was still lacking. Dr. Robert P. Hanson, participating U.S. scientist, commenting on the results, stated that even "...in absence of the completion of the serological testing and in view of the fact that statistical randomness could not be achieved in selection of samples, it is nonetheless reasonable to conclude that Tierra del Fuego was probably free of FMD in April 1963. It seems unlikely that an epizootic of FMD has occurred on the island in recent years." (Document No. 13 of "Documentation of Argentine, U.S. and Pan American FMD Center Reports on FMD, 1961-64").

The cured beef experiments were reported by Dr. M. Shahan. It was generally agreed that vaccination and the curing process considerably reduced the infectivity of lymph nodes tested from the selected animals challenged with live virus, as described by the protocol.

The Commission also acknowledged certain summary reports submitted by Drs. John H. Graves and Norman D. Heidelbaugh, on long-range research projects, developed by them in Argentina over several months, mainly initial experiments on FMD virus resistance to certain physical and chemical conditions.

The subject of meat technology was also analyzed, particularly a report prepared by Dr. Victor Conquest, specialist in meat technology, who had delivered lectures on foot technology in Buenos Aires, with special emphasis on meat technology.

Finally, the Commission recommended the publication of two bilingual papers, one of them to cover, in monograph form, the cured meat experiment and the Tierra del Fuego survey, the other a compilation of the more important documents relating to the activities of the Commission, both in the U.S. and in Argentina, beginning with the agreement between Presidents Kennedy and Frondizi and the Harrar Mission in Argentina.

The monograph was printed by the U.S. National Academy of Sciences in 1966 in one volume. The first part, in English, covers XXII + 90 pages, with the title of "Studies in Foot-and-Mouth Disease." The Spanish version, with the same number of pages, is titled "Estudio sobre Fiebre Aftosa."

The compilation of documents, in two volumes, contains 22 items, in English and in Spanish.

On June 1 and 2, 1966, an informal meeting was held in Buenos Aires to analyze the possibilities of new activities to be sponsored by the Joint Commission; several projects were studied.

November 30 and December 1, 1966, another meeting convened in Buenos Aires; the results of the previous meeting were discussed, as well as several projects submitted by Argentine research groups. The Commission recommended three main areas: (1) vaccines and virus; (2) epidemiology; and (3) meat technology. Some of the projects contained detailed cost estimates. At the time of the meeting neither of the two groups had funds available for the projects.

Somewhat later INTA and SELSA, in Argentina, started experiments on new vaccines including one involving both the Pan American Center and PIADL, on a large group of cattle held in Peninsula Valdes. These new facilities had been recently finished. Several of the members of the Argentine Group had an opportunity to visit them.

The experiment and its results were discussed at Buenos Aires on March 2-6, 1970, with the presence of members of both groups of the Joint Commission.

In June 1972, a new experiment was started on oil-adjuvant concentrated vaccines, PIADL and INTA, cooperating. This experiment will last until June 1974, depending on the results obtained during its course.

The future of the Commission was discussed at the end of the meeting by the members present. Although no definite agreement was reached, the Argentine Group, represented by all its members, and its Secretary, expressed its desire to put an end to the official activities of the Joint Commission, taking into account that U.S. and Argentine institutions are already cooperating on experiments and will continue doing it in the future.

Consensus was reached on the convenience of substituting for the Commission some Inter-American organism, which could act as a branch of one of the international organizations already existing, guiding the efforts of the Pan American countries interested in the research on foot-and-mouth disease. In some aspects, something to this effect is underway through the meetings of experts, Secretaries of State and others.

The members of the Argentine Group think that the Joint Commission has had some indirect influence on certain aspects which have favored Argentina.

One of them is the close cooperation between U.S. and Argentine research institution, and with the Pan American FMD Center, working together on vaccines with better and more prolonged protecting power.

The Commission also had a certain influence on the granting by USAID, of a loan for the building of two laboratories at the National Research Center of INTA, Castelar, co-financed by the Argentine Meat Board and INTA.

The several visits by U.S. meat experts evidently awakened a lot of interest in Argentina. Many of the meat industries got in touch with INTA and INTL. The latter institution created a Meat Research Center, with the help of the Argentine Meat Industry.

Finally, it should be pointed out that during the course of the Commission's activities, a good exchange of scientists was achieved between the U.S. and Argentina. Many Argentine scientists, both junior and senior, travelled to the U.S.; in more than one case the trip was financed by the U.S. Group.

The Argentine Group of the Joint Commission feels that the Commission has achieved the objectives of its mission and at the same time has been instrumental in the integration of the main research groups in the Americas concerned with foot-and-mouth disease.

Each of the members of the Argentine Group individually, and all of them jointly, agree that the mission of the Group can be terminated. Nevertheless, they remain ready to help any officer or institution involved in the problem of foot-and-mouth disease, if it is considered that the experience they have acquired should be used.

DR. VENANCIO DEULOFEU

PARERA 77
BUENOS AIRES - ARGENTINA

March 23, 1974

Dr. William R. Hinshaw
National Research Council
Commission on Natural Resources
2101 Constitution Avenue
Washington D.C. 20418, U.S.A.

Dear Doctor Hinshaw:

Many thanks for sending the information of your meeting in Washington on 5-March.

As you request I am pleased to send to you a copy of our report to the Minister of Agriculture. It was signed by all members of the Argentine Group except Dr. Garcia Mata. I am sorry that it is in Spanish but Dr. Durlach is taking care of a translation in English. As soon as it is finished I will send a copy to you. I hope the copies in the two languages will say the something.

With my best regards,

Sincerely yours.

NATIONAL RESEARCH COUNCIL
COMMISSION ON NATURAL RESOURCES

2101 Constitution Avenue Washington, D. C. 20418

BOARD ON AGRICULTURE AND
RENEWABLE RESOURCES

28 June 1974

MEMORANDUM

SUBJECT: Report of Final Meeting of U. S. Component of Argentine - U.S. Joint Commission on FMD, held at the USDA, Plum Island Animal Disease Center (PIADC), 25 June 1974.

BY: William R. Hinshaw, Staff Officer

The members of the U.S. Component of the Argentine - U.S. Joint Commission on FMD attended by invitation the annual conference of consultants to PIADC, 25-28 June 1974. Since four of the members, C. A. Brandly, R. P. Hanson, S. H. Madin, and M. S. Shahan, are also consultants for PIADC, NAS travel expenses were limited to those of Victor Conquest, member, and W. R. Hinshaw, Staff Officer.

On the evening of 25 June 1974, a meeting of the Joint Commission members was held under the Chairmanship of Dr. S. H. Madin. Also attending was Dr. John Graves, Assistant Director of PIADC. During the week a number of informal discussions relating to the Project were also had with Dr. J. J. Callis, Director of PIADC, Dr. Peter McKercher and other members of the PIADC Staff. During the meeting of the PIADC Consultants, Drs. Callis and McKercher presented a summary of the results of the USDA - Argentina FMD Vaccine Evaluation Field Trials recently completed in Argentina. These were the same as were presented to the U.S. Joint Commission Group at the March 5-6, 1974 meeting.

At the 25 June meeting, the Draft Copy of the Final Report to AID for contract AID/la-4 which terminates 30 June 1974 was reviewed. Suggestions for revisions made will be incorporated.

The Final Report (February 1974) of the Argentine Component received from Dr. V. Deulofeu in February 1974 which was first discussed at the 5-6 March meeting of the U.S. Component was again reviewed. The U.S. Members agreed once again to concur with the Argentine Members that the mission of the Joint Commission has been accomplished and should be terminated on 30 June 1974 - the final date of NAS Contract AID/la-4.

Dr. Madin agreed to write a draft of a letter for consideration by Dr. Handler, President of NAS, to be sent to President Nixon to inform him of the termination of the Project started in 1962 by agreement of U.S. President John F. Kennedy and Argentine President Arturo Frondizi.

28 June 1974

SUBJECT: Report of Final Meeting of U.S. Component of Argentine - U.S. Joint Commission on FMD, held at the USDA Plum Island Animal Disease Center (PIADC), 25 June 1974.

At the 5-6 March meeting, it was suggested that any available duplicate files of the Joint Commission should be sent to the PIADC Library for filing. By permission of the NAS Archivist, Miss Jean St. Clair, the writer sent about one file cabinet drawer of reports, letters and memos to PIADC. These arrived on 24 June and were made available to the group for review by the PIADC Librarian, Robert J. Uskavitch. These historical documents will supplement the more complete files in the NAS Archives.

Dr. Shahan stated that even though the mission of the Joint Commission has been accomplished, there is a need by NAS/NRC for a continued participation in an advisory capacity on foreign animal diseases including FMD. As an indication of this need he called attention to the fact that several government agencies have repeatedly emphasized this continued need to members of this group. The members concurred with him and suggested that this function could be assigned to the newly organized Committee on Animal Health in the Board on Agriculture and Renewable Resources.

The group expressed the need for continued cooperation of the USDA, PIADC, with Latin American countries on foot-and-mouth disease, as well as other diseases, and in the field of meat technology, especially as it relates to animal disease control. This cooperation could involve continued cooperation in AID supported programs and with the Pan American Health Organization Foot-and-Mouth Disease Laboratory in Rio de Janeiro.

Dr. Brandly called attention to the recommendation made at the 2-6 March 1970 meeting of the Argentine - U.S. Joint Commission meeting in Buenos Aires, that an Interamerican Commission on Foot-and-Mouth Disease, patterned after the European Commission on FMD be established. The U.S. Component has on a number of occasions repeated this recommendation and again went on record in favor of the 1970 recommendation. It was the general consensus of the group that the recently established Latin American Commission, although recognized as an important step in FMD control, it is not a substitute for a total Interamerican Commission such as was recommended by the Argentine - U.S. Joint Commission in 1970.

Finally, the group expressed its appreciation for the splendid cooperation of numerous agencies during the 1962-1974 existence of the U.S. Advisory Committee on Foot-and-Mouth Disease and the U.S. Component of the Joint Commission.

APPENDIX 4*

FROZEN COOKED BEEF EXPORTED TO THE U.S. FROM ARGENTINA

<u>Year</u>	<u>Metric Tons</u>	<u>Value:</u> <u>U.S. \$ x 1000</u>
1961	4.168	5.300
1962	4.476	5.600
1963	4.822	6.000
1964	3.183	3.800
1965	6.876	8.500
1966	12.932	16.000
1967	16.019	17.500
1968	24.911	29.900
1969	24.362	33.400
1970	25.567	39.600
1971	19.972	38.800
1972	17.400	31.500

Source: Junta Nacional de Carnes.

* This table is listed as Appendix 1 in Dr. Deulofeu's report (Appendix 2) page 16. It was supplied by him.