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ORIGINAL: ENGLISH

TUBERCULOSIS RESEARCH OFFICE, COPENHAGEN

In May 1951 the Fourth World Health Assembly decided that the Tuberculosis Research Office should be maintained, subject to a review of the situation by the Executive Board every two years.[1] The Board is reminded that at its seventh session it made a recommendation to this effect to the Assembly.[2]

The Director-General therefore submits the attached report on the Tuberculosis Research Office for the consideration of the Board.

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[1] Off. Rec. World Hlth. Org. 35, resolution WHA4.7

[2] Off. Rec. World Hlth. Org. 32, resolution EB7.R85

REPORT OF TUBERCULOSIS RESEARCH OFFICE, COPENHAGEN

September, 1952

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Annexes

1. Establishment of the office and authorities

Early in the autumn of 1948, Dr. C.E. Palmer, Medical Director in US Public Health Service (in charge of the Field Research Branch of Division of Chronic Disease and Tuberculosis), came to Europe at the invitation of UNICEF and ITC, and made a survey of the need and potentialities of medical research in connexion with the mass BCG vaccination programmes being carried out in many countries. He presented a report on this survey to the Joint Health Policy Committee UNICEF/WHO at its second session on 20 October, 1948. Accepting this report, the Committee recommended that the attention of the Director-General of WHO be drawn to the importance of scientific research in the BCG campaigns. The WHO members of the Committee at the same time reported the matter to the Executive Board. In recognizing a unique opportunity to further scientific knowledge in tuberculosis, the Board, at its second session, decided to accept responsibility for promotion of medical research in the BCG programme and to create a tuberculosis research office. In February 1949, the Research Office was officially opened in Copenhagen.

Relevant references in official documents, correspondence and agreements concerning the origin of TRO and its subsequent operations are given in Annexes A and B.

2. Method of investigation

The work of TRO is essentially one of "operations research", to borrow a term used during the late world war for the application of scientific methods to military problems. TRO has been, and still is, dealing almost exclusively with technical problems connected with the BCG programme or arising from its field operations. Its approach is international in character. TRO has assisted and co-operated with many national and international organizations. Special mention should be made of the Danish National Health Service, State Serum Institute and National Anti-Tuberculosis Association, the Finnish National Anti-Tuberculosis Association, the Tuberculosis Control Service of the Icelandic Government, the Union Mission Tuberculosis Sanatorium at Madanapalle, India, the BCG Pilot Station at Paris, the International Tuberculosis Campaign, and the WHO Tuberculosis Section which has taken over the work of ITC.

To obtain reliable results, great care is exercised in the design and execution of each investigation and in the analysis of observational data. This requires carefully trained technical staff and assistants to assure uniform techniques, accurate and unbiased observation, groups of sufficient numbers and comparable controls, appropriate statistical concepts and methods, and, above all, critical judgement in drawing conclusions. What is said is, of course, nothing new, but it cannot be over-emphasized in clinical and public health research.

As the WHO/UNICEF BCG programme is extended to many countries where BCG has been scarcely used, and reliable information on the nature and prevalence of tuberculous infection and disease is lacking, the need of scientific enquiry becomes more apparent and urgent. TRO's experiences have repeatedly shown that what is found to be true in one area frequently fails to hold in another area where people live under different environmental, economic, and social conditions. If serious mistakes are to be avoided in the conduct of large-scale BCG campaigns, preliminary surveys and

BCG trials should be made by competent pilot teams in order to determine suitable techniques and criteria for vaccination and the type of results to be expected.

TRO has hitherto put great emphasis on human field studies, though the need of basic laboratory research has been recognized for a long time. Arrangements have now been completed to undertake a closely co-ordinated programme of laboratory and field investigations so that the results and observations from the laboratory and the field can be correlated, compared and evaluated.

3. Development of research activities

When the mass BCG campaign was started, the procedures and techniques for tuberculin testing and vaccinating were formulated largely on the basis of previous experiences from the Scandinavian countries, although it was clearly recognized that changes might have to be made as the work was extended into different parts of the world. This actually proved to be the case. The methods and criteria of tuberculin testing were repeatedly modified, and critical problems were encountered when the vaccination results were found to differ widely from what was expected. The research programme developed by TRO therefore involved a variety of short-term and long-range investigations which comprised almost the whole subject of BCG vaccine and vaccination from the tuberculin test to the efficacy of mass BCG vaccination in the prevention of tuberculosis. Its object was to place tuberculosis immunization on a rational and scientific foundation.

The first series of the BCG studies was undertaken because of the finding of unusually poor results in one of the campaign countries. As the most serious deficiencies occurred during the summer, it was thought that they might be due to a failure to use sufficiently fresh vaccine, to difficulties in keeping the vaccine cold, or possibly to a reduction in the potency of the vaccine. In view of these possibilities only empirical and provisional changes could be made in the production and handling of the vaccine by the Danish State Serum Institute. At the same time, plans and arrangements were made for intensive study by TRO of questions relating to the allergenic potency of the vaccine and the effects of various physical factors, particularly temperature and duration of storage. More questions arose as the

studies progressed. To date 27 projects have been carried out and approximately 44,000 school children have been tuberculin-tested, and non-reactors vaccinated and retested. These studies have provided a wealth of data from which much has been learned about BCG vaccine and vaccination.

Concurrently with the vaccine studies, projects were developed to evaluate the immediate and long-range effects of BCG vaccination. In co-operation with ITC, specially trained teams were sent to Greece, Syria, Egypt, India and Ecuador to retest samples of the vaccinated populations. It was obviously necessary to determine whether the earlier uncertain and unsatisfactory results were being repeated in other countries. In Denmark and Finland long-range projects were designed to study the changes of tuberculosis morbidity and mortality in relation to mass BCG vaccination campaigns. It should be noted that neither project is a control study. A national roster of the tested and vaccinated has been set up to permit direct matching of current morbidity reports in Denmark and death reports in Finland. Tuberculosis morbidity or mortality of the vaccinated can thus be compared with that of the non-vaccinated (natural reactors to tuberculin) and with the expected trends in the general population.

As a great deal of the epidemiological and clinical work in tuberculosis as well as BCG vaccination, is based on the premise that the tuberculin test calls forth a specific reaction, the occurrence of non-specific tuberculin sensitivity raises many problems and much uncertainty. Material from some of the tropical countries indicates that ordinary tuberculous infection cannot be the only cause of tuberculin allergy; there are most likely other causes, though they have not yet been identified. To clarify this problem, comparative studies of tuberculin allergy are being conducted on an international scale and, recently, groups of tuberculous patients were tested with uniform techniques in various parts of the world. Such comparative studies are leading toward a better understanding of the usefulness - and limitations - of the tuberculin test.

Because tuberculosis is an important public health problem - and still the leading cause of death in almost all the Asian, East Mediterranean and Latin American countries - the importance of scientific research in tuberculosis need not be stressed.

Taking advantage of the excellent facilities available in a tuberculosis sanatorium in Madanapalle in India, a co-operative field research station has been set up with the assistance of the Indian Government to study the epidemiology of tuberculosis in a rural Indian population. The work is necessarily limited in scope, but it is expected that precise knowledge can be obtained concerning the nature, prevalence and spread of tuberculosis in that part of India and the role played by BCG vaccination in affecting the course and frequency of the disease.

For organization chart and summary of present activities see Annexes C and D.

4. Results so far achieved, and their significance

Now, what has TRO achieved during the past three and a half years? It would be absurd even to suggest that final answers have been found for the complex problems of BCG and tuberculosis immunization. But it can be said that a good many important questions are now clarified and suitable facilities have been developed for studies that need to be done.

One of the first responsibilities of TRO was to direct the collection of BCG campaign statistics and the preparation of the material for publication. At the conclusion of ITC in June 1951, a total of 38,000,000 children and adolescents had been tuberculin-tested, and 18,000,000 vaccinated with BCG in 23 countries of the world. This was the first time in medical history that mass immunization of such a magnitude had been carried out and it offered an unprecedented opportunity for world-wide collection of information on tuberculin sensitivity. The Mantoux test was given with relatively uniform technique and a standard tuberculin produced by a single laboratory. The record forms were also standardized. Up to now, 11 reports documenting the campaigns by individual country have been published and 4 more will be completed in 1952. These reports provide a permanent record of the work done and contain statistical information of great epidemiological value for comparison of tuberculin sensitivity between countries and between areas within a country, perhaps the best single index of tuberculosis that can be obtained for many countries today where morbidity and mortality statistics are either not available or unreliable.

During the early ITC campaigns some retesting was performed in various countries, but no conclusions could be drawn because of the marked variability of the methods and results. Since the autumn of 1950, in co-operation with ITC, specially trained teams have been sent to several countries to make systematic surveys of post-vaccination tuberculin allergy. Analysis of the results revealed significant geographic differences, even when the same batch of BCG vaccine had been used. Subsequent studies have shown that exposure of BCG to sunlight has a very damaging effect on the vaccine and this may explain, to a large extent, the low level of post-vaccination allergy found in some of the tropical and subtropical countries.

The results of the BCG studies have proved different in many respects from what was generally accepted. For example, it was believed that BCG vaccine had to be kept cold and used within a short time after preparation, that large numbers of living BCG organisms were needed to obtain a satisfactory allergic response, and that the potency of a given vaccine could be adjusted simply by minor changes in the amount of BCG per unit volume. None of these has been confirmed. Instead, it has been shown that the vaccine can be kept for 10 weeks at 2-4°C without significant loss of its allergenic potency; and storage at 20°C for a month or 37°C for 5 days causes only a slight reduction in the level of tuberculin allergic response. Vaccine could be diluted 10-fold, or given in half or twice the usual dose, without causing a significant change in allergy.

On the other hand, the depth of injection of vaccine was found to have considerable practical consequence. Though the level of allergy was not affected, the size of the local lesions at the vaccination site, as well as the frequency of abscesses increased with the depth of the injection. Differences in technique of injection may well explain why a greater proportion of complications was found in some of the campaign areas, even though the same vaccine was used.

In seeking an explanation for the low levels of post-vaccination allergy found in some of southern countries, in contrast to Denmark, exposure of the vaccine to sunlight was naturally considered a possible important cause of a qualitative change in the vaccine. A series of experiments was carried out to determine the

effect of sunlight on BCG. The results showed that light has a devastating effect on the vaccine. After 30 minutes' exposure, the post-vaccination Mantoux reactions decreased in mean size from 20.5 mm to 8.6 mm and the vaccination lesions from 9.0 mm to 5.5 mm; and the colony count of BCG organisms was reduced approximately a thousandfold. A substantial decrease in colony count was seen after exposure of the vaccine to the sun for only 5 minutes.

Although it has been common knowledge that many biological products are harmed by light and undue exposure of BCG vaccine should be avoided, the significance of the effect of light was not recognized until the extremely poor results in Egypt prompted the search for some powerfully destructive agent. Subsequent laboratory studies in the State Serum Institute have shown that exposure to ordinary daylight through the laboratory windows during the course of preparation of vaccine causes a large reduction in the number of viable organisms. Vaccines prepared under artificial light, on the other hand, contain a relatively stable number of live organisms. This work has already resulted in modifications of the laboratory procedures of preparation and handling of the vaccine, and at the same time, precautions are being taken in the field to prevent exposure of the vaccine to light.

Differences have been observed between vaccines produced by different laboratories. Some workers claim that these are due to variations between strains of BCG. Field studies have shown that dead bacilli produce much lower levels of allergy than living bacilli, and mixtures of the two can produce allergy over a wide range, depending on the relative proportion of each component. It is therefore conceivable that a great deal of the observed variations between vaccines may be explained by different proportions of living and dead organisms.

The usual method for assessing the degree of post-vaccination allergy has been to determine the percentage of persons in the vaccinated group whose reactions are above (or below) a certain size. This technique would work quite well if a definite criterion could be established to define what is a satisfactory level of allergy from BCG vaccination. As a matter of fact, BCG vaccination produces allergy of a broad range and, at the present time, there is no indication of what

constitutes satisfactory post-vaccination allergy. Fixing a criterion at some specific point on the scale is therefore meaningless. It is more rational to express the results of BCG vaccination in terms of the frequency distribution of the size of the reactions, thus indicating the level of allergy on the spectrum of tuberculin sensitivity. It is expected that this improved method of expressing post-vaccination allergy will be widely adopted by critical workers.

In applying the Mantoux test in an unvaccinated population in the Scandinavian countries, the pattern of the distribution of reactions clearly shows that there are two groups in the general population - one group with little or no reaction and the other with strong reactions. Using the same test, the same tuberculin, and the same person reading the reactions, a different pattern has been found in some of the campaign countries. Though the distribution again indicates that there is one group with strong reactions, the other group has a low level of sensitivity instead of having no reaction at all. The latter have apparently been infected by some agent that causes a tuberculin sensitivity which is not specific for infection with human tubercle bacilli. This difference in the pattern of the distribution of tuberculin reactions raises a perplexing situation as to the selection of persons for vaccination. In the Scandinavian countries the persons who have no reaction can be considered non-infected and may be vaccinated. In these other countries, should those with the low-grade sensitivity be vaccinated? There is no answer to this question at the present time. In the current BCG campaigns, the criterion which has worked well in the Scandinavian countries cannot be used with justification in areas where this low-grade sensitivity is present. For example, using the Mantoux 5 TU test in Ecuador, persons selected for vaccination by the 5 mm criterion constitutes 55 per cent of the group showing a low-grade of allergy. The remaining 45 per cent will not be vaccinated. This shows that such a criterion is not applicable. Similar difficulties have been encountered in Egypt and in some parts of India. The tuberculin test must be carefully studied in different parts of the world to determine the pattern of the distribution of reactions and what criterion can be suitably applied.

5. Future tuberculosis research

The work of TRO has perhaps brought forth more perplexing questions on tuberculosis immunization than it has actually answered or clarified. It may be appropriate, therefore, to examine broadly the direction of future research which will best serve the needs of international tuberculosis control programmes.

Since Koch's discovery of the tubercle bacillus, repeated attempts have been made to vaccinate against the disease, but the outcome of most efforts has been disappointing. The protective value of BCG in man is still a highly controversial subject. The great difficulty is that, with few exceptions, there has been a failure to realize the necessity for using a comparable group of unvaccinated controls with which to measure the effect of BCG in the vaccinated. It now becomes imperative that more control studies of this kind be made, in places where the prospect of success is good and co-operation is obtainable. WHO, in accepting the responsibility for technical guidance in mass campaigns conducted in many countries, has an obligation to assess the efficacy of the methods used

Another pressing problem is the need for much more exact knowledge of the basic nature of tuberculosis immunity. It is of tremendous importance to improve BCG vaccine or to develop a more potent prophylactic which can be relied upon to prevent tuberculosis in man. Only through a clear understanding of the mechanism of tuberculosis immunity is it likely that this can be achieved. It is basically a task for the laboratory, to be studied by intensive animal experimentation.

For practical BCG work, it is of great importance to know whether or not vaccinated individuals showing a high degree of tuberculin allergy are better protected than those with a low-grade sensitivity. This is a serious question, in view of the fact that retesting surveys have revealed in a number of countries an unusually low and possibly unsatisfactory level of allergy among the vaccinated population. The same finding may obtain in other countries where no systematic retesting has been made or where BCG programmes are being, or will be, performed. Should those below a certain level of allergy be re-vaccinated? WHO has a responsibility to provide an answer to this question for the use of its tuberculosis technical advisers. The relation between allergy and immunity is yet obscure,

although much work has been done in recent years. The solution of this problem must be worked out jointly by laboratory and field investigators.

Finally, a conspicuous opportunity to carry out medical research has arisen in connexion with the intensive efforts against tuberculosis being made by international organizations. There are many countries today where tuberculosis is the leading public health problem and where reliable knowledge about the disease is lacking. It is naive to believe that orthodox measures of tuberculosis control, though they may have been effective in West Europe or North America, are necessarily applicable in other countries where conditions of life are widely different. The only rational approach, perhaps also a more economical one in the end, is to combine the practical assistance programmes in such countries with a simultaneous programme of scientific research. Undoubtedly the same can be said about other phases of international public health work. What is practicable in one country may fail in another, unless a sound basis for application has been found, or the results of preliminary trials support its use.

ANNEX A

Excerpts from Official Documents Concerning the Origin of TRO

The Joint Health Policy Committee UNICEF/WHO adopted at its second session the following resolution (JC2/UNICEF/WHO/3: Report on 2nd Session):

> "The Joint Committee on Health Policy of UNICEF/WHO notes with interest the medical research aspects of the BCG campaign, and recommends that the attention of the Executive Director of WHO be drawn to the unique opportunity that exists in the present BCG campaign for answering many questions of basic importance in the control and epidemiology of tuberculosis through intensive and continuing study in connexion with these campaigns."

Furthermore, the WHO members of the Joint Health Policy Committee reported as follows to the Executive Board concerning this item (Off. Rec. 14, p.49):

> "Dr. Carroll Palmer, who has been studying the research potentialities of the European BCG programme, presented a report which indicated certain lines of investigation which seemed to the WHO members of the Committee to present to WHO a unique opportunity for furthering medical knowledge in the field of tuberculosis (see outline appended). In view of this, Dr. Holm and Dr. Palmer were invited to attend the second session of the Executive Board in connexion with its consideration of the report of the Expert Committee on Tuberculosis."

The Executive Board, at its second session, accepted this report, and adopted a resolution, the relevant part of which reads as follows (Off. Rec. 14, p. 17):

> "In regard to research in connexion with the current UNICEF-BCG programme, similar approval of the UNICEF members of the JHPC shall be sought for initiation of a research programme. On receipt of this approval, the Director General is authorized to make an allocation not exceeding $100,000. This will further be implemented by the Executive Board upon receiving recommendation from the appropriate experts and from the JHPC."

During its third session the Joint Health Policy Committee approved the proposal (JC3/UNICEF/WHO/33). This initial appropriation for 1949 was later increased to $150,000 by the Executive Board at its fourth session and the following resolution was adopted (Off. Rec. 22, p. 2):

> "The Executive Board authorizes the Director General to allot from the UNRRA Special Fund an amount not to exceed $150,000 to implement the WHO tuberculosis research programme."

Outline of Programme Presented to the Eighth Meeting of the Second Session of the Executive Board by Dr. Carroll Palmer Tuberculosis Research Expert

Six types of medical research which could be incorporated in the general BCG programme:

1. Investigation of the criteria for vaccination, and what could be considered as a positive tubercular reaction. For example, would not a single tuberculin test be sufficient for screening purposes?

2. Development, testing and use of a preserved vaccine in the long-range view of immunization against tuberculosis, by the collection of precise medical scientific information on the efficiency of different vaccines, preserved vaccines and methods of administration.

3. Re-vaccination and the value of criteria in the selection of groups to be re-vaccinated. What were the criteria for saying that one group or other was completely immunized by BCG vaccination?

4. Collection of statistical material. The reports of the BCG campaign should be prepared in a uniform way showing the level of tuberculin sensitivity of adults, and in particular of children, in the various countries.

5. Research to be made on the effectiveness of BCG, as one of the techniques in the control of tuberculosis. Indirect presumptive evidence could be obtained on the value of BCG by comparison of the results on vaccinated and non-vaccinated persons.

6.1 Miscellaneous studies, such as family and racial differences in susceptibility and resistance to tuberculosis, response to artificial immunization, and the worldwide prevalence of fungus infection in its relation to tuberculosis.

6.2 Preservation of records.

6.3 General evaluation of the effect of the programme and the possibility of obtaining better morbidity and mortality statistics.

ANNEX B

Official Correspondence and Agreements between WHO and the Danish Government

Excerpt from WHO's letter of 24 October 1950, to Danish Ministry of Interior, signed by the Acting Director-General:

"WHO highly appreciates the co-operation and assistance that the Danish Government, its Health Department, its State Serum Institute, the school authorities and school physicians, and the medical profession of the country have extended to WHO Tuberculosis Research Office in Copenhagen under the direction of Dr. Carroll Palmer. This collaboration has proved of great value in carrying out research in the field of BCG vaccination at a high scientific level. To make full use of the excellent atmosphere created by this collaboration, WHO proposes to retain the Tuberculosis Research Office in Copenhagen, and looks forward to a continuing association with the Danish Government and medical profession in carrying forward and expanding the activities of the Tuberculosis Research Office.

... ...

WHO expresses the sincere hope that the Danish Government and medical profession will continue to co-operate with the Tuberculosis Research Office in Copenhagen and with its field studies in Denmark so that the research programme may be developed and expanded. Furthermore, BCG country programmes will thus continue to be closely associated with laboratory research, with field and statistical studies, and specialized laboratory facilities will be at all times available for the study and comparison of vaccine and tuberculin from different sources."

Excerpt from reply of Danish Government of 12 January 1951, signed by the Minister of the Interior:

"The Danish Government notes with satisfaction that WHO has decided to retain the Tuberculosis Research Office in Copenhagen, and on the basis of this decision, suitable premises have now been procured which will be placed at the disposal of the Tuberculosis Research Office, rent free, the maintenance costs to be borne by WHO.

Various Danish institutions and the medical profession of Denmark are already in close collaboration with the Tuberculosis Research Office, particularly in connexion with field studies on evaluation of BCG vaccine and the Danish BCG vaccination campaign. The Danish Government will gladly assist in maintaining and extending this association, and for this purpose plans connected with laboratory research in the field of vaccination against tuberculosis are at present under active consideration."

AGREEMENT BETWEEN THE GOVERNMENT OF DENMARK AND THE WORLD HEALTH ORGANIZATION FOR THE ESTABLISHMENT OF A TUBERCULOSIS IMMUNIZATION RESEARCH CENTRE

Whereas it is recognized that the role of immunizing agents is of vital importance in the world-wide effort to eradicate tuberculosis,

Whereas the campaigns of mass BCG vaccination have shown the necessity of further scientific investigation for determining the most satisfactory means of immunization,

Whereas the Government of Denmark, recognizing the importance of such research, has proposed, and the Secretary-General of the United Nations has agreed, that funds of the Danish UNAC collection presently available be used for laboratory research, and

Whereas the World Health Organization has requested that special emphasis be given to control studies for determining the value of BCG vaccination,

Now therefore, the Government of Denmark (hereinafter called "the Government") and the World Health Organization (hereinafter called "the Organization")

HAVE AGREED AS FOLLOWS:

Article 1

Purpose

There is hereby established within the State Serum Institute in Copenhagen a centre for international tuberculosis immunization research (hereinafter called "the Centre") which shall:

(i) undertake laboratory and related research on tuberculosis immunization;

(ii) co-operate with the Organization's field research on tuberculosis immunization;

(iii) co-operate with other centres and laboratories.

Article 2

Organization

For the purpose of co-ordinating laboratory and field research and general supervision of the Centre, a Committee shall be established composed of four representatives, two nominated by the Government and two nominated by the Organization.

The Committee shall adopt its own rules of procedure.

The Director of the Centre shall be the Secretary of the Committee.

The duties of the Committee shall also include:

(i) the recommendation for the selection of the Director of the Centre to be designated and appointed in accordance with the procedure determined in the supplementary agreement provided for in Article 6 hereof;

(ii) the approval of appointments, on the recommendation of the Director, to the professional and technical staff of the Centre;

(iii) the approval of the annual budget estimates to be submitted by the Director to the Government;

(iv) the transmittal, together with the Committee's comments, of the annual report of the Director to the Government and to the Organization on the progress of work;

(v) such other duties as may be determined in the supplementary agreement provided for in Article 6 hereof.

Article 3

Personnel

(1) Subject to the provisions of paragraph (ii) of Article 2 of this Agreement, the Director shall appoint the staff of the Centre.

(2) Staff other than officials of the Organization shall be appointed under conditions to be determined in the supplementary agreement provided for in Article 6 hereof.

(3) Subject to the availability of funds, officials of the Organization may be assigned to perform duties in the Centre.

Article 4

Establishment of the Laboratory

(1) Suitable premises for the Centre shall be constructed in close proximity to the State Serum Institute by the Government using the UNAC funds for this purpose upon land being the property of the Institute or placed at the disposal of the Centre by the Government gratuitously.

(2) The provision of equipment for the Centre shall be determined in the supplementary agreement provided for in Article 6 hereof.

Article 5

Operation of the Centre

(1) Subject to the availability of funds the Government shall be responsible for the necessary expenses in connexion with the operation of the Centre.

(2) Subject to the availability of funds, the Organization shall assist the Government in the provision of personnel and supplies for the Centre.

(3) The implementation of the provisions of this Article shall be determined in the supplementary agreement provided for in Article 6 hereof.

Article 6

Execution of the Agreement

(1) In execution of the provisions of this Agreement, a supplementary agreement (Plan of Operations) shall be concluded by the duly authorized representatives of the parties.

(2) This supplementary agreement shall also provide for interim arrangements pending the completion of the new premises for the Centre.

Article 7

Privileges and Immunities

The privileges, immunities and facilities provided in the Convention on the Privileges and Immunities of the Specialized Agencies, together with its Annex VII (revised), as acceded to by the Government on 25 January 1950 and on 22 May 1951, shall be accorded to the Organization, its personnel, property and assets, in connexion with the performance of this Agreement.

Article 8

Entry into force and Termination

(1) This Agreement shall enter into force upon signature by the parties.

(2) This Agreement may be terminated by either party upon written notice to the other and shall terminate 6 months from the receipt of such notice.

(3) The termination of this Agreement shall constitute termination of any supplementary agreement hereto.

(4) In the event of such termination the parties shall mutually determine the ultimate utilization of the new premises and the equipment of the Centre provided from UNAC funds or from the funds of the Organization.

IN WITNESS WHEREOF the Government and the Organization through their duly appointed representatives have signed this Agreement at Copenhagen on 30 November 1951, in four copies, two in English and two in Danish, the English text alone being authentic.

For the Government of Denmark: Aksel Møller

and at Geneva on 5 December 1951

For the World Health Organization: Brock Chisholm

SUPPLEMENTARY AGREEMENT FOR THE OPERATION
OF A TUBERCULOSIS IMMUNIZATION RESEARCH CENTRE

(Plan of Operations)

The Government of Denmark (hereinafter referred to as "the Government") and The World Health Organization (hereinafter referred to as "the Organization")

Acting in pursuance of Article 6 of the Basic Agreement signed on 5 December 1951 between the Government and the Organization concerning the establishment and operation of a Tuberculosis Immunization Research Centre

HAVE AGREED AS FOLLOWS:

(1) Appointment of the Director

In accordance with the provisions of paragraph (i) of Article 2 of the Basic Agreement, the Government shall designate the Director of the Centre upon the recommendation of the Committee from the staff seconded by the Organization to the Centre.

(2) Functions of the Director of the Centre

The Director shall:

(i) direct the activities of the Centre;

(ii) select the professional and technical staff for approval by the Committee and appoint all other staff;

(iii) prepare the budgets for approval by the Committee;

(iv) prepare an annual report on the activities of the Centre.

(3) Personnel

(i) The professional and technical staff of the Centre (other than officials of the Organization referred to in Article 3(2) of the Basic Agreement) will be appointed after approval of the Committee under the conditions of service of the Institute;

(ii) All personnel assigned to the Centre shall conform to the rules and regulations of the Institute.

(4) Establishment of the Laboratory

(i) The building of the laboratory, inclusive of usual laboratory installations, animal stables, etc., will be paid for from UNAC funds and from other sources.

Until the construction of the new laboratory is completed, temporary laboratory space will be provided by the Institute and paid for from UNAC funds.

(ii) Capital laboratory equipment and supplies shall be provided from:

(a) The Organization's funds, but not exceeding US $20,000;

(b) UNAC funds to a maximum of 100,000 Danish Kroner;

(c) Such additional funds as may be available.

(5) Operation of the Centre

(i) The Government from UNAC or other funds will provide to the Centre (a) such facilities as are part of the general maintenance of the Institute, e.g., water, heat, electricity, gas, cleaning services; (b) procurement, transportation, accounting and other common services of the Institute.

(ii) Within its yearly budgetary allocations and subject to the availability of funds the Organization will defray personnel expenses for the Director and for the personnel seconded by the Organization and for such equipment, supplies and other expenses as must be paid in other than Danish currency.

This contribution to the Centre shall not exceed US $30,000 per annum.

(iii) Operating expenses, not exceeding Danish Kroner 300,000 per annum, will be defrayed from UNAC funds.

(iv) Such additional funds as may be available may be provided for further necessary operating expenses.

(6) Accounting and Auditing

(i) Accounting Accounts for the Government contribution and UNAC funds will be kept by the Institute, and for the Organization funds by the Organization. The Institute and the Organization will furnish annual statements of accounts to the Director of the Centre for presentation to the Committee, to the Institute and to the Organization in the form of a joint statement.

(ii) Auditing Accounts for the Government contribution and UNAC funds will be audited by the auditors of the State Serum Institute; accounts for the Organization's funds will be audited by the Organization's auditors.

The two auditing bodies should consult each other as necessary, it being understood that access by the auditors to the accounts of both parties is to be provided.

(7) Amendments

This agreement may be amended from time to time as necessary by the parties, subject to the provisions of the Basic Agreement.

IN WITNESS WHEREOF, the undersigned, being duly authorized for that purpose, have signed this Agreement, at Copenhagen, on 15 December 1951.

For the Government of Denmark: .Zeuthen.

and at Washington on 27 December 1951

For the World Health Organization: .Carroll.E..Palmer.

ANNEX C

ORGANIZATION CHART
WHO TUBERCULOSIS RESEARCH OFFICE COPENHAGEN

DIRECTOR'S OFFICE
Medical Director
Asst. Medical Director

WHO/DANISH GOVERNMENT COMMITTEE

BCG VACCINE STUDIES
3 Medical Officers
1 Statistician
1 Asst. Statistician
2 Research Assistants
2 Technical Assistants
3 Clerks
1 Driver

STUDIES ON TUBERCULIN ALLERGY AND TUBERCULINS
2 Medical Officers
1 Statistician
2 Asst. Statisticians
2 Clerks

BCG CAMPAIGN STATISTICS
1 Asst. Statistician
2 Clerks

STATISTICAL PROCESSING POOL
1 Head Clerk
6 Clerks
1 Draftsman

ADMINISTRATION (INCLUDING SECRETARY POOL)
1 Administrative Officer
1 Asst. Adm. Officer
1 Accounting Officer
1 Accounting Clerk
1 Asst. Translator
2 Secretaries
2 Stenographers
1 Typist
1 Office Assistant
1 Telephone Operator

TUBERCULOSIS IMMUNIZATION RESEARCH CENTRE (LABORATORY)
TRO staff seconded to Centre:
1 Director
1 Immunologist
1 Bacteriologist

Joint Projects
with National or Local Organizations

BCG EVALUATION STUDIES

1. Denmark

   in co-operation with Danish National Health Service and Anti-Tuberculosis Association:
   1 Research Associate
   1 Asst. Statistician

2. Finland

   in co-operation with Finish National Anti-Tuberculosis Association
   1 Asst. Statistician
   1 Clerk

EPIDEMIOLOGICAL STUDIES

1. Madanapalle, India

   in co-operation with Union Mission Tuberculosis Sanatorium assisted by Indian Government;
   1 Consultant (part-time)
   Local personnel

2. Iceland

   in co-operation with Icelandic Government

Staff members as provided in 1953 budget.
Chart made in September, 1952.

ANNEX D

SUMMARY OF PRESENT ACTIVITIES

WHO TUBERCULOSIS RESEARCH OFFICE COPENHAGEN

SEPTEMBER 1952

Type of Activity	Purpose	Organization	Place of Operation	Progress*	Remarks
I. Statistical documentation of mass BCG campaigns.	To assist ITC in organization of field statistical work and training of local statistical personnel; to compile statistics and prepare reports on tuberculin testing, vaccination and post-vaccination testing of national campaigns; to handle WHO/UNICEF campaign statistics; to analyse material collected from vaccination programmes.	Co-operation with ITC and participating national organizations. Since Jan. 1952 co-operation with WHO TB-section and Regional Offices and national organizations. Assistance and guidance to regional BCG statisticians working in American, South-East Asian and Eastern Mediterranean countries.	Central Office in TRO Copenhagen. Prior to 1952, statistics from 23 countries in Europe, North Africa, Middle East, Asia and Latin America. At present, statistics from Aden Colony, Egypt, Iran, Pakistan, India, Burma, Thailand, Formosa, Hongkong, Philippines, Malaya, Costa Rica, El Salvador, Jamaica and Trinidad.	Monthly and annual statistical summaries for ITC and, since Jan. 1952 for WHO TB-section. Individual reports published for 9 countries, for Lebanon and Palestine Refugees in ITC Second Annual Report. Four additional reports to be completed this year. Simplified procedures introduced for collection of field statistics. Collection and analysis of pre- and post-vaccination testing results on sample basis.	Expenditures for publication of individual country reports paid by ITC. After 1952, work to be conducted on reduced scale and no budget provisions made for preparing and publishing similar reports for WHO/UNICEF campaigns.
II. Evaluation studies of BCG vaccination in prevention of TB.	A. Danish Mass TB Campaign. To develop a national roster of the tuberculin tested, x-rayed and vaccinated for long-range follow-up of TB morbidity. Special studies of relationship of allergy and x-ray findings to incidence of TB.	Joint programme with Danish National Health Service and Anti-TB Association.	Country-wide in Denmark, except Copenhagen.	Campaign started early in 1950 to cover 1.5 million persons 1-6 and 15-34 years of age and including tuberculin testing, vaccination, and x-ray examination of adults. Work on roster begun July 1950. So far punch card records made for 1.2 million persons half of whom vaccinated during the campaign or previously. Special studies conducted to evaluate and improve methods of tuberculin testing, x-ray examination, and selection of persons for vaccination. Improved compulsory national notification of pulmonary TB. Campaign to be completed Dec. 1952 and completion of roster in 1953, after which compilation and analysis of statistics, and follow-up work will be the main concern.	3.4 million kroner appropriated by Danish state and local authorities for the campaign. For developing the roster and research, kr. 400,000 plus annual allocation of kr. 25,000 from the state and kr. 100,000 a year from TRO. In 1954 and succeeding years follow-up work will be based largely on existing facilities of clinical examination, diagnoses and reporting and research activities financed through annual allocations from Danish Government and TRO.
	B. Finnish Mass BCG Campaign. To study long-range effect of mass vaccination on TB mortality through setting up national roster of the tested and vaccinated.	Co-operation with Finnish Anti-TB Association and National Office of Vital Statistics.	Operation of a statistical office in Helsinki and analysis of TB mortality statistics in Copenhagen.	Work on roster begun September 1948, including copying of some 1 million cards for population 1-25 years of age. Punch card records completed for 850,000 tested and vaccinated. Matching of TB death certificates against roster already begun; steps being taken to verify TB deaths for acute forms of the disease. Study of Finnish TB mortality with special reference to BCG vaccination well advanced and manuscript on results being prepared	Finland has high TB mortality and good vital statistics with strong central leadership and interest in international collaboration in research.

*A separate list of TRO publications is given elsewhere.

Type of Activity	Purpose	Organization	Place of Operation	Progress*	Remarks
III. BCG Vaccine and Vaccination Studies.	To investigate basic factors influencing allergenic potency of BCG vaccine with particular reference to problems arising in international BCG campaigns. Factors studied including dosage and age of vaccine, exposure to light and heat, qualitative differences between living and dead bacilli, vaccination techniques, etc. To compare vaccines prepared by different laboratories.	Studies conducted by TRO under joint auspices of ITC, Danish State Serum Institute and TRO. Programme consists of testing, vaccination and periodic retesting of school children supplemented by laboratory work (DSSI) on vaccines used. Close co-operation with national and local health services and officials, other BCG production laboratories, BCG Pilot Station, Paris.	Chiefly in Denmark, also in Mexico, South India and Egypt.	Approximately 44,000 school children tested and non-reactors vaccinated in 27 projects. Retesting after 6-12 weeks completed in all projects; one year retesting completed in 17; two year retesting in 7. A monograph being prepared for publication. Plans to continue work in Denmark on reduced scale, and extension to other countries depending on available facilities and future budget.	Field expenses paid by ITC in 1949-51, and in 1952 by a grant of $40,000 from UNICEF. Future work necessarily limited unless extra-budgetary support obtainable.
IV. Laboratory investigation.	To undertake laboratory research on TB immunity and immunization with particular reference to BCG. To co-operate with TRO and other research centres.	A TB Immunization Research Centre (TIRC) established by agreement (Dec. 1951) between WHO and Danish Government. Supervision and co-ordination by a joint committee of 4 members, two from each of co-operating parties. 2.3 million kroner allocated by the Government from its UNAC fund and about $30,000 contribution a year from TRO budget.	A special laboratory within premises of Danish State Serum Institute, Copenhagen.	TIRC Committee met in May and July 1952 on matters of appointment of staff and commencement of work. Director of Centre (temporary) and asst. bacteriologist appointed. Newly constructed laboratory of 5 rooms and $20,000 equipment ready for use; work expected to begin about 1 Oct. 1952.	Field studies on BCG have clearly shown need for basic laboratory investigations. Since 1950 TRO has made repeated effort to provide a research laboratory. Later offer by Danish National Health Service of the balance of Danish UNAC fund made it possible to establish TIRC. Use of the UNAC contribution approved by UN Secretary-General after consultation with UNICEF and WHO.
V. Epidemiological studies of TB in widely different communities	To investigate prevalence, nature and spread of TB and certain methods of control 1) in Madanapalle, a rural Indian community of 52,000 population 2) in Iceland, an insular country of 140,000 population.	Madanapalle Field Station. Co-operation with Union Mission TB Sanatorium, assisted by Indian Government.	Madanapalle and 175 surrounding villages.	Approximately 42,000 persons tuberculin-tested and x-rayed, including BCG vaccination of 11,000. Retesting and x-ray re-examination of 10,000 persons in 1951-52. 185 TB patients diagnosed and treated. Basic information transferred onto punch cards for individual identification and annual follow-up. Analysis of material underway.	Madanapalle offers excellent facilities for long-term studies of TB occurring under conditions very different from those prevailing in Europe and America and for investigations of immediate problems arising in connexion with mass BCG vaccination being carried on in India.
		Iceland project. Co-operation with Icelandic Government.	Country-wide, central office at Reykjavik.	National roster developed to include information on tuberculin sensitivity and x-ray findings for the population by household grouping. Plans being made for follow-up of TB morbidity and mortality. Detailed records for many years being transferred onto punch cards.	Unusual insular position of the country favourable for follow-up with excellent facilities for complete coverage TB control. Precipitous decline in TB mortality in recent years despite very little BCG vaccination.

*A separate list of TRO publications is given elsewhere.

Type of Activity	Purpose	Organization	Place of Operation	Progress*	Remarks
VI. Studies of tuberculin test and tuberculins.	To study specificity of the tuberculin test with particular reference to selection of non-infected persons for vaccination in different parts of the world. To investigate causes of non-specific reactions observed in tropical and subtropical countries. To develop suitable methods for field standardization and comparisons of tuberculins.	Work carried out by special teams directed by TRO operating in co-operation with national and local health authorities.	Denmark, Egypt, Finland, Holland, Iceland, India, Mexico, Norway USA.	In addition to children tested in connexion with vaccine studies, approximately 93,000 children and adults, and 4,100 tuberculous patients were tested with standard PPD; many with duplicate tests using varying doses and different antigens.	Work of TRO has demonstrated urgent need for and importance of more precise information on tuberculin sensitivity in different parts of the world. Such data are basic for a rational application of BCG vaccination and for international comparison of tuberculin sensitivity as an index of TB infection.
VII. Consultation and training	To advise on technical matters of mass BCG vaccination carried out previously by ITC and now by WHO/UNICEF, and to assist WHO TB-section and Regional Offices in training a number of selected doctors, nurses and statisticians for BCG work. To acquaint health officers from member states and WHO fellows with TRO work and methods of investigation.	Undertaken by senior staff members on an individual basis making use of TRO facilities including statistical evaluation projects, field vaccine studies, and co-operative research programme connected with Danish TB campaign.	Copenhagen as centre, field visits to other places in Denmark.	Increasing number of international and national officials visit TRO for conferences and discussions on technical matters related to BCG vaccination. Requests for training of BCG personnel also increasing. During past year 36 health officers from 23 countries and 15 WHO staff members and fellows have spent from a day to 2-3 months in TRO. Currently, 2 doctors and 4 nurses are being trained for BCG work.	The WHO TB-section programme of sending more fellows to Denmark and increasing requests for training in TRO make it necessary to expand this activity on an organized basis. This would require an additional staff of one professional and one administrative assistant to be provided beyond present budget.

*A separate list of TRO publications is given elsewhere.

ANNEX E

Publications - WHO Tuberculosis Research Office, Copenhagen 1949-52

GENERAL

1. Prospectus of Research in Mass BCG Vaccination - Carroll E. Palmer. Public Health Reports. 64: 40, 1250-1261, Oct. 7, 1949.

2. WHO Tuberculosis Research Office, Copenhagen, Progress Reports. Chron. World Hlth Org. 4: 11, 331-335, Nov. 1950, 6: 9, 254-259. Sept. 1952.

3. Annual Reports for 1949, 1950, and 1951. Off. Rec. World Hlth Org., No. 24: p. 61-62, No. 30: p. 52-54, and No. 38: p. 38-40

BCG VACCINE STUDIES

1. Report of BCG Vaccine Studies, Denmark. Second Annual Report of the International Tuberculosis Campaign, 1950. pp. 301-321.

2. BCG Vaccine Studies 1: Effect of Age of Vaccine and Variation in Storage Temperature and Dosage on Allergy Production and Vaccination Lesions Ten Weeks after Vaccination - Lydia Edwards and Anna S. Gelting. Bull. World Hlth Org. 1950, 3, 1-24.

3. BCG Vaccine Studies 2: Effect of Variation in Dosage of BCG Vaccine on Allergy Production and Vaccination Lesions Nine Weeks after Vaccination - Lydia B. Edwards and Anna S. Gelting. Bull. World Hlth Org. 1950, 3, 279-300.

4. BCG Vaccine Studies 3: Preliminary Report on Effect of Sunlight on BCG Vaccine - Lydia B. Edwards and Knud Tolderlund. Bull. World Hlth Org. 1952, 5, 245-248.

5. BCG Vaccine Studies 4: Further Observations on the Effect of Light on BCG Vaccine - Lydia B. Edwards and Inger Dragsted. Bull. World Hlth Org. 1952, 5, 333-336

6. BCG Vaccine Studies 5: Field Studies of the Significance of Dead Bacilli in BCG Vaccine - Sven Nissen Meyer and Carroll E. Palmer.
Bull. World Hlth Org. (in press).

7. BCG Vaccination and Tuberculin Allergy - Carroll E. Palmer.
The Lancet. 1: 19, 935-940, May 10, 1952.

TUBERCULIN SENSITIVITY AND TESTING

1. Studies of Pulmonary Findings and Antigen Sensitivity among Student Nurses. V. Doubtful Reactions to Tuberculin and to Histoplasmin - Carroll E. Palmer and O. Strange Petersen.
Public Health Reports. 65: 1, 1-32, Jan. 6, 1950.

2. Studies of Pulmonary Findings and Antigen Sensitivity among Student Nurses. VI. Geographic Differences in Sensitivity to Tuberculin as Evidence of Non-specific Allergy - Carroll E. Palmer, Shirley H. Ferebee and O. Strange Petersen.
Public Health Reports. 65: 35, 1111-1131, Sept. 1, 1950.

3. Experimental Error in the Determination of Tuberculin Sensitivity - Sven Nissen Meyer, Anna Hougen and Phyllis Edwards.
Public Health Reports. 66: 18, 561-569, May 4, 1951.

4. Research Contributions of BCG Vaccination Programs. II. Tuberculin Sensitivity at Different Altitudes of Residence - LeRoy Bates, Thøger Busk and Carroll E. Palmer.
Public Health Reports. 66: 44, 1427-1441, Nov. 2, 1951.

5. The Finnish Trambusti Test - A Comparison with the Mantoux Test - Phyllis Q. Edwards and Severi Savonen.
Public Health Reports. 66: 49, 1625-1641, Dec. 7, 1951.

6. Tuberculin Sensitivity. A Study on 245 Tuberculous Patients - Phyllis Q. Edwards and Johs. Guld.
Acta Tuberculosea Scandinavica. 25: 5, 463-473, 1951.

7. The Effect of Universal Carbon-Arc Light Therapy on Tuberculin Sensitivity - Phyllis Q. Edwards and K. Magnus.
Ugeskrift for Laeger. 20: 631-634, May 15, 1952.
(To be published in English in Acta Ped. Scandinavica.)

8. The Effect of Certain Infectious Diseases on Tuberculin Sensitivity - Johanne Weis Bentzon.
(Submitted to Tubercle)

9. A Method of Standardization of Tuberculin Preparations by Intracutaneous Reactions in Humans - Comparison of Two Purified Tuberculins - Sven Nissen Meyer.
Amer. Rev. Tuberc. 66: 292-313, Sept, 1952.

10. Tuberculin Testing in Relation to BCG - Carroll E. Palmer.
(To appear in Transactions of the Annual Meeting NTA, Boston, May 25-29, 1952).

11. Quantitative Aspects of the Intradermal Tuberculin Test in Humans. I. The Dose-Response Function within the Range 1-10 Tuberculin Units, Determined by Duplicate Tests. - Johannes Guld.
(Submitted to Human Biology)

12. Tuberculin Sensitivity of Tuberculous Patients - Carroll E. Palmer and LeRoy Bates.
Bull. World Hlth Org. (in press)

OTHER RELATED STUDIES

1. Research Contributions of BCG Vaccination Programs.
I. Tuberculin Allergy as a Family Trait - Carroll E. Palmer and Sven Nissen Meyer.
Public Health Reports. 66: 9, 259-276, March 2, 1951.

2. Significance of Familial Factors in the Development of Tuberculin Allergy - Sven Nissen Meyer and Chr. Munch Jensen.
Amer. J. Human Genetics. 3: 4, 325-331, Dec. 1951.

3. On the Reliability of the Reading of Photofluorograms and the Value of Dual Reading - E. Groth-Petersen, A. Løvgreen and J. Thillemann.
Acta Tuberculosea Scandinavica. 26: 1-2, 13-37, 1952.

4. Geographic Distribution of Histoplasmosis and Histoplasmin Sensitivity - Alessandro Mochi and Phyllis Edwards.
Bull. World Hlth Org. 5: 259-291, 1952.

5. Results of Mass X-Ray Survey in a Rural Population at Madanapalle, India - J. Frimodt-Møller, P. Benjamin and P. Mathew.
Proceedings of the 9th TB Conference, Lucknow, India. February 1952.

STATISTICAL DOCUMENTATION OF MASS BCG CAMPAIGNS

1. Mass BCG Vaccination in Czechoslovakia 1948-49. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Jørgen Nyboe. ITC country report series 1, 1950. 103 pp.

2. Mass BCG Vaccination in Poland 1948-49. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Jørgen Nyboe. ITC country report series 2, 1950. 134 pp.

3. Mass BCG Vaccination in Syria 1950. With special reference to statistics on BCG vaccination and pre- and post-vaccination allergy - I-Chin Yuan and Jørgen Nyboe. ITC country report series 3, 1951. 44 pp.

4. Mass BCG Vaccination in Israel 1949-50. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Mette Søegaard. ITC country report series 4, 1951. 34 pp.

5. Mass BCG Vaccination in Malta 1950. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Mette Søegaard. ITC country report series 5, 1951. 28 pp.

6. Mass BCG Vaccination in Tunisia 1949-51. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Jørgen Nyboe. ITC country report series 6, 1952. 42 pp.

7. Mass BCG Vaccination in Ecuador 1950-51. With special reference to statistics on BCG vaccination and pre- and post-vaccination allergy - I-Chin Yuan and Truls Zeiner-Henriksen. ITC country report series 7, 1952. 41 pp.

8. Mass BCG Vaccination in Austria 1948-50. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Erik Ebsen Petersen. ITC country report series 8, 1952. 39 pp.

9. Mass BCG Vaccination in Morocco and Tangier 1949-51. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Mette Søegaard. ITC country report series 9, 1952. 42 pp.

10. Mass BCG Vaccination in Greece 1948-51. With special reference to statistics on BCG vaccination and pre- and post-vaccination allergy - I-Chin Yuan and Jørgen Nyboe. ITC country report series 10, in press.

11. Mass BCG Vaccination in Yugoslavia 1948-51. With special reference to statistics on tuberculin testing and BCG vaccination - I-Chin Yuan and Mette Søegaard. ITC country report series 11, in press.

12. D-Form Statistics of the BCG Campaign in Lebanon. - Second Annual Report of the International Tuberculosis Campaign, 1950. pp. 252-255.

13. D-Form Statistics of the BCG Campaign for the Palestine Refugees. - Second Annual Report of the International Tuberculosis Campaign, 1950. pp. 265-271.

14. Pilot Report of the BCG Vaccination Campaign in Poland. - The Conference on European BCG Programmes, 1950. pp. 311-322.

15. Records and Statistical Data Connected with Mass Vaccination Programmes. - The Conference on European BCG Programmes, 1950. pp. 323-326.

16. Instructions for Field Statistical Work in Connexion with Mass BCG Vaccination Campaign. November 1949. Mimeographed. Published in Second Annual Report of the International Tuberculosis Campaign, 1950. pp. 73-92.

17. Monthly Statistics on Tuberculin Testing and BCG Vaccination. - Prepared for the International Tuberculosis Campaign from March 1949 to June 1951, and for WHO/UNICEF BCG campaign since July 1951.

18. Monthly and annual summaries on tuberculin testing and BCG vaccination for individual countries, published in Second Annual Report of the International Tuberculosis Campaign, 1950, and Final Report of the International Tuberculosis Campaign, 1951.

19. Comparisons between Moro-patch and Mantoux tests. Second Annual Report of the International Tuberculosis Campaign, 1950. pp. 140-144.

20. Graphic illustrations of tuberculin sensitivity for various countries. - Second Annual Report of the International Tuberculosis Campaign, 1950. pp. 146-151.

21. Tuberculin sensitivity in graphic form for various countries. - Final Report of the International Tuberculosis Campaign, 1951. pp. 107-117.

22. Retesting programmes in certain countries. - Final Report of the International Tuberculosis Campaign, 1951. pp. 118-119.

23. Instructions for Statistical Work in a Mass BCG Campaign. (Simplified statistical schemes and procedures for WHO/UNICEF BCG campaigns). Mimeographed and issued July 1951.