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COMMITTEE ON PROGRAMME AND BUDGET

PROVISIONAL MINUTES OF THE ELEVENTH MEETING

Palais des Nations, Geneva
Monday, 16 March 1964, at 2.30 p.m.

CHAIRMAN: Dr S. RENJIFO (Colombia)

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Note: Corrections to these provisional minutes should be submitted in writing to the Chief, Records Service, Room A.843, within 48 hours of their distribution.

1. GENERAL PROGRAMME OF WORK COVERING A SPECIFIC PERIOD: Item 2.3 of the Agenda (Resolution WHA13.57; Official Records No. 102, Annex 2: Document A17/P&B/1)

Dr LAYTON, representative of the Executive Board, recalled that Article 28 of the Constitution required the Executive Board to submit to the Health Assembly for consideration and approval a general programme of work covering a specific period. At its thirty-second session the Executive Board had reviewed the third general programme of work, which covered the period 1962-1965 inclusive, and had decided to recommend to the Seventeenth World Health Assembly that it extend it until the end of 1966. A draft resolution for the Committee's approval was included in document A17/P&B/1, but the word "general" had inadvertently been omitted from operative paragraphs 1 and 2. He therefore read out a corrected version, as follows:

The Seventeenth World Health Assembly,

Having considered the recommendation of the Executive Board,

1. CONCURS in the suggestion of the Executive Board that the third general programme of work for a specific period be extended to include 1966; and

2. DECIDES to extend the third general programme of work for a specific period to include 1966.

Decision: The draft resolution was approved.

2. CLINICAL AND PHARMACOLOGICAL EVALUATION OF DRUGS: Item 2.8.1 of the Agenda (Resolutions WHA16.36 and EB33.R21; Document A17/P&B/3)

Dr BAROYAN, Assistant Director-General, introducing the item, said that the question of drug safety was now being discussed by the Health Assembly for the third time. He recalled that the Sixteenth World Health Assembly had passed a detailed

resolution on the subject and had asked the Director-General to pursue the matter and report to the Executive Board and the Health Assembly. Because of the short interval since the Board's session, the Director-General's report to the Executive Board (document EB33/12) was presented as an annex to document WHA17/P&B/3.

Delegates had before them the following draft resolution sponsored by the delegations of Australia, Denmark, Finland, Iceland, Netherlands, Norway, Sweden, the United Kingdom and the United States of America:

The Seventeenth World Health Assembly,

Having examined the report by the Director-General on the clinical and pharmacological evaluation of drugs;

Having noted the resolution on the clinical and pharmacological evaluation of drugs of the Executive Board;

Desirous of a rapid development of a rational programme by which WHO can contribute to the protection of man against hazards arising out of the medical use of drugs;

Appreciative of the assistance given in this respect by Member States, the Advisory Committee on Medical Research and the Section on Pharmacology of the International Union of Physiological Sciences; and

Convinced that international collaboration and co-ordination are indispensable for the achievement of such a programme,

1. INVITES all Member States:

(1) to communicate to WHO any decision to refuse the approval of a new drug, or the withdrawal or restriction of the availability of a drug already in use as specified in resolution WHA16.36, in so far as they have not already done so, and to ensure that the justification for such action is communicated at the same time;

(2) to develop, as quickly as possible, with a view to eventual international collaboration, their arrangements for the systematic collection and evaluation of information on serious adverse drug reactions observed during the development of drugs and, in particular, after their release for general use; and

(3) to communicate to the Director-General the general principles and requirements which they consider essential for the evaluation of the safety and efficacy of drugs; and

2. REQUESTS the Director-General:

(1) to continue to collect and disseminate decisions relating to adverse drug reactions as specified in resolution WHA16.36 and to report to the Executive Board if and when changes in these arrangements appear desirable;

(2) to pursue, with the assistance of the Advisory Committee on Medical Research and with a view to eventual international co-ordination, discussion on satisfactory methods for monitoring adverse reactions, especially late toxic effects, to drugs already in use; and

(3) to undertake, with the assistance of the Advisory Committee on Medical Research, the formulation of generally acceptable principles and requirements for the evaluation of the safety and efficacy of drugs.

Dr ENGEL (Sweden) said that, as the delegate who had introduced the subject under discussion to the Fifteenth World Health Assembly, he had been particularly pleased to study the documents presented by the Director-General and to observe the interest shown by Member States and the progress that had been made.

Experience in the past two years had, however, made clear the many legal, economic and medical difficulties in clinical and pharmacological evaluation of drugs, as well as in registration of toxic effects and dissemination of information on them.

An international reporting system on serious adverse reactions would for a long time be the main weapon in protecting mankind against deleterious drug effects, and he emphasized the need for an effective and systematic collection and evaluation on the national level as a prerequisite to the fulfilment by WHO of its activities

as a communication centre. Reliable information on the subject could come only from hospitals, since they alone were in a position to make sufficient observations and to analyse them adequately. It was true that the development of an effective reporting system depended on factors that varied from country to country. The United Kingdom delegate had mentioned that his country was developing such a system on late toxic effects of drugs already in use. While such information was most important, and difficult to obtain, reporting could not be limited to those effects. He had in mind particularly the early-appearing effects on the blood-forming system. To evaluate the adverse effects of drugs already in use, it was extremely important to be able to estimate the amount of consumption of different drugs. Immediately-available figures were needed for a sound judgement to be formed of the importance of an adverse effect observed in the use of a particular drug.

His country had for many years had a reporting system on congenital defects apparent at birth, but it had been of limited value at the time of the thalidomide disaster because it had not been kept up to date. Such registration should be established in a manner that would make possible its immediate utilization.

When Member States communicated to WHO action taken because of adverse effects of drugs, it was very important for the justification for that action to be adequately presented.

The Fifteenth World Health Assembly had requested the Executive Board and the Director-General to study the subject of clinical evaluation of drugs with the assistance of the Advisory Committee on Medical Research. His own country had had to work out its own principles and statutory regulations with little guidance from

WHO or from the patterns of other countries. Its regulations were based on the conviction that the responsibility for all preclinical evaluation of a new drug should lie with the manufacturer; clinical trials were carried out by a hospital doctor - a clinician in a leading position - who, guided by the directives given by the National Board of Health, was responsible for the patient's safety and the safe keeping of the drug. He was expected to work in close contact with the manufacturer and to be remunerated by him. Adverse effects were immediately reported to the national health authorities. An attempt had been made for several years to establish a service for clinical pharmacology at each teaching hospital to assist the clinical investigator in his trials and to promote rational pharmacotherapy in general. Such measures were highly desirable.

An agreement on a sound advertising policy had been reached with Swedish drug manufacturers and with representatives of foreign pharmaceutical industries; it was published as a codex of praxis in the pattern of advertising and information in general.

The draft resolution before the Committee represented a slight but positive modification of the resolution recommended by the Executive Board, and stressed some of the points he had mentioned.

Drawing attention to operative paragraph 1(1) of the draft resolution before the Committee, he said that the wording that had been intended by the sponsors was:

> "(1) to arrange to communicate to WHO any decision to refuse the approval of a new drug or to withdraw or restrict the availability of a drug . . . "

Professor BABUDIERI (Italy) said that the international information system on adverse drug reaction had, during its first year's operation, proved useful. There were some imperfections that were largely due to deficiencies at the national level. He suggested that Member States, in reporting restrictive action taken in relation to specific drugs, should provide as much information as possible on the reasons for such action (the nature and extent of the reactions, for example), and should include the non-proprietary names as requested by the Sixteenth World Health Assembly.

His delegation realized the present administrative and financial difficulties in the way of an extension of the international information system, but hoped that it might be made possible in the future.

Dr WEBB (Australia) supported the remarks of the delegate of Sweden as one of the co-sponsors of the draft resolution.

Dr DOUBEK (Czechoslovakia) said that his delegation had noted with satisfaction that WHO was giving due attention to the subject, but it was clear from the Director-General's report (document A17/P&B/3) that the activity would have to be strengthened in the future.

It was not enough passively to collect information, the significance of which could not always be clearly defined. It was important to know also the amount of consumption of drugs in a given population and to estimate the incidence of side effects. The Executive Board, in resolution EB33.R21, had requested the Director-General:

> "to pursue, with the assistance of the Advisory Committee on Medical Research and with a view to eventual international co-ordination, discussion on satisfactory methods for monitoring adverse reactions of drugs already in use . . . "

It would be useful to employ in drug evaluation the same methods that had been used in evaluating vaccines or in assessing methods for tuberculosis control or malaria eradication. Such programmes were easier to apply in countries where the population received drugs free of charge from the government. Toxicological investigation had so far been concentrated mainly on the toxicity of drugs from the point of view of mortality of laboratory animals. Although that type of investigation was important, it failed to show the side effects. It was necessary to organize more effectively international collaboration under the auspices of WHO.

The question of the quality of imported drugs was also important for some countries. The Director-General's report on standards of drugs (document A17/P&B/4) mentioned that the best safeguard of quality would be by means of a national control laboratory. That was not a realistic approach in existing circumstances. His country had a national laboratory for the study of drugs in which a large number of highly qualified specialists worked. Not all countries, however, could establish such an institution. Apart from the programme envisaged by WHO, it was important that individual governments should agree that the quality of drugs intended for export should be the same as that for home consumption. The Organization could, with the agreement of the governments concerned, send its own experts to ensure that that was so. That would give a guarantee to developing countries of the quality of imported drugs, particularly if the firm exporting them knew that they might be subject to control. It was vital for all countries to have quality control of drugs, and the Organization should insist upon it. The commercial aspect did not, of course, affect the socialist country from which he

came, but it was extremely interested in all questions concerned with the possibility of extending the knowledge of the effects of drugs. To ensure their quality and effectiveness was a moral duty towards humanity.

Dr SAUTER (Switzerland) said that his delegation had noted the Director-General's report (document A17/P&B/3) with interest.

The Federation of Swiss Doctors had set up a central body responsible for the systematic collection of information on adverse drug effects, but it was as yet too early to assess the results.

He drew attention to operative paragraph 1(1) of the draft resolution before the Committee, which read:

"1. INVITES all Member States:

(1) to communicate to WHO any decision to refuse the approval of a new drug, or the withdrawal or restriction of the availability of a drug already in use as specified in resolution WHA16.36 . . ."

Resolution WHA16.36, however, made reference only to decisions taken "as a result of serious adverse reactions", and he feared that the text of the draft resolution might give rise to difficulties of interpretation. Should the expression "as specified in resolution WHA16.36" be taken to mean that future action should be limited to decisions taken as a result of serious adverse reactions, or, since those effects were not specified, that action should be taken to communicate all decisions to refuse a drug, for whatever reason?

Operative paragraph 1(2) made reference to serious adverse drug reactions "observed during the development of drugs". Such development was a long and complicated process during which the active substances, solvents, preservatives, etc.

might be repeatedly changed or modified with the very object of eliminating harmful or undesirable effects. The text of the draft resolution appeared to suggest that Member States were expected to assemble all the observations made during that long process. His delegation was doubtful about the possibility of administrations being able to fulfil that task, and would be grateful for clarification on the subject.

Operative paragraph 2(1), unlike operative paragraph 1(1), mentioned adverse effects. Since those two paragraphs were closely related, he considered that their texts should be made more consistent.

Dr MURRAY (United Kingdom of Great Britain and Northern Ireland) said that the Fifteenth and Sixteenth World Health Assemblies had discussed the subject, and following the studies made by the Executive Board and the Director-General, WHO's role in it was now becoming clearer. All those with health administrative responsibilities had a duty, in view of the worldwide trade in pharmaceuticals, not only to the populations of their own countries but to others also, to do everything possible to ensure the safety and efficacy of drugs put on the market. Much could be done by critical examination and investigation to ensure the highest possible degree of safety and freedom from harmful effects.

Since the Sixteenth Health Assembly, the United Kingdom had made significant progress to that end by co-operation between the pharmaceutical industry and the medical profession. A committee on the safety of drugs had been set up, with three sub-committees: one on toxicity, one on clinical trials and therapeutic efficacy and one on adverse reactions. The pharmaceutical industry had agreed that from 1 January 1964 no new drug would be marketed or put to clinical trial against

the advice of the committee. It was hoped that doctors would only use drugs that had been cleared by the committee.

A system of reporting of congenital abnormalities had also been started. Doctors had been asked to watch for and report on adverse reactions, and the first notice to the medical profession on such reactions had been published in February 1964, when a short note had been sent to all practitioners concerning liver damage observed following the use of some monoamine oxydase inhibitors. A copy had been sent to the Director-General under the terms of resolution WHA16.36.

The United Kingdom committee on the safety of drugs received advice from the Medical Research Council and from the British pharmaceutical industry, and every drug submitted to the committee was considered individually. His delegation would be pleased to communicate information on the matter to the Director-General if it were thought to be of value to him in his formulation of principles.

The United Kingdom delegation commended for adoption the resolution before the Committee.

Dr EL BORAI (Kuwait) said that he had noted that, in response to resolution WHA16.36, information communicated by four governments on nine drugs which had then been disseminated to Member States, but that some of the information was not clear or satisfactory. The Congress of the International Pharmaceutical Federation that had been held in Prague in August 1963 had stressed the need for devising some measures that could be taken before disseminating such information. It was anticipated that the scientific group that the Organization was proposing to convene would make some proposals for devising a workable programme on the subject.

His delegation supported the draft resolution before the Committee, and particularly operative paragraph 2, and looked forward to the formulation of generally acceptable principles and requirements.

He referred to the observation by the Director-General that it would not be feasible at present to collect and disseminate satisfactorily all data on new drugs owing to financial limitations. It was important to try and find an appropriate solution to that problem in order to move forward towards the very important goal.

Dr SCHINDL (Austria) thanked the Director-General for his excellent report, from which it could be seen that efforts had been made to overcome at least partially the difficulties with regard to toxicity and dangerous side effects of drugs.

The draft resolution before the Committee attempted to provide for the formulation of generally acceptable principles and requirements for evaluation of the safety and efficacy of new drugs. But even if such principles and requirements were established, he questioned whether freedom from chronic toxicity, cancerogenic, teratogenic and mutagenic side effects could be guaranteed with absolute certainty. Although sad experience had confirmed certain side effects of a drug, it could not be reliably affirmed that a new drug, even after normal clinical and toxicological examination, was free from side effects.

In his country, where strict clinical and pharmacological evaluation was carried out, the possibility was being considered of excepting such possible mutagenic and teratogenic effects from certification of safety and efficacy.

The time had come to warn people on an international basis of the serious effects of drugs. He supported the draft resolution before the Committee.

Dr CHADHA (India) said that his delegation appreciated the difficulties that had been experienced in implementing the suggestions made in the Fifteenth and Sixteenth Health Assemblies. It had been stated that information regarding adverse reactions appeared from time to time in a large number of medical journals all over the world. That was not a convenient method of bringing the information to the notice of the average busy medical practitioner, nor was it possible for a single drug control organization to go through all the medical journals of the world. WHO was the most appropriate body to carry out the task. Paragraph 3.4 of the Director-General's report (document EB33/12) stated: "It does not seem that a satisfactorily complete collection and dissemination by WHO of data on new drugs (as contemplated in resolution WHA16.36) is at present feasible."

Although his delegation appreciated the difficulties involved, it would plead that at least a beginning should be made; the additional staff, machinery and expenditure would be fully justified.

It was very necessary that all countries - particularly the more advanced - should exercise greater vigilance and control over the manufacture and sale of drugs. He felt strongly that something tangible could be done in that direction.

Dr MORSHED (Iran) expressed support for the draft resolution before the Committee. However, in view of the importance of the subject, particularly for the developing countries which were being flooded with new drugs produced abroad, and for the sake of clarification, he proposed the following amendments: in sub-paragraph 1(1), to replace the opening words, "to arrange to communicate to WHO"

by the words, "to arrange to communicate urgently, as they do for quarantinable diseases, to WHO"; and in sub-paragraph 2(1), after the word "disseminate", to insert the words, "by daily radio-telegraphic diffusion and the weekly epidemiological reports".

Dr BERNHARDT (Federal Republic of Germany) said that his delegation had been interested in WHO's plans for a programme regarding drug safety ever since its inception. His country had participated with great interest in the regional symposium on the subject held in Moscow three weeks previously. His Government agreed that the information service at present provided by WHO with regard to certain types of governmental decision on drug safety could be made of greater value by fuller co-operation on the part of those supplying the information. Justifications for decisions concerning the withdrawal of drugs from general use should be an integral part of the information supplied to WHO in the first instance. He therefore endorsed the recommendations to that effect contained in resolution EB33.R21 of the Executive Board.

With regard to the drawing up of generally acceptable principles for the experimental evaluation of drug safety and the development of satisfactory methods of tracing and registering adverse reactions to drugs already in general use, he agreed that the time had come to move forward from studies on the feasibility of the suggestion to some practical action on the lines indicated in the Director-General's report to the thirty-third session of the Executive Board (document EB33/12).

Referring to sub-paragraphs 1(c) and 2(c) of resolution EB33.R21, which were reproduced as sub-paragraphs 1(3) and 2(3) of the draft resolution now before the Committee, he said he understood that what was meant by the efficacy of drugs was therapeutic efficacy. If so, he did not feel it would be possible to formulate generally acceptable principles and requirements for its evaluation, as the therapeutic efficacy of a particular drug in the case of a particular patient often depended not only on objectively determinable pharmacological factors but also, for example, on psychological factors. He therefore thought it unlikely that the attempt to formulate such principles would give any practical results.

With the above reservation, his delegation supported the draft resolution before the Committee.

Professor ŽDANOV (Union of Soviet Socialist Republics), after expressing appreciation of the Director-General's report on the item, observed that the problem under discussion was a very complex one. He would not himself go into any details but merely recall the lengthy discussions at the last World Health Assembly and the concern expressed by many delegates, particularly from under-developed countries, regarding the danger of importation of drugs that had not been properly tested. The task that had been introduced to the Director-General was difficult but worthwhile. Progress was slow but unmistakable.

After referring to the effective centralized drug control in his own country, where a special commission was responsible for examining the safety of all home-produced pharmaceutical products and the few that were imported, he recalled a symposium held in Prague in August 1963 shortly after the Congress of the International Pharmaceutical Federation and suggested that its report should be communicated to Member governments of WHO as soon as possible.

The draft resolution before the Committee would not of course solve all problems, but it represented a further step forward. The report by the Director-General showed that as a result of past decisions by WHO certain improvements had already been introduced in national legislation regarding the control of drugs, which showed the value of the Organization's continuing work on the subject.

Dr HAQUE (Pakistan) referred to paragraph 4(c) of resolution WHA16.36, in which the previous World Health Assembly had requested the Director-General "to continue the study of the possibility of formulating, and of seeking international acceptance of, basic principles and requirements applicable to the toxicological, pharmacological and clinical evaluation of drugs". In other developing countries the same tendency had probably been noted as in his own: namely, that numerous pharmaceutical firms established branches within the territory and began the production of a wide range of drugs, producing pamphlets emanating from universities and academic figures that no member of the government concerned had ever heard of to prove that the drugs had been adequately tested. In Pakistan, under legislation introduced four years previously, no new drug could now be introduced without the authorization of the Ministry of Health. Any drug allowed by the United States Food and Drug Administration, which was known to be an extremely cautious body, was admitted without further question, but otherwise all drugs were subjected to tests within the country, which was a long and expensive matter. His Government would therefore be interested to know whether in the opinion of the Director-General there were in other countries bodies which were as strict as the United States Food and Drug Administration and whose indications could therefore be followed.

He considered it a matter of urgency that basic principles and requirements for the toxicological, pharmacological and clinical evaluation of drugs should be formulated, so that when the governments of the developing countries did undertake testing for themselves they could be sure that they were following the methods recommended by WHO.

Dr ALDEA (Romania) stressed the danger of fallacious advertising of drugs and proposed that the draft resolution before the Committee be amended by the insertion in paragraph two of a new sub-paragraph reading:

> To study possibilities of controlling advertising of pharmaceutical preparations and report on the matter to the Executive Board with a view to presenting proposals to the Health Assembly.

Dr SMITH (United States of America), after observing that his delegation was one of the joint sponsors of the draft resolution under consideration, said that nowadays drugs were in fact international. Many of the new ones being introduced were potent pharmacodynamic agents with potential toxicity and, in view of the variations in response of different patients, unexpected reactions were possible even with doses in the therapeutic range. To permit all countries to benefit from the experience of each regarding such reactions, prompt exchange of information was necessary. The United States of America had at present an expanding programme for the collection and dissemination of reports on adverse reactions and some of the information concerned - that specified in resolution WHA16.36 - had already been transmitted to WHO and other Member countries.

He recognized that, as pointed out by the delegate of the Federal Republic of Germany, the formulation of generally acceptable principles and requirements for evaluating the safety and efficacy of drugs would be difficult. However, he considered that the effort might give some valuable results and would at least show the possibilities and limits. If it were possible to develop principles and requirements acceptable to many countries, there would be increased confidence throughout the world in the safety and efficacy of useful drugs investigated under such conditions. Moreover, valuable guidance would be provided for countries which did not yet have evaluation services but wished to develop them.

Dr CAMERON (Canada) expressed support for the draft resolution and appreciation of the realistic report submitted by the Director-General.

The clinical and pharmacological evaluation of drugs was probably one of the most complicated administrative fields that the Organization could enter. No national organization, even, could guarantee that all drugs available in its own country were entirely safe and up to the standard laid down. In his own country the Department of Health included a division of food and drug control established under legislation dating back more than eighty years, and the conclusion reached in the light of experience was that the Government's essential function in the matter was to police the distribution of drugs. He apologized for the term "police", but felt it was the best description of what could actually be done: namely, to conduct spot checks, observe the level of quality maintained by the various manufacturers and keep a special watch on those that seemed to require it. The great majority of

manufacturers - the conscientious ones - welcomed such surveillance. The governments that had not yet been able to establish control systems would do well to bear in mind that it would never be possible to dispense completely with the principle: "Let the buyer beware."

Some delegations seemed to have the idea that all side effects observed in the use of any drug should be reported to WHO. He felt that any such system could become a bureaucratic monster that would not give results commensurate with the expense. When the matter had first been raised the idea had been that only unusual occurrences calling for drastic action should be reported. If all Member States could remember that, the Organization would be able to keep to its proper role.

Finally, he observed that in the case of established drugs, bought from reputable manufacturers, with proper labelling and descriptions for the guidance of the medical profession, there would never be much danger. However, if doctors and patients wanted to have the benefit of all the latest and most potent drugs, there would always be some element of risk and no action even by WHO could prevent it, as there were reactions that would not show up until a drug had been tried on thousands of patients, as in the unfortunate case of thalidomide. He said that only to discourage exaggerated hopes of eliminating all hazards.

Dr AMMUNDSEN (Denmark), speaking as a co-sponsor of the draft resolution under consideration, thanked delegates for their support and the Director-General for his positive attitude. The position of her delegation had been adequately stated in the intervention of the delegate of Sweden, so she would confine herself to pointing out a problem that had arisen in the implementation of resolution WHA16.36. In the last paragraph of section 2.2 of the report submitted to the thirty-third session of the Executive Board (document EB33/12), it was stated that only one case of withdrawal of a drug had at that time been communicated to WHO, which would seem to indicate that the reporting systems of the Member countries, including her own, were not yet adequate. However, knowing that the use of a certain drug in Denmark had been discontinued because of carcinogenic properties, she had inquired why the fact had not been communicated to WHO and had been told that, the decision having been made by the manufacturer, who had himself noted the defect in time, and not by the Government, the requirement to report to WHO had not been considered to apply. The same interpretation, due to a misunderstanding of the English text, in other countries might account for the small number of notifications received.

Professor GONZALEZ TORRES (Paraguay), after expressing support for the draft resolution under consideration, said that in his country there was practically no pharmaceutical industry and regarding the safety and efficacy of drugs it was necessary to rely on the information provided by the producing countries. When a

drug was withdrawn from use, as in the case of thalidomide, the decision was taken on the basis of reports in scientific publications, as there was no testing institution in the country. He stressed the value for countries like his own of a reliable centralized source of information.

Dr OLGUÍN (Argentina) also supported the draft resolution and emphasized the value of international exchange of information on drug safety and efficacy through WHO. The recent establishment in his country of an Institute of Pharmacology and Assay of Medicaments would enable it to co-operate more effectively.

Dr CHARLES (Trinidad and Tobago) said that his country was a small one and did not have the necessary funds and staff to undertake biological assay of drugs on its own account. It did, however, at present receive information on the results of tests for safety and efficacy from Canada, the United Kingdom and the United States of America, and would be glad if any other countries possessing the necessary facilities could make such information available to his government as well as to WHO.

Dr PEREZ MAZA (Cuba) said that his country, following the same humanitarian principles on which the draft resolution was based, was endeavouring to eliminate the dangers involved in the use of therapeutic drugs. The task was made easier by the fact that the pharmaceutical industry was in the hands of the state and the drugs were produced not for profit but to serve the public. All relevant information was disseminated by the Ministry of Health and labelling of drugs was compulsory. A laboratory had been established to assay all drugs, whether locally produced or imported, and though not yet fully equipped it was providing valuable services.

Dr PERERA (Ceylon) said that most of the therapeutic drugs used in his country were imported. For testing efficacy and toxicity the Department of Health had set up a Drug Formulary Commission which met regularly to consider any new drugs brought on to the market and distributed its findings to all medical practitioners. The service had come to be generally appreciated

His delegation supported the draft resolution before the Committee.

Dr SHRAIBI (Morocco) said that, as a result of previous decisions of the World Health Assembly regarding safety and efficacy of drugs, the Ministry of Health in his country, before authorizing the use of any drug, now required evidence that its sale and general use were permitted in the country of origin. Furthermore, it was planned shortly to establish a national laboratory for chemical and bacteriological assay.

Regarding the draft resolution now under consideration, he felt that many countries, lacking the necessary facilities for full laboratory analysis, would find it difficult to obtain all the information called for. To overcome those difficulties, closer collaboration and fuller international exchange of documentation would be required, and the regional offices of WHO must provide technical guidance for those countries that would be establishing national assay laboratories.

He considered that the resolution would spur both the Organization and its Member countries to greater efforts and he therefore supported it.

Dr WAKIL (Lebanon) observed that the question under discussion was complicated by the fact that there were two different sorts of countries: the drug-producing countries and the drug-importing countries The producing countries ought to exercise a very strict control over the manufacture, and the importing countries ought to lay down certain conditions, in particular that any drug imported should be really in use in the country of origin. The national legislation of Lebanon, which imported about twenty thousand proprietary drugs, required for each drug a certificate of origin vouching that it was on sale in the producing country and subject to the necessary control.

His delegation supported the draft resolution.

Mr RISQUEZ (Venezuela) also endorsed the draft resolution. His country had had for more than fifteen years a commission composed of doctors, pharmacologists, pharmacists and consultants from the pharmaceutical industry which was responsible not only for authorizing the use of new drugs but also for reviewing those already in use and withdrawing the permit where adverse reactions had been observed. Standards were severe and up to forty per cent. of the drugs submitted for approval were rejected. He took the opportunity of thanking the Food and Drug Administration of the United States of America which had assisted his Government in establishing the service.

He suggested that a further paragraph should be added to the draft resolution requesting the Director-General to invite Member governments to communicate to him any information that could assist other Member States in drafting national legislation on drug control.

The DEPUTY DIRECTOR-GENERAL said that, before the Chairman called on the Assistant Director-General, Dr Baroyan, to answer the questions raised, he wished to apologize for the fact that, as had been pointed out by the delegate of Sweden, an unfortunate editorial change had been introduced into the text of the draft resolution under consideration. In sub-paragraph 1(1), the words "to communicate to WHO any decision to refuse the approval of a new drug, or the withdrawal or restriction of the availability" should be corrected to read, "to arrange to communicate to WHO any decision to refuse the approval of a new drug, or to withdraw or restrict the availability". There was also a typing error: in sub-paragraph 2(2) the words "late toxic effects, to drugs" should be corrected to read, "late toxic effects of drugs".

Secondly, he wished to assure delegates that their remarks had been carefully noted and to thank, on behalf of the Director-General, those Member governments which had provided valuable information on the action taken in the light of earlier resolutions. Finally, he would point out, again on behalf of the Director-General, that the value, accuracy and speed of the information that could be supplied to Member States depended largely on the value, accuracy and speed of the reports received by the Secretariat.

Dr BAROYAN, Assistant Director-General, said that for the past three years the Director-General, in response to the decisions of the Health Assembly and the Executive Board, had done all in his power to develop the activities of WHO in the field of clinical and pharmacological evaluation of drugs. The results obtained

were fully set out in the reports before the Committee. The keen interest shown during the discussion was understandable, since the subject was one that closely concerned the health of the entire world. Representatives of producing and importing countries had spoken from their respective points of view but had shown a common concern with the need to ensure the harmlessness of the pharmaceutical products used by mankind everywhere. The comments made would serve as valuable guidance to the Director-General.

Replying to particular points raised, he noted that the delegate of Canada had drawn attention to some of the difficulties involved and to the impossibility of solving all the problems of ensuring with absolute certainty the safety of a new drug. In view of those difficulties he did not think it would be possible to put into effect the proposal for the establishment under WHO auspices of a laboratory which would assume responsibility for authorizing the use of pharmaceutical products throughout the world. As to the proposal of the delegate of Romania regarding the control of advertising, the matter had been raised at the symposium recently held in Moscow and it had been agreed that control of pharmaceutical advertising should be the responsibility of national governments.

Reference had been made to the desirability of speedy communication by telegram. He could assure the Committee that any such information received was immediately communicated to Member States, though, as the Deputy Director-General had pointed out, its value and accuracy depended on the Member government supplying it.

Regarding the question, raised by the delegate of India among others, of the assistance that could be provided by WHO in the development of national laboratories, it would be seen in connexion with item 2.8.2 of the agenda that assistance was being given in connexion with the different matter of drug standards.

Dr SCHINDL (Austria) explained, in connexion with the remarks of the delegate of Denmark, that the product in question was "bio-protein". It had been withdrawn as being of poor quality because a defect in the manufacturing process had resulted in the barium, added at one stage, being incompletely removed later. His Government had considered the case serious enough to warrant reporting to WHO.

Dr ALDEA (Romania) thanked the Assistant Director-General for his explanation and withdrew his amendment.

Decision: The draft resolution, as duly corrected, was adopted.

3. STANDARDS OF DRUGS: Item 2.8.2 of the Agenda (Resolutions WHA16.38 and EB33.R28; Document A17/P&B/4)

Dr BAROYAN, Assistant Director-General, said that in accordance with resolution WHA16.38 the Director-General had submitted a report to the thirty-third session of the Executive Board which, in turn, had requested the Director-General to continue his study and report to the following session of the Executive Board.

A circular letter would be sent to Member States in accordance with that resolution and the Director-General would report to the thirty-fourth session of the Board which would then be in a position to refer the matter to the following World Health Assembly.

Dr EL BORAI (Kuwait) informed the Committee that, although his Government was in full agreement with resolution WHA16.38, it was taking steps of its own to ensure that imported drugs were of acceptable standards. There was already a small laboratory under the supervision of one chemist which was being rapidly developed in order to be able to provide effective quality control. Five of the country's best chemists and pharmacists had been sent on missions to large firms and laboratories in Europe in connexion with the expansion of laboratory facilities and with a view to the home production of some drugs in current use.

Professor BABUDIERI (Italy) said that the need for the quality control of imported drugs was universally recognized, but, as was very well brought out in the Director-General's report, the difficulty was to provide a continuous control of every batch of exported drugs.

He fully agreed that exported drugs must comply with the quality requirements of the exporting country, but as its control could not extend beyond its own boundaries, quality control should be effected in the importing country. He fully realized that the establishment of control laboratories and the training of efficient staff were expensive and difficult, but it might be possible for two or more neighbouring countries to establish such a laboratory. In other cases, developing countries might be able to arrange for drugs to be tested on their behalf in the more developed countries. His Government would be willing to assist in that way.

Dr GJEBIN (Israel) expressed his disappointment that, in the words of the Director-General's report, there was "no other effective and practical way of controlling the quality of drugs imported . . . than by checking it in an official control laboratory of the importing country" and that no, more positive, suggestion was made. For the developing countries, that meant an additional burden in terms of expense and utilization of qualified personnel which, if available at all, would be sorely needed elsewhere. Faced with the situation in which certain countries were heavily dependent on overseas suppliers and were being supplied with drugs, not all of which had complied with the quality requirements of the producing country for its own use, WHO should do more to influence the governments of exporting countries to abandon current practices, and insist that no drug be exported unless it had complied with all the requirements for home use. The best solution would be, of course, to have quality control laboratories in every country but that was unattainable for many Member States. He fully agreed with the previous speaker on the value of inter-country laboratories and did not doubt that WHO had already done much to promote their establishment. At the same time, he had the impression that much remained to be done. WHO should be less defeatist and should not rest content with placing the burden of quality control on the importing countries. It was the duty of WHO to assist those countries which had no laboratory of their own, and it might do so along the lines he had suggested.

Dr AL-WAHBI (Iraq) said that, like other importing countries, Iraq had had the opportunity to appreciate the need for quality control. On one occasion imported sulfadiazine had been found, fortunately in time, to be of double the potency expected. He therefore welcomed the offer by the delegate of Italy, which was exactly the kind of aid he had had in mind when he had suggested, at the thirteenth meeting of the thirty-third session of the Executive Board, that WHO might assist developing countries by arranging with the producing countries for drugs to be tested prior to exportation until such time as the developing countries could set up their own public health laboratories. He appealed to other exporting countries to follow that lead.

Dr SMITH (United States of America) said that under the Federal Food, Drug and Cosmetic Act, the Food and Drug Administration of the United States had authority to exercise control over drugs in state and inter-state commerce. That included drugs exported from or imported into the United States. An exemption in the Act allowed export of a drug if it met the standards and did not go against the laws of the importing country. A drug exported in compliance with that exemption was not required to meet the standards required for its distribution in the United States. That exemption might be used to cover exportation of antibiotic drugs without batch certification or compliance with United States standards. That exemption did not apply to new drugs approved for distribution under the new drug procedure of the Federal Food, Drug and Cosmetic Act. Such drugs, if exported, had to meet the standards set in the approved new drug applications. An application however might provide for a different set of standards to meet the requirements of a foreign government. There was therefore a dual situation whereby some drugs had to meet United States standards before they could be legally exported whereas others had to meet the standards of the importing country.

Each system might be subject to criticism. It was agreed, however, that only drugs meeting adequate standards should be exported, whether that was achieved by laboratory control in the exporting country, in the importing country, or by an independent laboratory. It was the responsibility of the importing country to ensure that the drugs imported complied with an acceptable standard. It was moreover quite conceivable that, under certain circumstances, an importing country might demand or permit higher or lower standards than those of the exporting country.

Dr AWOLIYE (Nigeria) congratulated the Director-General and his staff on an excellent report.

His delegation fully shared the view that drugs exported should, of necessity, comply with the standards of the countries exporting them and that the export of substandard drugs should not be permitted.

On independence, the drug market of his country had been thrown open and it had become necessary to ascertain the standards of drugs. The drugs imported were not all of the British Pharmacopoeia or British Pharmacopoeial Commission standards owing to the different formulations used in overseas countries. References to other pharmacopoeias and national formularies were not unusual. Nigeria as a developing country was continuing to use the standards applied before independence until such time as it had been able to evolve its own on lines similar to those in use internationally or adapted to local needs. Meanwhile it was planning to control the quality of the drugs imported by having a pharmaceutical inspector at ports to take samples which would be tested for quality before being released for use in the country. A medical supplies committee had been established in Lagos over eighteen months previously with, among other duties, that of ensuring that substandard drugs were not used in the hospitals and public health service of his country and were not

prescribed privately. During his chairmanship of that committee he had had the opportunity of appreciating the need for that control. He therefore suggested for consideration by WHO the possibility of providing central control of drug standards and financial assistance for peripheral control.

Dr CHARLES (Trinidad and Tobago) associated himself with the comments of the delegate of Israel.

Dr CHADHA (India) expressed his delegation's deep concern at the position revealed in the Director-General's excellent report. It was particularly difficult for the developing countries to understand how human beings whose need was so great could be supplied with substandard drugs when the developed countries were able to control the sale and export of the drugs they were producing. It was particularly alarming to see that "evidence establishing the safety and effectiveness of one or more batches of a drug has no significance with respect to the safety of subsequent batches of the drug . . .". If that were so every batch should be tested. To suggest that every developing country should have its own quality control laboratory was not a constructive suggestion, desirable though that might be. It would be more helpful, in the circumstances, to suggest that the quality control should be carried out by the exporting country. He therefore put forward an urgent plea for more substantial and effective action to promote quality control before export.

Mr ABRAR (Somalia) thanked the Director-General for his report. His country was totally dependent on foreign drugs which it imported from as many as ten different countries. His delegation had expressed its concern at the previous Health Assembly. The subject was particularly important for the developing countries. Dozens of drugs, the standard of which they were unable to control,

were coming on to their markets and his delegation felt that unless international control was established their cause might well be lost. It was the responsibility of WHO rather than of individual or of exporting countries to assist the developing countries in solving that important and complex problem.

Dr HAQUE (Pakistan) agreed with the delegate of Israel that the report submitted by the Director-General made no suggestions of a positive nature. With regard to the issuing of certificates by exporting countries, he gave an instance of experience in his own country where that had not in fact proved a sufficient safeguard; a consignment of drugs to the value of two million rupees bearing a certificate from the exporting country had been examined and half the quantity had proved substandard, possibly due to deterioration, and had had to be returned. Drugs provided by the largest producing laboratories had given no trouble, although they were subjected to examination in Pakistan nevertheless. It was extremely difficult for the small developing countries to have their own laboratories and he would therefore urge WHO to consider what positive steps it could take to ameliorate the situation. It was moreover in the interests of the new pharmaceutical companies themselves that their drugs should not be rejected.

Dr AL-WAHBI (Iraq) felt obliged to intervene again in view of the trend of the discussion. He asked whether the drug-producing countries would be willing to help the importing countries by undertaking quality control if they were requested officially to do so by the governments of the importing countries. Such an offer would be evidence of a spirit of international understanding and co-operation in favour of the developing countries until they were in a position to establish independent facilities.

Professor MUNTENDAM (Netherlands) expressed a sense of disappointment with the conclusion stated in section 6 of document A17/P&B/4. He agreed with the sentiments expressed by the delegate of India.

Dr BAROYAN, Assistant Director-General, said that the statements and suggestions made by delegations at the present meeting would be taken into account by the Director-General. However, the questions raised appeared to be covered by resolution EB33.R28 as well as by the report submitted by the Director-General, which showed the action being taken by the Organization.

Laboratories for quality control were being set up in the developing countries also. He referred to the extremely favourable report made by a WHO expert on the well-equipped laboratory for the control of drugs established in Iraq. The control facilities existing in India had also been commended. WHO was taking the necessary steps for sending consultants to a number of countries where such laboratories and activities were being developed.

Dr WAKIL (Lebanon) shared the feelings of disappointment voiced. There could surely be no valid reason for allowing a state of affairs to continue where the same standards were not applied to drugs according to their place of consumption. The problem was an immense one for the importing countries, including his own. He recalled that in fact a committee had been set up in Lebanon after complaints had been made by the pharmacists' association, press and general public, and discussions with the Lebanese Ministry of Health had led to the recognition of the need for control of all imported drugs, which was no easy matter in view of the large number of types involved.

He emphasized the need for WHO to assist in arriving at some solution of the problem, possibly by establishing laboratory facilities, on a regional basis at least, for quality control of drugs.

Dr CHADHA (India) was grateful for the explanations provided by Dr Baroyan. Nevertheless, he did not think that the conclusions stated on page 6 of document A17/P&B/4 were adequate to meet the situation and it seemed to him that no progress had been accomplished over the past year. While there could be no doubt that the work being done by the central drug laboratory in India was good, the point at issue was essentially the need for adequate control in the exporting countries. He expressed the fervent hope that WHO would take some tangible action in that respect.

Dr CAMERON (Canada) wished to correct any possible misunderstanding regarding the position of the exporting countries. Canada was a small drug-producing country and its exports were therefore correspondingly small. He assured the Committee that tests were not undertaken in respect of every single batch of drugs sold in Canada, neither were they certified. There were exceptional instances where every batch was tested, such as with regard to the Salk vaccine for poliomyelitis, for example. On the whole, however, the authorities tried to police the market, to inspect drug-producing firms and to maintain standards. No distinction was made as between drugs sold abroad and in Canada. There was accordingly no negligence or lack of goodwill in the exporting countries. It was essentially a simple matter of supervising that industry and maintaining it in good condition whether production was for home or abroad.

Dr AL-WAHBI (Iraq) thanked Dr Baroyan for his favourable comment regarding the nucleus of a control laboratory set up in Iraq. It was to be hoped that one day that laboratory would indeed be able to be responsible for the analysis of all drugs; at present, that appeared to be a somewhat over-optimistic evaluation.

He associated himself with the wise remarks made by the delegate of India. He was also disappointed with the conclusions stated on page 6 of the Director-General's report. He would have hoped that a more constructive and factual answer could have been provided in the interests of the millions of people in real need of high quality drugs.

The CHAIRMAN believed that there was a consensus that the question called for further study. He accordingly requested the Rapporteur to read to the Committee a draft resolution on the subject.

Dr MOLITOR (Luxembourg), Rapporteur, submitted the following draft resolution for the consideration of the Committee:

> The Seventeenth World Health Assembly,
>
> Having noted resolution EB33.R28 on the need to continue studies in order to secure a high standard of drugs for human use in all countries;
>
> Noting that there will be a further consideration of the matter by the Executive Board,
>
> REQUESTS the Executive Board to report thereon to the Eighteenth World Health Assembly.

Decision: The draft resolution was adopted.

4. DRAFT FOURTH REPORT OF THE COMMITTEE ON PROGRAMME AND BUDGET (Document A17/P&B/19)

Dr MOLITOR (Luxembourg), Rapporteur, read the draft fourth report of the Committee (document A17/P&B/19).

Dr AL-WAHBI (Iraq) requested an opportunity after the adoption of the draft fourth report to revert to the subject of the resolution on standards of drugs.

Dr CHADHA (India) believed that the Committee had had insufficient time to come to a decision on the resolution, which had just been adopted, on standards of drugs, particularly as it had not been circulated. The matter was of great importance and he would have wished to have an opportunity to speak on that resolution.

Sir George GODBER (United Kingdom of Great Britain and Northern Ireland), drawing attention to the first resolution, "Medical research programme: proposal for the establishment of a World Health Research Centre", contained in the draft fourth report of the Committee before the meeting, presumed that the words "communications, science" in the second line of the second paragraph of its preamble, should be construed to read "communications-science".

The CHAIRMAN said that the resolution would be corrected accordingly.

Decision: The report was adopted.

5. STANDARDS OF DRUGS (resumed)

Dr KAUL, Assistant Director-General, Secretary, at the request of the Chairman, read out Rule 68 of the Rules of Procedure which was relevant in connexion with the remarks made by the delegates of Iraq and India following the adoption of the resolution relating to standards of drugs.

The CHAIRMAN asked whether the delegates of Iraq and India wished to move a formal proposal to reconsider the question in accordance with Rule 68.

Dr AL-WAHBI (Iraq) said that it was the general custom for important resolutions such as the one adopted to be circulated before any decision was taken. It was difficult for the full import of the text to be appreciated immediately, particularly since many delegations had to use the interpretation facilities. He would therefore request, with a view to facilitating the Committee's work, that the discussion be reopened so as to provide delegations with the possibility of submitting amendments. He considered that a fair request.

Dr CHADHA (India) expressed the opinion that the resolution had been disposed of too rapidly to allow time for adequate consideration. It would have been preferable for it to have been circulated in writing so that any amendments desired could have been presented.

The CHAIRMAN put to the vote the motion for reconsideration of the proposal relating to standards of drugs.

Decision: The motion was adopted by 37 votes to 2, with 26 abstentions.

The CHAIRMAN said that the text of the resolution adopted on standards of drugs would be circulated early the following morning.

The meeting rose at 6 p.m.