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TWENTY-SECOND WORLD HEALTH ASSEMBLY

INDEXED

COMMITTEE ON PROGRAMME AND BUDGET

PROVISIONAL SUMMARY RECORD OF THE SIXTH MEETING

Sheraton-Boston Hotel, Boston, Massachusetts
Thursday, 17 July 1969 at 9 a.m.

CHAIRMAN: Professor B. REXED (Sweden)

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Note: Corrections to this summary record should be submitted in writing to the Chief, Records Service, Room 326, within 48 hours of its distribution.

1. DRAFT FIRST REPORT OF THE COMMITTEE ON PROGRAMME AND BUDGET TO THE COMMITTEE ON ADMINISTRATION, FINANCE AND LEGAL MATTERS (A22/P&B/Conf.Doc. No.2)

The CHAIRMAN put to the meeting the draft first report of the Committee on Programme and Budget to the Committee on Administration, Finance and Legal Matters.

Decision: The report was approved unanimously.

2. QUALITY CONTROL OF DRUGS (Resolution WHA21.37; Document A22/P&B/12) (continued)

Dr GATMAITAN (Philippines) said that a thorough study of the report and its appendices revealed the time and effort spent on that valuable document. His delegation subscribed to the proposed Principles of Pharmaceutical Quality Control and the Good Practices in the Manufacture and Quality Control of Drugs contained in Appendices I and II of the report respectively. The importance of proper quality control was appreciated by pharmaceutical manufacturers, who realized that it was needed to guarantee the uniformity and efficacy of their products. With the expansion of the drug industry, there had been great improvements in quality control; that was all to the credit of manufacturers. Most local manufacturers in his country that were subsidiaries of reputable manufacturers insisted on strict quality control before the drugs could be released. In certain cases the mother companies even required government laboratories to analyse their products or check the analysis of local laboratories.

While such laboratories were well equipped, those of Philippine-owned companies still left much to be desired in respect of analysis; many of them still failed to appreciate the fact that quality must be maintained, irrespective of cost. Quality control was no longer confined to qualitative and quantitative analysis, but also extended to the combination of ingredients. That was vital, as incorrect combinations could result in unsuitability of the product or at least reduce its efficacy. It was deplorable that local formulations often included numerous diverse ingredients merely to present an impressive formula, often of sub-standard potency. The growth of the Philippine pharmaceutical industry would depend greatly on its appreciation of the importance of quality control.

Drug control in his country was vested in the recently established Food and Drug Administration, a department of the Ministry of Health. No drug could be placed on the home market unless registered with that department. All drugs had to be analysed by the Food and Drug Administration, whose laboratories - while not the most modern - were adequate, and whose requirements were stringent. Only drugs conforming to that body's minimum requirements were licensed. The requirements were laid down in the administrative Orders issued by the Philippine Ministry of Health, prescribing regulations for the enforcement of the Food, Drug and Cosmetics Act - under the headings of requirements for drug and cosmetic establishments, and requirements for pharmaceutical drug manufacturing laboratories - particularly in respect of premises, equipment, raw materials, production and control procedure, packaging and labelling, and laboratory control. Those regulations and requirements, which provided the legal and technical basis for the maintenance of a satisfactory manufacturing procedure, were based on the Good Practices in the Manufacture and Quality Control of Drugs established by the WHO Expert Committee, and included in the appendix to the report.

Dr FELKAI (Hungary) approved the report and appendices wholeheartedly. The requirements contained in Appendices I and II had been implemented in his country, where legislation ensured Ministry of Health control of the manufacturing process, premises and equipment, and storage conditions.

The State Institute of Pharmacy was responsible for taking samples of all products. Before any drug could be registered, factories were checked as to suitability; chemical, biological and microbiological controls were also made to ensure the efficacy of quality control. All Hungarian factories had well-equipped control laboratories with well-trained staff; many of them were well-known researchers and some served on the Pharmacopoeia Commission as well.

He supported the recommendations for a certification scheme. Certificates for individual batches had for some years been issued at the request of importing companies by the Hungarian Ministry of Health. The second edition of the International Pharmacopoeia had greatly developed the part on drugs and control methods, and should become the standard reference work for the international trade in pharmaceutical products. The 1967 edition would greatly assist the quality control of drugs in developing countries.

The standard colour-matching solution which figured in national pharmacopoeias should be included in the addendum to the International Pharmacopoeia; that would allow data which could not be obtained, even from tests with highly sensitive instruments, to be obtained in a simple manner.

The standards of the Hungarian Pharmacopoeia would be based on WHO standards. To that end, the National Pharmaceutical Institute maintained close contact with the WHO institute in Stockholm.

WHO courses held in Copenhagen in 1968 on quality control of drugs had been very useful; he was convinced that the further course to be held in Copenhagen on the same subject would be most helpful, especially to drug control experts in the developing countries.

His country would willingly provide specialists from developing countries with facilities to study the Hungarian drug-control system; it was also ready to make specialists available to assist in the establishment and improvement of drug control laboratories.

Professor PENSO (Italy) said that the Italian delegation entirely agreed that it was necessary to establish rules of good practice for the manufacture and quality of control of drugs, but pointed out that those proposed by WHO were considerably less strict than those required under Italian law.

In Italy prior authorization from the Ministry of Health was required for the production of drugs. A would-be manufacturer must first possess a factory; provided that the factory was approved by a group of experts from the higher Institute of Health, he would receive the requisite authorization. However, a special licence application must be made for each drug, which latter had to be tested in respect of its value and so as to ascertain that it was both active and innocuous. Once the drug was approved, the factory was visited by a group of experts whose task it was to establish that the necessary machinery was available for the production of the specific drug. Those regulations applied to all products for sale at home and abroad.

For certain groups of products, namely immunological products, sera, vaccines; biological products, hormones and so forth; antibiotics, and products (such as catgut) used in surgery, the inspector appointed by the manufacturer had to send his credentials to the Ministry of Health, which would decide whether or not he was fitted for his task. In addition health officers were sent by the State to the factory to take samples; those were then sent to the Higher Institute for Health where they were controlled batch by batch.

Some explanation of the word "batch" was required. In document A22/P&B/12, the word "batch" was defined in section 2 of Appendix II. However, the definition did not cover all contingencies. It was stated that a batch was "a quantity of any drug produced during a given cycle of manufacture." But it was common knowledge that in some factories drugs were produced on the conveyor-belt system, which meant that the raw materials went in at one end and the finished product came out, ready for marketing, at the other. For instance, in various European and American factories there was serial production of catgut for twenty-four hours out of twenty-four, and the definition quoted could not be applied thereto, not indeed to various antibiotics or sterile products.

As the Committee knew, the eight countries of the European Community, signatories to the Partial Agreement, which had the most highly developed pharmaceutical industries in Europe, were preparing a European Pharmacopoeia which was to have legislative force in those eight countries. A batch of sterile products was defined therein as being a homogeneous collection of closed containers, so prepared as to ensure that the risk of contamination was identical for each of the component units. Several delegates had already raised the question of the safety of products defined as sterile, and there were other points in the document which raised doubts. Control of products was mentioned in the report, but it was not stated on how many samples control had to be carried out. Unless control followed established biometrical laws, it was valueless and could give no guarantee to those who bought and used the drugs.

The World Health Organization had at its disposal a whole series of documents prescribing the number of samples on which control must be carried out in order to be valid; all that was needed was to apply the resolutions of the expert committees of WHO.

No account was taken in the report of countries such as Italy where there was State control of the most important products, yet the report considered such details as labelling. In modern production procedures the name of the product was often printed on the container, and labels were no longer employed. He considered such details anachronistic.

What was important, was that drugs exported to countries with difficult climates needed to be packaged differently from those manufactured for the cold or temperate climates in which they had been produced. The rules applicable to the European countries were not applicable to countries with a tropical climate. Insistence must be placed on the adaptation of the packaging to the conditions of the country where the drug was to be used.

It was also necessary to consider rules for the proper conservation of drugs. Drugs which had been properly prepared and tested had often, when they arrived in certain countries, pharmacies or hospitals, been stored under such inadequate conditions that the product had deteriorated. Italy had had protests from importers, and on going into the question had found that deterioration was due to the conditions in which the product had been stored. He thought therefore that regulations were needed for packaging and storing, as well as for production, and should form the subject of a special WHO recommendation to improve the distribution of drugs throughout the world.

In respect of the certificate stating that manufacturers had respected the rules of good practice, he said that in the big European drug-producing countries including his own - all drugs were prepared in conformity with legislation imposing such rules. If each small consignment - of which there might be thousands daily - had to be provided with such a certificate, it would be necessary to open up a special office for the purpose. He thought it would be preferable to indicate on the package that the product had been produced in accordance with rules recommended either by WHO or by the producer country, as was the case with certain other

products such as foodstuffs. Much the same procedure applied in Common Market countries in respect of wine: each bottle had to be provided with a stamp, certifying that the wine conformed to Common Market rules. The same could be done for drugs prepared in countries where those rules were fully applied.

Moreover, as the certificate required that the quality conform to WHO regulations, certain Italian exporters had had their products returned, as the certificate issued by the Higher Institute of Health did not correspond to the minimum requirements of WHO. For example, because WHO admitted 500 microbes per millilitre for smallpox vaccine, while Italy admitted only 100, or because titration had been carried out on twenty guinea-pigs, instead of on ten, as stipulated by WHO. If a certificate was to be required, it should be stated that the rules must be similar, not identical, to those recommended by WHO.

He hoped the Secretariat would revise and improve the document on the basis of technical data already published by WHO and its technical committees.

Dr AKIM (United Republic of Tanzania) said that the quality control of drugs had been under discussion by the Executive Board and various World Health Assemblies since 1963. International trade in drugs would be one-sided for many years to come, as drugs were usually manufactured in developed countries, and developing countries had little hope of becoming self-supporting in that respect for a long time. The latter were thus particularly anxious to see that the proposed specifications for the quality control of drugs were effectively implemented under Article 21 of the Constitution of WHO. His delegation had studied that Article in conjunction with Article 22, and had compared it with Article 23, which had been mentioned during the Committee's discussion. It was quite clear that under Article 21, as qualified by Article 22, and under Article 23, Member States had the option to reject the recommendations. He thought the difference was one of degree; if Article 23 was to be taken as the basis, any response from manufacturing countries would be discouraged from the very beginning.

He had tried to understand the objections of various speakers to implementing the proposals under Article 21. He had failed to do so - since it had been stated that the proposals were acceptable in principle and that most of the manufacturers would have little difficulty in meeting the proposed requirements. Italy had even mentioned that these requirements were less stringent than existing ones. It had also been stated that there was inadequate agreement on the proposals and that they must therefore come under Article 23. However, there appeared to be solid support for those proposals in the Committee, and he felt that they should be accepted under Article 21.

He thought that the possible objection that some exporting countries might not be in a position to meet the requirements immediately was immaterial, since the adoption of the recommendations under Article 21 would merely facilitate the identification of quality for the buyer. It imposed no other obligations.

He also pointed out that the problem extended to medical equipment, and asked the Director-General what had become of the Organization's attempt to produce suitable X-ray equipment for rural health services in developing countries. No information had been given as to its outcome.

Dr KIVITS (Belgium) said that his delegation agreed with the proposals submitted in respect of quality control and of good practices, and with the suggestions of the Secretariat regarding certification of the quality of pharmaceutical products. It also agreed with the proposal of the delegate of the United States of America, supported by the delegations of Czechoslovakia, the Federal Republic of Germany, and others, suggesting that the proposals submitted be adopted as recommendations under Article 23 of the Constitution.

He had one question to put to the Secretariat regarding the Good Practices in the Manufacture and Quality Control of Drugs (Appendix II to document A22/P&B/12). The first sentence of section 10 (page 9) of the report, read: "Every establishment that manufactures pharmaceuticals should have a quality control department that is autonomous in the areas of responsibility assigned to it." In the following paragraph it was stated: "A quality control laboratory must also be available." His delegation thought that might cause confusion. It could mean that there were two services which exercised mutual control over each other. He thought, however, that it was intended to mean that the control service should include a laboratory. Consequently, he thought the wording should be modified.

Dr URATA (Japan) said that the world was evolving rapidly; so were pharmaceutical products. New ones were constantly being introduced and had become of major importance in international trade. His Government considered it most important to take measures to guide and supervise drug manufacture, and to introduce some kind of certification for local and imported drugs. His Government did not object in principle to further study of the possibility of quality control, and would be most happy to assist in any way.

However, he recommended that the Committee should be very careful in respect of the quality control of drugs. The definition of drugs in section 2 of Appendix II of the report, for instance, did not cover all contingencies. That was true also of the definition of starting materials and of "half-finished" products. The problem of how to interpret those definitions in concrete cases remained. He was sure that the Committee agreed with the report, but it could not be denied that the recommendations contained loop-holes. His delegation considered that the proposals should be adopted as recommendations, not as regulations; it was indeed high time to consider adopting WHO guidelines which, in his delegation's opinion, could be attained from the appendices now before the Committee.

Dr DAS (Nepal) said that many developing countries had no laboratories of their own for the analysis and assay of drugs, nor had they sufficient staff, equipment or money. But as pharmaceutical firms were springing up like mushrooms in certain countries, it was essential to have proper control. To ensure a suitable certification scheme, he suggested that WHO explore the possibility of setting up regional or inter-regional laboratories; he was glad that other delegations had voiced similar views.

Mr GLOKPOR (Togo) said that his delegation was most interested in any international action to guarantee the quality and therapeutic safety of important drugs, and he thanked the Director-General and the Secretariat for their work in submitting to the Committee a system of certification for pharmaceutical products sold internationally. Unfortunate experiences had high-lighted the potential threat to health of drugs; moreover, their cost was high, and the consumer had the right to be sure of both the quality and the therapeutic safety of the drugs he was buying.

His delegation agreed with the system proposed and was willing to trust the health authorities of the exporting countries in respect of control. Problems remained, however, such as the stability of pharmaceutical products to the extent that it depended on factors such as climate, since imported drugs were usually manufactured in countries with climates which differed from that of the importing country. In adopting the proposed system, the importing countries would still have the power to exercise control on imported products; he agreed with the Director-General who had said in the introduction to his Annual Report for 1968 that it was "generally recognized that, even after the most careful evaluation of its therapeutic safety during the initial stages of testing, a drug should be kept under close surveillance for possible adverse reactions". The delegation of Togo therefore supported the request of the Indonesian delegation that WHO should assist countries with insufficient resources by making available, even if only at regional level, laboratories to ensure the necessary control over imported drugs as well as over those produced locally.

Dr CHAVEZ (Panama) emphasized that the problem of drug control was of great importance for all countries. In Panama a laboratory for the analysis of pharmaceutical products and foodstuffs, attached to the Faculty of Science of the University and working in close co-operation with the Ministry of Health, had existed for some ten years. All imported drugs had to be submitted for analysis to that laboratory, and, unless they conformed to the requisite qualitative and quantitative requirements, they were withdrawn and their sale prohibited. Around 10 000 drugs had already been analysed and registered. By agreement with the Higher Council for Health of Central America and Panama, his country had made the services of that laboratory available to all Central American countries. Moreover, as from 1969, a drug quality control department was to be established at the University of Panama. The report submitted to the Committee, setting forth regulations and standards for the quality control of drugs, would certainly give the programme further impetus, and he hoped that those regulations would be put into practice on a world scale.

Professor SENAULT (France) said that the Director-General's report on the quality control of drugs, and its appendices, which embodied the conclusions of the relevant expert committees, clearly showed the common concern to find satisfactory control methods.

The delegate of Italy had stated that, particularly in certain European countries, the national requirements were considerably more strict than those submitted in the Director-General's report. That, however, did not constitute an obstacle; the Director-General, on the advice of the expert committees, had put forward minimum requirements, and countries whose requirements were more severe would have no difficulty in conforming to them. The delegation of France was, therefore, prepared to accept the Director-General's proposals, including the Certification Scheme on the Quality of Pharmaceutical Products in International Commerce, provided that the scheme was adopted as recommendations under Article 23 of the Constitution.

Professor GERIĆ (Yugoslavia), congratulating the Director-General on the work accomplished, recalled the discussions at previous sessions of the Executive Board and the Health Assembly and the hesitation, and even opposition, that quality control of drugs had encountered. Considerable progress had been made, but much remained to be done, since the final goal was the institution of international regulations. His delegation approved the proposals contained in the Director-General's report and hoped that WHO would persevere in its work.

Dr TEOUME-LESSAN (Ethiopia) said that his country, as one which depended, and would depend for several years to come, on imported drugs, was grateful to the Director-General for his excellent report.

Until a few years previously, his country had had no means of controlling the very large number of imported drugs. A drug control department had been set up but would have to be further developed before it could cope with its responsibilities. It had already been found, however, that many of the drugs imported on the basis of the information provided by the exporting country or the manufacturing firm were unsatisfactory. Sometimes the chemical content did not correspond to that given in any pharmacopoeia, and sometimes even the physical properties did not conform to specifications. He mentioned the case of a large batch of aspirin - supposedly tablets - which when opened had been found to have disintegrated into powder; the manufacturer had been informed and another shipment had been obtained - of tablets so hard that they did not even pass a simple disintegration test.

He failed to understand why producing countries that had national control requirements more stringent than those proposed in the report before the Committee were unwilling to accept the suggested Certification Scheme on the Quality of Pharmaceutical Products in International Commerce as regulations under Article 21 of the Constitution.

He referred to a point already raised by the delegate of Norway in connexion with the footnote[1] to the clause of the second certificate in the draft certification scheme saying that he would like to know the reasons for which a drug was not authorized for sale in the manufacturing country. He personally would not be willing to buy any such drug. The footnote should be deleted.

The delegate of Italy had drawn attention to the need for rules for packaging and storage of drugs. It was for the manufacturer to state the temperature at which a given drug should be stored - and it would not be sufficient to state merely "room temperature", since that would vary according to place. Manufacturers should test their drugs at various temperatures, so that the maximum permissible temperature would be known.

He supported the view of certain delegations, among them the delegation of the United Republic of Tanzania, that the certification scheme should be adopted as regulations under Article 21 of the Constitution. Under that Article, Member States were not compelled to accept the regulations, but importing countries would know which countries had not done so, and could take measures accordingly.

Dr HEMACHUDHA (Thailand) said that there was nothing untoward in the proposals made in the Director-General's excellent report and that the requirements envisaged were certainly already complied with by all reputable pharmaceutical manufacturers. However, it was one thing to adopt requirements, and another to get them implemented. Implementation entailed a great deal of paper-work, co-operation with quality control departments of manufacturing firms, and responsible supervision on the part of the national health authorities.

The pharmaceutical industry in his country was not developed, so it had to depend upon imported drugs, and there had been some difficulties caused by the importation of sub-standard products. The relevant legislation had been amended but had not given ideal results.

Referring to the remarks of the delegate of Ethiopia on the footnote to the last clause of the second certificate in the suggested certification scheme, he said that he shared the concern of that delegate that drugs not authorized for sale in the country of manufacture should still be exported. If such drugs had been shown by test to be unreliable, why was it permitted to export them? He asked whether WHO had taken, or intended to take, any steps to discourage that practice and thus protects its Member countries, which might have been misled by deceptive pharmaceutical advertising.

Dr DALY (Tunisia) said that his delegation approved the proposals contained in the report of the Director-General and its appendices. His Government had been concerned by the problem of quality control of drugs for several years and had taken a certain number of measures. One administrative measure, which in his opinion, was extremely important and which had facilitated all the others, was the centralization of import. It had been made the monopoly of a single body, which had all the imported pharmaceutical products at its disposal, and a control laboratory had been set up. Centralization was perhaps not possible in large countries, but in small ones such as his own it facilitated control.

Another administrative measure taken had been the limitation of the number of products in circulation. That work had taken nearly ten years, at the end of which the number of products had been reduced from some 30 000 to 4500. It was considered that a further reduction would be possible. That work had been accomplished not without difficulty, owing to the number of importers and to differences in medical opinion.

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[1] This footnote reads: This paragraph must be deleted if the sale of the drug is not authorized in the exporting country.

The third measure, which was both technical and administrative, had been the laboratory control of quality. At present, control was carried out by the importing body, which was under state supervision. The system was not yet perfect, and the Government intended to set, up its own laboratory to supervise the work of the importing body, which was evolving towards manufacture.

With regard to the suggested certification scheme annexed to the Director-General's report, his delegation did not think it would be possible to go further than adopt it as recommendations under Article 23 of the Constitution.

Dr JOYCE (Ireland) said that the Requirements for Good Practice in Manufacture and Quality Control of Drugs and the Certification Scheme on the Quality of Pharmaceutical Products in International Commerce contained in the Director-General's report were acceptable to his country, which was in the course of preparing draft legislation on those matters. His delegation would agree to both being adopted as recommendations under Article 23 of the Constitution.

Dr AL-AWADI (Kuwait) congratulated the Director-General on his report, which was the result of two years' discussions on drug control procedures. It was an attempt to answer two important questions raised at previous Health Assemblies - one being how to safeguard the consumer from the large number of drugs in international commerce, and the other being how to improve the standards of drug-manufacturing firms. The report actually dealt with the latter aspect. It remained to be seen what could be done to safeguard the consumer, since such protection depended upon the establishment or development of control laboratories on a national or regional basis, with which the Health Assembly, in sub-paragraphs (iii) of its resolution WHA21.37 had requested the Director-General to assist.

As regards Annex 2 to Appendix II of the report - Good Practices in the Manufacture and Quality Control of Drugs - the producing countries, as had already been stated, had requirements stricter than those recommended, and yet some of the consumer countries were still experiencing difficulties with imported products. His delegation was not satisfied with the definition of "drug" given in that annex, which read as follows:

> Drug. Any substance or mixture of substances that is manufactured, sold, offered for sale, or represented for use in (1) the treatment, mitigation, prevention, or diagnosis of disease, an abnormal physical state, or the symptoms thereof in man or animal; or (2) the restoration, correction or modification of organic functions in man or animal.

Why did that definition refer only to "an abnormal physical state", and why did it not cover also an abnormal physiological or mental state:

The proposals in the report were good, but he wondered what the Organization could do to assist in implementing them. Would it be possible for WHO to maintain a list of manufacturing firms?

He noted that the certification scheme could be adopted either as regulations under Article 21 of the Constitution or as recommendations under Article 23, but would like to have some explanation of the difference, in terms of practical application, between the two methods.

Dr GÓMEZ (Ecuador) said that the Director-General's report dealt very clearly with a problem that was complicated by the fact that the interests of commercial firms and exporting countries were involved. The requirements, considered as a general guide, were quite acceptable. The certificate of the manufacturer respecting good practices in manufacture and quality control of drugs received his delegation's entire support. He thought that WHO, when it had the complete list of manufacturers satisfying the requirements of good practices, should publish it and circulate it to Member States.

With regard to the certification of individual batches of drugs, he considered that the batch number should be omitted from the certificate, since, as the delegate of Italy had stated, it would be too much to expect national health authorities to take responsibility for every batch. The certificate should merely state that the drug had been approved by the competent institute and that a visa had been obtained.

He agreed with the delegate of Ethiopia that the footnote to the last clause of that certificate should be deleted, since it did not seem logical for a country to export a drug that could not be sold on the home market. His delegation could approve the certificate, with those two amendments.

Dr EVANG (Norway) said that the delegate of Ethiopia had apparently misunderstood his delegation's suggestion regarding the last sentence of the second certificate (concerning individual batches) in the certification scheme. The suggestion, in fact, had been to strengthen that sentence by introducing into it a few words that would have the effect of putting at the disposal of the importing country in all cases a copy of the text of the permit given, for use in the country concerned.

Moreover, there were legitimate cases when a drug that was exported was not authorized for use in the exporting country. For instance, some countries produced drugs that were excellent but were nevertheless not used in the country because they were for treatment of a disease that was not present in that country.

In general, he agreed with the delegations of importing countries that progress in protecting them from unsatisfactory imported drugs had been slow. The proposals before the Committee represented only a first step towards the adoption of more stringent and binding regulations.

Dr HASAN (Pakistan) said that, since it attained independence, his country had developed its own pharmaceutical industry; a Drug Act had been passed, with supporting legislation, standards had been drawn up, and quality control was being carried out. His country would have no difficulty in complying with the requirements set forth in the Director-General's report. Drug laboratories had been developed near most centres of the pharmaceutical industry, and the drug inspection force in the field had been considerably reinforced.

He understood that a regional seminar on the quality control of drugs was to be held in Pakistan and he was looking forward with interest to its report.

Dr N'DIAYE (Senegal) said that nearly all the drugs and specialties consumed in Senegal were imported. The country had as yet no pharmaceutical industry and the establishment of factories for compounding, packaging, etc. was contemplated. There were no laboratories that could carry out effective control of the products imported. There was a law regulating the entry of such products into the country, but it offered no scientific guarantee. For those reasons, his delegation welcomed the Director-General's report.

His country had confidence in the exporting countries, but insisted that the products imported should have proved their worth in their country of origin. In that connexion, he strongly supported the remarks of the delegate of Ethiopia.

The delegate of Italy had raised the very pertinent matter of packaging products according to the climate of the country in which they were to be used. That was of interest to his country, where difficulties in keeping pharmaceutical products had been experienced owing to the warm climate, but it was to be hoped that more suitable packaging would not result in increased prices.

Professor PENSO (Italy) said that his criticism of the requirements set out in the Director-General's report had been constructive ones. He had wished to make the requirements more stringent, so that they would afford real protection to importing countries. He had wished also to introduce some element of statistics into the quality control of drugs, for the reason that, if a certificate were issued for a drug on the basis of examination of one sample in a lot of, say, one hundred thousand, that certificate would be valueless. He had also requested the introduction of some more precise requirements as to packaging and storage of products intended for export, especially to tropical countries.

The delegate of Ethiopia had raised a very important question that had been answered in part by the delegate of Norway. Italy, for instance, produced drugs for the treatment of schistosomiasis, which did not exist in the country. When such drugs were exported, a visa and an export permit had to be obtained, for which a tax was levied; but it would be stupid to make manufacturers pay for a permit to allow the sale on the domestic market of products for which the country had no use.

The delegate of Ethiopia's remarks on packaging were extremely pertinent. However, to some extent the importing countries were responsible if the packaging was not satisfactory. In some cases, instead of ordering direct from the manufacturer and specifying that the product was for use in a hot and humid country, they ordered from wholesalers who did not specialize in the trade and who then placed an order with the manufacturers, without specifying that the drug was for a tropical country. He invited importing countries to co-operate, in their own interests, by placing all orders direct with the manufacturers.

Dr RAMZI (Syria) said that the Syrian Ministry of Health was organizing, with the help of WHO experts, the work of its quality control laboratory. Legislative and administrative measures to facilitate such control had been taken, including the setting-up of special governmental bodies responsible for import of drugs and the establishment of a technical committee to reduce the number of specialities imported.

Dr MARTÍNEZ (Mexico) said that his delegation accepted without reservations the proposals on the quality control of drugs. Mexico was both an importing and an exporting country and was convinced that the only way of ensuring good quality of drugs was by national control, carried out through properly organized laboratories. It was recognized, however, that for some time certain countries would be unable to set up their own laboratories and the Organization, therefore, should assist in improving national laboratories that would carry out analysis and control for countries wishing to avail themselves of their services.

His delegation considered that the certification scheme should be adopted as recommendations under Article 23 of the Constitution. It would be much more difficult to attain unanimity in the Health Assembly for its adoption as regulations under Article 21 and, even if adopted, it would have only limited application.

The scheme represented a step forward in the quality control of drugs. It provided a procedure that was simple and practical, and he was sure that it would give fruitful results. However, as had already been stated, it should not be considered more than a preliminary step. Drugs in themselves were not harmful, but the publicity concerning them was. He hoped that, during the next stage, WHO would study the possibility of promoting a common stand with the purpose not so much of avoiding the export of drugs of poor quality as of preventing the mental disorientation of the public and the medical profession. The resolution adopted on the present item of the agenda should contain a provision to the effect that WHO should continue its study of the matter.

On the question of the improvement of control laboratories, although his delegation agreed that WHO should assist in the establishment and development of national laboratories that would undertake control work for other countries, it could not agree to any such laboratories eventually forming part of the Organization, because of the budgetary problems involved.

Dr TEOUME-LESSAN (Ethiopia) said that the delegate of Norway, in correcting the misunderstanding that had arisen, had not appeased his apprehensions. The footnote in question stated that the last paragraph of the certificate had to be deleted if the sale of the drug was not authorized in the exporting country; in his opinion, there was a considerable difference between a drug not being authorized and not being used. All drugs exported should be authorized, whether they were used in the country of origin or not. One way of doing that might perhaps be to make it compulsory for manufacturers, in order to put a drug in circulation, to obtain a visa, which would be certified by the national health administration, and a copy of which could be obtained by the importing country for its first shipment only.

Dr N'DIAYE (Senegal), referring to what had been said by the delegates of Italy and Norway concerning the export of drugs not authorized in the country of origin, said that naturally his country permitted the import of drugs against diseases that were prevalent in Senegal but unknown in countries producing the drugs. However, in order for a visa for such drugs to be obtained, they had to be introduced by a physician holding an official position in a university.

His delegation agreed with what the delegate of Italy had said regarding packaging but pointed out that suitable packaging often increased the price of the drug. Economically weak countries, such as his own, were anxious that proper packaging should not make the price of the drug prohibitive.

Dr FAKHRO (Bahrain) supported the delegate of Ethiopia in his view that the certification scheme should be adopted as regulations under Article 21 of the Constitution.

Every year the authorities having the responsibility for buying drugs were faced with the difficulty of trying to decide which manufacturers were reputable and whether one country offered better guarantees of quality than another. Naturally, they were wary, because unfortunate accidents had occurred with certain imported drugs, resulting in substantial financial loss.

The other problem facing importing countries was the emergence of new pharmaceutical companies in some of the developing countries. The importing countries found it difficult to buy from them, because they were unknown, but nevertheless wished to encourage them, especially if they manufactured for countries with similar climatic conditions and disease patterns.

In his view, the proposals under discussion, if they were really implemented, and not merely recommended, but be a first step in the right direction.

Professor VALDIVIESO (Chile) thought that WHO's efforts to ensure quality control and to introduce a certification scheme were most praiseworthy but should be considered only as a first step in a field in which much needed to be done. Many manufacturers had commendably tried to maintain a high standard of quality, but were doing so more in the interests of the firm's reputation and profits, and probably at greater cost to the consumer. Certification of quality should be based on a drug's primary ingredients and made compulsory as soon as possible. Far more drugs than were necessary for therapeutic purposes were on sale in the world, and since many of those drugs were no more than placebos to be prescribed to

hypochondriacs, they should not be so highly priced. Moreover, many drugs of the same composition were on sale under different brand names, and it was not for physicians to state whether one drug was better than another. For that reason, a permanent committee within WHO, to establish criteria for the therapeutic effectiveness of drugs, would be highly desirable.

A recent survey by the national Academy of Science of the United States showed that some manufacturers made exaggerated claims for the efficacy of their products. Of 349 antibiotic preparations tested, some ninety had been found to be a combination of various antibiotics, the combined action of which was nil, or at most no more than a single one of the components, while the others merely served to increase the price of the finished product. In spite of opposition from physicians and the Food and Drug Administration, such products continued to be available. Chile itself had set up a special commission to inquire into the efficacy of drugs and their cost. That type of body required the support of an international authority such as WHO, which could serve as a court of appeal in doubtful cases.

Dr NOORDIN (Malaysia) considered that a minimum standard should be set in the requirements for good manufacturing practice. If a certification scheme were adopted as regulations under Article 21 of the Constitution, drug manufacturers would no doubt require a period of time in which to conform with those regulations, and this might place an additional burden on local health authorities. Furthermore, since the wheels of justice moved slowly at all times, amendments to existing legislation might take as long as three to four years. His delegation was therefore in favour of the requirements being adopted as recommendations under Article 23 of the Constitution. The situation might be reviewed at a later stage, when the advisability of adopting regulations could be given further consideration.

Dr AMMUNDSEN (Denmark), referring to remarks made on drugs whose sale was not authorized in the exporting country, pointed out that in many such countries, including her own, abuse and misuse of drugs was a major public health problem. It had therefore been found necessary to set a limit inside the country on the sale of a large number of drugs having similar effects. But that in no way reflected on either the substance or the purity of such drugs, and no restrictions were therefore placed on their export to other countries.

Dr HENRY (Trinidad and Tobago) said that his country was an importer of drugs and had no machinery to distinguish between one drug and another. According to existing legislation, wholesalers were not permitted to import a drug which did not carry a certificate saying that it had been manufactured in accordance with good manufacturing practice. His delegation therefore fully supported the Director-General's recommendations.

Dr MONDET (Argentina) said that WHO had devoted some twenty years to malaria eradication. And yet, in his country, the plethora of drugs available was as serious as a problem to health authorities as was malaria, and absorbed about one-third of the health budget. His delegation therefore considered the quality control of drugs to be of major importance. He heartily endorsed the statement made by the delegate of Ethiopia, and supported the suggestion put forward by the delegate of Chile for an over-riding authority to be set up by WHO.

Referring to the comment of the delegate of Denmark, he would point out that 22 000 drugs had been banned in Argentina but that 400 control laboratories had been necessary for that purpose, a figure which was excessively high for a country with a population of 23 million, fifty-two per cent. of those drugs were manufactured in Argentina, and the remainder was manufactured locally under licence from foreign manufacturers.

He hoped that certification by WHO, if instituted, would be an effective instrument and not merely a bureaucratic piece of paper. The establishment of inter-regional control laboratories to which several countries could send samples was highly desirable, since experience in Argentina showed that the expense of maintaining the requisite number of such laboratories was a heavy burden for a single country.

Dr TATOČENKO (Union of Soviet Socialist Republics) said that in the USSR the principles for the control of pharmaceutical preparations provided first of all for governmental control of all drugs, whether manufactured for domestic use or for export. Such control ensured equally high standards of quality of all drugs. For that reason the adoption of the proposed certification scheme would not constitute any difficulty for the USSR. There were in his view a number of inaccuracies in the proposed certification scheme, which should be eliminated, considering that it represented an important legal document; however, he did not think that it would be advisable to do so at the present stage.

The Soviet delegation would support the proposal for adoption of the Director-General's proposals as recommendations in accordance with Article 23, provided that the scheme was revised after a suitable period of time, when Member countries had adopted appropriate legislation and when the regulations had already been actually tried out.

Dr BRZEZINSKI (Poland) said that, since most of the delegates who had spoken appeared to regard as premature the adoption of the proposals as regulations under Article 21 of the Constitution, his own delegation, in order to help the Committee to reach a conclusion speedily, would now be prepared to support their adoption as recommendations under Article 23.

Dr TABBAA (Saudi Arabia) said that the problem of quality control of drugs and their prices might be solved if each importing country, of which Saudi Arabia was one, were to set up control laboratories empowered to ban the sale of doubtful or excessively expensive drugs.

Dr HALBACH, Director, Division of Pharmacology and Toxicology, said that, in his attempt to answer the various points raised by delegations, he would group them according to content.

The delegate of the United Kingdom had questioned the meaning of the expression "a given drug" in the explanatory portion of Section B of Appendix III. Possible confusion might perhaps be eliminated if the paragraph were to begin with the words "In appropriate cases, the responsible public health authorities...". If this addition were acceptable to the Committee, the third paragraph in Section B would consequently have to be reworded as follows: "In the case of a drug for which batch certification was appropriate and which had already received an authorization...".

The establishment of national control laboratories had been discussed in several Health Assemblies and WHO was aware of the difficulties involved. The possibility of inter-regional laboratories was being studied at the present time. One such laboratory had been started in Panama for the countries of Central America and one which would have special facilities for training was under consideration for Montevideo. In that connexion WHO was grateful to the Government of India for having offered to make available the central control laboratory at Calcutta for regional control. Thanks were also due to the Government of Hungary for having offered training facilities.

It was clear that the Director-General's recommendations should be regarded as minimum requirements liable to revision from time to time.

The delegates of Italy and Czechoslovakia had mentioned the need for more specifications on sterile products to be included in the International Pharmacopoeia; and the delegate of Australia had asked that such procedures should be presented in a special code of practices. Those suggestions had been duly noted but would, he believed at this stage, be outside the scope of good manufacturing practices.

The point raised by the delegation of Belgium concerning Section 10 of Appendix II was perhaps more clear in the English version, which stated in the first paragraph the need for a quality control "department that is autonomous..." and which would be responsible for seeing that the necessary controls were carried out; and went on in the next paragraph to specify the role of the quality control "laboratory" as an instrument to do the analytical work.

He was grateful to the delegate of Japan for having stressed the need for good will in the interpretation of the recommendations, which was indeed desirable in order to achieve the desired goal.

The date of expiry for the use of a drug was a matter for mutual agreement between the manufacturer and the consumer, and depended not only on the composition of the drug but also on local climatic conditions. Keeping records was also a national responsibility.

In reply to the delegate of Kuwait, he said that effective supervision by WHO would have to be based on treaty regulations. In that connexion he recalled the Narcotics Control treaties for which the International Narcotics Control Board acted as watchdog by supervising the legal international trade in narcotics. It also kept a record of firms authorized to produce narcotic drugs in various countries.

With regard to the point raised by the delegate of Italy on the use of the word "batch", he would refer him to the English text, which stated that the essence of a manufacturing batch was homogeneity during "a given cycle of manufacture" i.e., with no specification of the length of such cycles.

With regard to the discrepancies between national pharmacopoeias and the International Pharmacopoeia, it was to be hoped that, with improved communications between scientists and intensified international trade, those discrepancies would in time disappear.

The question of price control was a delicate one. It was to be expected that, as more national health schemes developed with free or low-cost distribution of drugs, the question of their prices would also be gone into.

Many pertinent remarks had been made on the therapeutic safety and efficacy of drugs - which was not a pharmaceutical matter. In that field, the Division of Pharmacology and Toxicology had a continuing programme including, inter alia, the monitoring of drugs and the formulation of principles for the experimental and clinical evaluation of the safety and efficacy of drugs. In connexion with the latter, ethical problems had been dealt with in several WHO scientific group reports to the extent possible, though delegates had expressed the wish that WHO could have been more explicit on that matter. In that connexion the Council for International Organizations of Medical Science had convened a round-table conference in 1967, at which both WHO and UNESCO had been represented. It had been the unanimous conclusion of that conference that it was neither advisable nor feasible to formulate detailed ethical guidelines applicable to all foreseeable circumstances. On the other hand the conference had emphasized that in the case of a difficult decision, a "judgement of peers" should be sought.

The question of drug consumption raised by the delegate of Chile had preoccupied WHO for some time. The Regional Office for Europe had sponsored a study on how to measure drug consumption, which would be followed by a seminar later in 1969. The ultimate purpose was to determine whether present consumption was reasonable or beyond actual therapeutic needs, and whether it should therefore be reduced.

A number of delegates had stressed the need for some kind of permanent body in WHO to pass judgment on the therapeutic safety and efficacy of drugs. Action of this nature at present being taken in the United States, under the sponsorship of the National Research Council, indicated that what was feasible at the national level and could therefore also be considered at international level. That question however needed a great deal of study and would certainly have important financial implications. Until such a body could be set up, the best course to follow was to improve available information and its dissemination. It was to be hoped that WHO's efforts to make clinical pharmacology the discipline responsible for evaluating drugs would further that aim.

The amendments proposed by the delegates of Ethiopia and Norway to the wording of the certificate in Appendix III, section B2, would require a corrigendum to document A22/P&B/12.

Dr BERNARD, Assistant Director-General, Secretary, said that he would make a few comments complementing those of Dr Halbach.

The present discussion, like those which had taken place at the two previous Health Assemblies, had revealed the complexity of the problem and the importance and urgency which delegations attached to its solution. It was the earnest desire of the Director-General that the Organization should play a decisive role in this regard. Indeed, the preparation of the documents now before the Committee had taken almost two years.

Those documents were still by no means perfect. Some members of the Committee, such as the delegate of Italy, had expressed the view that the proposed requirements could be made more stringent; others - so great were the differences between countries - felt that, even as they stood, they would be difficult to apply. The Director-General had had to take into account a whole range of situations, and the proposals presented were, in his opinion, the most generally applicable. Those proposals could be modified on some points but a broader revision, obviously, was not practicable at the Health Assembly.

The Committee was called upon to decide whether the requirements for good manufacturing practices and the proposed certification scheme should be considered for adoption as regulations under Article 21 of the Constitution or as recommendations under Article 23. Article 21 empowered the Health Assembly to adopt regulations concerning inter alia the safety and purity of pharmaceutical drugs. Article 22 stated that any regulations adopted pursuant to Article 21 would come into force for all Members after due notice had been given of their adoption by the Health Assembly, except for such Members as might notify the Director-General of rejection or reservations within the period stated in the notice.

In that connexion he drew attention to Rule 10 of the Rules of Procedure, under which the Director-General was required to consult the United Nations and the specialized agencies, as well as Member States, on international conventions or agreements or international regulations proposed for adoption which might affect the activities of those organizations; and to bring the comments of those organizations to the attention of the Health Assembly together with the comments received from governments. If the Health Assembly were to decide on the application of Article 21, a period of time would be necessary to conform with the provisions. The procedure under Article 23 was simpler and speedier, as the Health Assembly had the authority to make recommendations to Members on any matter within the competence of the Organization, and this applied to any resolution which the Committee might adopt on quality control. But one procedure did not rule out the other. The Health Assembly could at one of its sessions adopt recommendations and at another, decide to modify them, or alternatively adopt the procedure of Article 21. It should be borne in mind that whatever solution was selected, the effectiveness of quality control would largely depend on measures taken at the national level to conform with the regulations or recommendations adopted.

The suggestions concerning further steps which could be taken by WHO, e.g. as regards the usefulness of drugs had been noted and would be studied. The technical, ethical and legal problems involved needed careful consideration and the Director-General would give these his full attention. On the other hand, WHO would continue to help countries to develop their control facilities. As stated by Dr Halbach, seminars and training courses had been sponsored

by WHO, and efforts were being made, in which the United Nations Development Programme was expected to participate, to develop control laboratories on a regional basis.

Dr SIDERIUS (Netherlands) said that, if the regulations were to be implemented, many countries would have to amend their legislation. The harmonization of national legislations would take some time, as was shown by the experiences of the Common Market. His delegation was therefore in favour of the proposals being adopted as recommendations under Article 23 of the Constitution. In the meantime the Director-General might be asked to submit a report to the Twenty-third World Health Assembly on improvements to the requirements in the certification scheme which he might consider necessary, and on ways and means of implementing the certification scheme. It was his intention to submit a draft resolution in that sense duly sponsored by other delegations, at a later stage.

Dr STRALAU (Federal Republic of Germany) said that, in the opinion of his delegation, it would be preferable to adopt the proposals as recommendations and, after a suitable lapse of time and in the light of experience gained, to consider their adoption as regulations.

Mr HAILE GIORGIS (Ethiopia) said that, although he had noted the remarks of the delegate of Denmark, his delegation was not satisfied with the wording of the last paragraph of Appendix III, and thought that it should be rewritten so that in cases where drugs were not authorized for the domestic market of the country in question, reasons for that decision should be given.

Professor PENSO (Italy) said that his delegation was in favour of adopting the proposals as recommendations. He reminded the Secretariat of the questions he had raised regarding the number of samples on which the control should be carried out, and the packaging of drugs exported to tropical regions, these being matters to which he attached great importance.

The SECRETARY said that the draft resolution which the delegate of the Netherlands would shortly submit would, if he understood correctly, refer to the annexes which should be attached to it, namely, annexes II and III of the Director-General's report. The Secretariat proposed to get in touch with all delegations who had suggested amendments in order to see what modifications could be incorporated in the annexes. The Committee might revert to the matter when it considered the proposed resolution.

The CHAIRMAN, concurring in the Secretary's suggestion, said that the Committee would resume the present discussion at a later stage.

The meeting rose at 12.35 p.m.