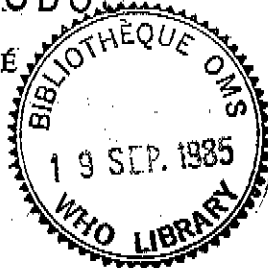




CONFERENCE OF EXPERTS ON THE  
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THE ROLE OF WHO IN THE TRANSFER AND DISSEMINATION OF INFORMATION ON  
DRUG QUALITY, SAFETY AND EFFICACY

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THE ROLE OF WHO IN THE TRANSFER AND DISSEMINATION OF INFORMATION ON  
DRUG QUALITY, SAFETY AND EFFICACY

WHO (AND ITS CONSTITUTIONAL MANDATE)

1. Within the terms of its constitution WHO acts as the directing and co-ordinating authority on international health work. Among its functions it is required to assist governments, upon request, in strengthening health services, and to provide information, counsel and assistance in the field of health. Virtually from its inception in 1948, the governing bodies of the Organization identified drug regulation and control as a field in which these responsibilities could be applied to useful effect. Over the years, and particularly after the thalidomide tragedy in the early 1960s, many formal resolutions have been adopted by the World Health Assembly which call for the establishment of international norms, exchange of information, and multilateral collaboration to support the drug regulatory apparatus of national governments.
2. The key resolutions are set out in the Annex and subsequent sections of this paper describe their implementation. However, in order to define the task of the Organization in a perspective that depicts contemporary concerns it is necessary briefly to review how current trends in drug control and drug development determine the structure of national markets.

THE STRUCTURE AND CONTROL OF NATIONAL DRUG MARKETS

The administrative control of pharmaceutical products

3. Contemporary approaches to the control of biological and pharmaceutical products have evolved in highly developed countries over more than fifty years. The course of the evolutionary path has been determined by the fact that the beneficial, therapeutic effects of marketed drugs are, in general, more readily demonstrable than their attendant hazards. Whereas it is incontestable that innovative development of new products has transformed the practice of medicine within the lifespan of a single generation of clinicians, it has become manifest that drugs are biologically active substances with an innate potential to exert adverse as well as beneficial effects at pharmacological dosage, and that therapeutic progress is inherently associated with risk. Evaluation of the costs, benefits, and hazards of drug treatment has consequently assumed a complexity that was formerly unappreciated.
4. As yet, the prediction, and even the detection, of some serious drug-related effects still presents a formidable technical challenge. Historically, drug control has tended to adjust empirically in response to unanticipated and dramatic incidents of drug-induced injury. The need for further adjustment will doubtless become apparent, but already the spectrum of controls applied to the research-based pharmaceutical industry is singularly comprehensive.
5. The greatest emphasis has been accorded to the need for exhaustive technical assessment of each new product prior to marketing. However, adequate assurance of quality, efficacy and safety is contingent on many other safeguards including the implementation of good manufacturing practices, efficient distribution and storage, informed use of products, and systematic collation and analysis of experience with marketed drugs. In highly developed countries controls are consequently exercised over manufacture and packaging, labelling and promotion, distribution, sale and use, and the reporting of post-marketing experience.

6. In turn, this requires not only a central agency to determine the conditions under which each product is accepted for registration, to oversee advertising and promotional practices, and to ensure adequate post-marketing surveillance, but also a highly educated cadre of doctors, nurses, and pharmacists qualified to prescribe and dispense the products with understanding and discretion, and a body of inspectors and chemical analysts to assure the quality of products throughout the distribution chain. The cost of the required administrative apparatus is burdensome even to the most affluent of countries and it is reflected in the prices of pharmaceutical products whether they are destined for domestic use or for export. Thus developing countries support an infrastructure of control, as well as a research base, in exporting countries that they are unable, for lack of resources, to institute themselves.

7. However, the need for drugs is no more forcefully apparent than in the developing world. To deny populations access to the benefits of medical technology for want of administrative capacity is inadmissible in concept. The problem has to be relieved by ensuring that national approaches to drug control and the provision of associated information to the profession and the public are optimally adapted to local circumstances. The extent to which success can be achieved is contingent upon the support offered by governments of exporting countries and by the manufacturers. If the technical competence of the pharmaceutical industry can be relied upon to advance exemplary promotional and marketing standards and to foster effective administration of drug control in developing countries, and not to exploit its weaknesses, progress will be greatly facilitated.

8. Meanwhile, governments in exporting countries are in a position to ameliorate the situation. They can ensure that their statutory provisions and regulations provide for adequate control of exported products without impeding the delivery or development of drugs legitimately needed elsewhere for which there is no domestic market. They can also assure the effective operation and further evolution of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce<sup>(1)</sup>, with a view to providing importing countries not only with an attestation of the quality of the product but also with authenticated information on its safe and effective use.

9. Finally, a complementary role exists for WHO in promoting contact and understanding between national drug regulatory authorities; in effecting the exchange of objective, unbiased technical information selected and presented in a manner that sustains countries in their quest for self-sufficiency; and in fostering and coordinating therapeutic research on an international basis, particularly within the developing world.

#### The technical assessment of pharmaceutical products

10. Whereas the WHO Model List of Essential Drugs contains less than 250 pharmaceutical substances, the number included in registered pharmaceutical products in some countries exceeds 3000. The total number of products available on these national markets is many times greater since most of these substances are offered in a variety of formulations - either singly or in combination - both as branded and as generic items. In many countries the number is further augmented by many herbal and other traditional remedies sold either as proprietary, labelled products or as extemporaneously dispensed concoctions. Traditional and unorthodox

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(1) WHO Official Records, No. 226, 1975. (Offprint - Good Practices in the Manufacture and Quality Control of Drugs and Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce).

systems of medicine retain recognition and considerable patronage in many highly developed countries. In the rural areas of some developing countries it is the traditional healers that provide the most readily available resource for the development of primary health care services. Also at issue, however, is an extensive and highly remunerative illicit trade in fraudulent or spurious medicines which is not confined solely to countries with weak regulatory systems. Exploitation of the law by deliberate evasion has been attempted within the most sophisticated legal systems.

11. Comprehensive national licensing systems that require marketed drug products to meet independently determined standards of quality, efficacy, and safety have been instituted only within the past two decades and priority has consistently been accorded to the assessment of newly developed products. Few national regulatory authorities have, as yet, reviewed every product currently available on their domestic market, but many are committed to do so within the next few years. The recent demonstration that a substance as widely contained in herbal remedies as aristolochic acid possesses a potent carcinogenic potential has disposed of the complacent assumption that prolonged use is, of itself, sufficient to establish the safety of a medicinal product.

12. Even the assessment of newly-developed products is still evolving. After the thalidomide disaster expectations were raised that the safety of drugs in man might reliably be predicted from animal models. Subsequent experience has demonstrated the inadequacy of this hypothesis. Adverse drug-induced effects are protean in their manifestations and serious complications of therapy have occurred, such as the practolol syndrome, that cannot be reproduced, even retrospectively, in animal models.

13. Analogous difficulties arise in assessing the efficacy of drugs intended for long-term administration in chronic disease. The development of products used in such commonly occurring conditions as ischaemic heart disease, hypertension, hyperlipidaemias, diabetes and rheumatoid arthritis, remains commercially viable only while the prospect exists of introducing them into routine use after a relatively short period of clinical assessment. Ultimate demonstration of their clinical value and of the possible risks of prolonged exposure can only devolve from observation of large populations of treated patients over many years.

14. The rational use of drugs evolves from a profound and secure understanding of their clinical performance. At present, much of this knowledge is superficial and incomplete. Whereas the deficiencies of the situation are manifest, perceptions of how to proceed have developed slowly. However, the emergence of epidemiologically-based approaches to the investigation of drug performance seems destined to create a shift of emphasis in drug assessment to a more balanced combination of pre-marketing evaluation and post-marketing surveillance.

15. The resources and organizational effort required to undertake such studies are daunting. Nonetheless, the development of computerized data bases of prescribing information on the one hand, and of patients' hospital records on the other, renders feasible the collection and analysis of more information on drug performance than has previously been possible. Governments, because of their general responsibility for their health services and pharmaceutical companies, because of their responsibility and liability for the safety of their products, have a direct interest in fostering such studies, and in exploring their logistic, financial and ethical implications.

16. Regardless of the approaches ultimately adopted, the efficiency with which the work is executed and the extent to which it influences the use of drugs globally will depend greatly on international coordination of efforts and timely exchange of information.

Economic factors as determinants of drug development and use

17. The concept of the rational use of drugs implies a need for socially oriented approaches to new drug development. The commercially-determined and competitive structure of the research-based pharmaceutical industry require research expenditure to be determined by the prospective return on investment as well as by medical need. The potential demand for a product tends to become an overriding factor in research planning, and the development of a drug intended to capture a share of an established market may hold more attraction than a bolder venture into therapeutic innovation.<sup>(1)</sup> The problem is compounded by other perceived disincentives to innovative research: the lack of secure scientific leads for new forms of therapy; rising costs of drug development at a time of general economic recession; stringent price controls imposed within the public sector; and short effective periods of patent protection coupled with selective encouragement of generic manufacture and prescribing.

18. The consequential pattern of drug development, with its emphasis on treatment and prevention of the common diseases of affluent communities, draws criticism as being ill-adapted to global therapeutic needs. Thus the Sixth Cumulative List of International Nonproprietary Names for Pharmaceutical Substances published by WHO in 1982,<sup>(2)</sup> shows that no fewer than 78 benzodiazepines and closely related compounds had been taken to an advanced stage of development. The inclusion in the list of 67 beta-adrenergic blocking agents, 53 non-steroidal anti-inflammatory agents of the ibufenac and ibuprofen groups, 57 penicillins and 42 cephalosporins offers revealing insight into the prevalence of repetitive research patterns. The thesis that molecular manipulation not infrequently offers dividends in terms of improved therapeutic performance is a valid but vulnerable argument. Large numbers of essentially interchangeable marketed products render effective therapeutic comparison impracticable. They create a situation in which therapeutic choice is determined by advertising pressure rather than objective evidence and, in the longer term, they threaten to frustrate evaluation of therapeutic performance.

19. Nevertheless, the recent introduction of drugs of uncontested value such as aciclovir, ciclosporin and clavulanic acid belies much pessimistic prognostication about the pace of therapeutic progress. Moreover, the ongoing clinical development of drugs such as ivermectin, mefloquine and praziquantel provides evidence of the commitment of some research-based companies to the advancement of tropical medicine. However, the gestation period for a new drug from the time of its first synthesis to its release for general clinical use commonly extends over a period of eight to twelve years. The full influence of prevailing economic pressures on the process may thus not become generally evident for several years. One disturbing trend is, nonetheless, already apparent: in recent years several leading manufacturers of vaccines have opted to withdraw from the field pleading reduced profitability and sharply increased liability for product-induced injury. At a time when the emergence of AIDS and legionnaire's disease provides a salutary reminder that infectious disease will never remain a static target; when vaccination holds encouraging prospect in the management of parasitic, as well as bacterial and viral infections; and when bioengineering techniques offer important new approaches to vaccine manufacture, this is an ominous portent.

20. Whether action is now required to redress these trends is an issue that is critical to the future of drug development. Some governments are either

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(1) Trends and Prospects in Drug Research and Development. XIth CIOMS Round Table Conference, Geneva, 8-9 December 1977, CIOMS, Geneva, 1978.

(2) International Nonproprietary Names (INN) for Pharmaceutical Substances. Cumulative List No. 6, WHO, Geneva, 1982.

contemplating, or have already introduced, measures that offer a degree of protection or inducement to companies prepared to address societal responsibilities. Possible prolongation of the period of patent protection for new drugs is widely debated. National compensation funds or mutual insurance schemes funded from levies on companies and administered under the aegis of the state, have been set up in a few countries to settle claims arising from drug-induced injury. Several governments have also provided direct financial incentives to stimulate the development and production of drugs for rare diseases that would otherwise offer no commercial attraction.

21. At global level the call to increase the responsiveness of pharmaceutical research to contemporary needs brings the problems of the developing world into sharp relief. The prevalence of malaria has probably doubled over the past decade as both the parasites and the vectors have developed resistance against the available drugs and insecticides. No lasting amelioration of the situation can be expected until new approaches to its containment are available. Other conditions such as measles and diarrhoeal diseases, which rarely result in death in affluent countries, remain major causes of infant mortality in developing countries. Even so, national populations are increasing in these countries, as elsewhere, at a rate that is imposing an intolerable strain on economic resources already extended to breaking point.

22. It is against this background that WHO has initiated major research programmes in the fields of tropical and diarrhoeal disease and in human reproduction,<sup>(1-3)</sup> in the expectation that much may be done on budgets that are modest by commercial standards to rationalize existing therapy and even to develop new therapeutic tools, both by coordinating and building upon resources that already exist within the academic world and industry and by judicious financial support of promising research.

23. Having established these programmes, WHO has become involved at first hand in the process of drug development. It now provides an important focus for technical collaboration between developed and developing countries in a complex multidisciplinary technical operation, offering a stimulus and a challenge to both academic departments and the pharmaceutical industry to address the health problems of the developing world through innovative research and reappraisal of current therapeutic practice.

24. Coincidentally with the early development of these research programmes, the World Health Assembly endorsed, in 1975, a report of the Director-General<sup>(4)</sup> pointing to the need for comprehensive centrally-directed drug policies within developing countries as a prerequisite to satisfying the basic health needs of under-served populations. Reference was made to experience gained in countries where schemes of basic or essential drugs<sup>(5)</sup> had been implemented and WHO was called upon to advise Member States on the selection and procurement, at reasonable

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(1) Special Programme for Research and Training in Tropical Diseases. Sixth Programme Report, 1 January 1983-31 December 1984. UNDP/World Bank/WHO, Geneva.

(2) Programme for Control of Diarrhoeal Diseases. Fourth Programme Report 1983-1984, WHO, Geneva.

(3) Special Programme of Research Development and Research Training in Human Reproduction. 13th Annual Report, December 1984, WHO, Geneva.

(4) WHO Official Records, No. 226, 1975, Annex 13, pp 96-110.

(5) WHO Technical Report Series, No. 685, 1983. The use of essential drugs: report of a WHO Expert Committee).

cost, of essential drugs of established quality meeting their national health needs. It remains the responsibility of governments to determine the extent to which selective procurement policies are implemented and to adapt the WHO Model List of Essential Drugs to specific local needs and policies. Wide contrasts in national circumstances render it impossible to draw up a drug list of general applicability and acceptability.

25. Since the essential drugs concept was first elaborated it has gained wide recognition. It has provided a rational yet flexible basis for systematizing drug procurement and use at national level and for establishing drug needs at specific points, or for specific purposes, within the health care system. Indeed, it offers substantial advantage in terms of economy and efficiency in many settings. Even in affluent countries, where large numbers of drugs are readily available, the compilation of hospital formularies - often as a result of spontaneous institutional initiatives - has long found favour as a means of reducing prescribing costs and simplifying dispensing practices. Analogous initiatives by professional organizations have resulted in the publication of various quasi-official national formularies and other reference sources intended to promote efficient and cost-effective prescribing among doctors at large.

26. Whether it is primarily a function of government or of professional self-discipline to constrain prescribing costs is a political issue. Many national drug regulatory authorities are required, in their licensing function, to confine their attention to matters of quality, safety and efficacy. Others are empowered also to consider, as a condition of registration, whether a product meets a perceived medical need. Nonetheless, public expenditure on drugs is everywhere identified as an important and potentially negotiable element in the overall cost of public health services. Increasingly, governments reveal a determination to reduce drug costs, not only through direct price controls and selective registration but also through selective reimbursement of prescription costs, compulsory generic licensing, or promotion of generic prescribing and dispensing. The dilemma that emerges for all governments is to reduce public expenditure on drugs as far as is practicable without eroding the standards of the health services they provide and yet assuring a socially-productive investment in new drug development.

#### The exportation of pharmaceutical products

27. A majority of Member States import large quantities of both finished pharmaceutical products and bulk substances. Many do not, however, possess the technical and financial resources to undertake a comprehensive and independent assessment of the drugs on which they depend.

28. The major drug exporting countries have adopted divergent positions in their legislative responses to this situation. One approach, which derives from the doctrine of state responsibility and the concept of international minimum standards, is to disallow the export of pharmaceutical products that have not been approved for domestic sale. The other, based upon the principle of comity of nations, is to accept the right of each sovereign to decide what medicines it will import having regard to its own assessment of its particular health needs, the diseases and health related characteristics of its population, the nature of its health care delivery systems, the availability of treatment and its own evaluation of benefits and risks.

29. Patterns of disease and the structure of medical care vary within wide limits from country to country. The balance of risk and benefit in using medicines varies correspondingly. The unacceptable burden of disease in many developing countries results from infections that either do not occur in developed countries or that are

effectively contained where highly evolved medical services are available. In consequence, the administrations of many exporting countries consider that they are inadequately informed to make value judgements on the safety and efficacy of medicinal products that are to be used under circumstances, and for conditions, that are alien to their experience.

30. Developing countries, nonetheless, rely upon drug exporting countries to develop legislative and administrative mechanisms that will effectively block the shipment of unacceptable or substandard products. Such provisions should neither impede the movement of valuable medicines where they are most urgently needed, nor provide a disincentive to the development of new drugs for diseases endemic exclusively in developing countries.

31. Both these principles are embodied in a resolution of the UN General Assembly (GA37/137) adopted in 1982 on problems of international trade in all hazardous products, with particular reference to pharmaceuticals. It records that products either banned or withdrawn on grounds of human health and safety within the country of origin have subsequently remained available in export markets, and that newly-developed products intended - but not yet approved - for domestic use have been released prematurely for export.

32. The resolution also acknowledges that a product unauthorized in one country may subserve a legitimate need elsewhere. It therefore calls upon governments to prevent the exportation of any pharmaceutical product not authorized for domestic use, save at the specific request of the competent authority within the importing country or when evidence is available that its use is officially sanctioned within the importing country. In either case governments are requested to ensure that the supporting information and labelling are adequate to provide for the safe and effective use of the product. To assist importing countries to identify imports that present undue or exceptional hazards the General Assembly called for the publication and regular updating of a consolidated list of products that have been banned, severely restricted or not approved in the country of origin.<sup>(1)</sup>

33. This listing complements the Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, which was established by WHO in 1975. The scheme provides an administrative mechanism whereby regulatory authorities in developing countries may obtain, on request, details of the regulatory status of any imported product in the country of origin. It requires the competent authority of the country of manufacture to certify pharmaceutical products intended for export by supplying, at the request of the importing country, assurances that:

- the exporting country has approved the product for domestic sale, or if not, why not.
- the manufacturing premises are subject to regular inspection and conform with standards set by WHO in its principles of good manufacturing practice.

#### International exchange of information

34. The complexity of the international drug market and the urgency with which messages sometimes need to be conveyed leave no doubt about the need to develop efficient international channels of communication between national drug regulatory authorities.

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(1) Consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by governments. UN, New York, 30 December 1983.

35. The development of such channels also needs to take account of the existence of profound differences both in the structure of national drug markets, and in the circumstances in which drugs are used. A decision taken in one country may not be immediately applicable elsewhere.

36. Efforts to assure the safe and effective use of drugs extend resources even in the most affluent societies. Nonetheless, they have a place in every community, regardless of its resources and cultural background. In every case the need for rational usage demands that access to appropriate drugs be carefully planned and controlled. In the longer term it demands the development of therapies and dosage forms specifically for use in circumstances where skilled care is at a premium. Depot preparations such as injectable contraceptives, drugs intended for intermittent administration such as praziquantel and repletion doses of retinol and, most importantly, vaccines that confer prolonged immunity to endemic disease are effective not only by virtue of their therapeutic activity but also because the dosage regimens allow for efficient delivery.

37. For the most part, however, developing countries are constrained to use products that have been designed for use within totally different systems of medical care. In such circumstances the process of drug control should embrace not only consideration of evidence generated elsewhere - and most frequently in highly developed countries - on the performance of candidate drugs, but evidence of their relevance to health care within the national context. In some developing countries the concept of prescription control may apply only to hospitals and similar institutions. The rational use of drugs in other settings, and particularly in primary health care, then involves balancing the need for access to therapy against the possibility of misuse and abuse. The many local variables provide for many different national solutions.

38. International systems of exchange of information relieve regulatory authorities in developing countries of the need to undertake fully independent assessments of the drugs registered under their aegis. They are thus allowed to focus their attention on the acceptability of products within the prevailing health care infrastructure. The extent to which WHO can facilitate the task of national authorities in their drug selection policies and in the generation of supporting information is developed further in subsequent sections of this paper.

39. No mechanism for international exchange of regulatory information can operate effectively, however, where there is no indigenous system of drug registration. Many developing countries have yet to create such a system. This may have been impracticable in the past, but advances in information science in recent years have yielded data storage and retrieval techniques that bring effective data management within the reach of virtually every country. International dissemination of technical information needs to be complemented by the development of information systems that can be readily adapted to the registration requirements of every national authority.

40. The purpose of central administration is to serve an effective peripheral infrastructure. This demands not only a flow of appropriate information to drug prescribers and the public but also the carefully planned, assured and controlled delivery of appropriate drugs at every level of the health-care system. In any situation, rational use of drugs is contingent on effective administration of health services and effective education of health care providers.

#### THE NORMATIVE FUNCTIONS OF WHO

##### Terms of reference

41. The primary responsibility for drug control, including the licensing of marketed products, the determination of the claims that may be made for them, and

the conditions of distribution and sale, lies within the competence of national authorities. Although these decisions are primarily technical in nature, the foregoing sections show that they are also influenced by administrative, economic and political factors.

42. Nonetheless, trade in drugs is internationally structured and the same basic criteria regarding quality, safety and efficacy are recognized throughout the world. It follows that, if common standards and methods of technical assessment can be developed, much will be gained in mutual understanding between regulatory authorities and in the efficiency of the regulatory process. Drug assessment, however, remains an essentially empirical exercise: although internationally applicable technical guidelines for the evaluation of the safety and efficacy of drugs have been elaborated from time to time under the auspices of WHO,<sup>(1)</sup> matters of detail are determined by national preference and divergences of view are inevitable. National authorities, moreover, do not always agree in their precepts or in their interpretation of the evidence. These differences have profound consequences. They have impeded attempts at harmonization and unification of regulatory procedures even among closely associated trading partners.

43. Not all the early ambitions of the World Health Assembly to develop international standards in this technically complex field have proved practicable, but several of WHO's related informational activities remain normative in concept. Their objectives are diverse: they facilitate international communication in drug control, and in medicine generally, through the development of common systems of nomenclature; they establish globally recognized standards of quality for pharmaceutical products; and they create internationally accepted guidelines for therapeutic research in human subjects.

44. Thus, the Organization assigns internationally recognized generic names (or International Nonproprietary Names) to drug substances; it has developed, within the context of the International Drug Monitoring Scheme, standardized systems for the classification of drugs and their adverse effects<sup>(2)</sup>; it provides specifications in the International Pharmacopoeia<sup>(3)</sup> for assuring the quality of drug substances; it promulgates standards for good pharmaceutical manufacturing practices as embodied within the Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce; and, not least for the purposes of its own drug development programmes, it has produced, in collaboration with the Council for International Organizations of Medical Sciences, proposed international guidelines for biomedical research involving human subjects,<sup>(4)</sup> and for the first administration of a new drug to man.<sup>(5)</sup>

#### International nonproprietary names for drug substances

45. The need to identify each pharmaceutical substance by a unique globally-accepted generic name is self-evident. It is of critical importance in

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(1) WHO Technical Report Series, No. 563, 1975. Guidelines for evaluation of drugs for use in man: report of a WHO Scientific Group.

(2) International Monitoring of Adverse Reactions to Drugs. Adverse Reaction Terminology. 30 June 1984. Unpublished WHO Document DEM/NC/84.153 (English and French) WHO, Geneva.

(3) The International Pharmacopoeia, Third Edition Vol. 1, 1979; Vol. 2, 1981. WHO, Geneva.

(4) Proposed International Guidelines for Biomedical Research Involving Human Subjects. CIOMS, Geneva, 1981.

(5) Safety Requirements for the First Use of New Drugs and Diagnostic Agents in Man. CIOMS, Geneva, 1983.

facilitating communication in medicine as well as in the labelling and advertising of medicinal products in international commerce.

46. Responsibility for the selection of International Nonproprietary Names (INNs) was first accorded to WHO in 1950 with the adoption of Resolution WHA3.11 by the Third World Health Assembly. With the subsequent publication of some 3000 names of newly developed drug substances, the task has gained considerably in complexity. The work is facilitated, however, by the confidence that governments have vested in the agreed procedures. Several countries have now disestablished their nomenclature commissions and automatically accept all recommended INNs. Whereas other national commissions remain extant, each has come to accept a common set of conventions for devising generic names, with the result that nationally assigned names now rarely differ from the INN.

47. The systematic development of the terminology is at risk, nonetheless, of becoming compromised. The procedure for selection requires that no conflict shall occur with licensed trademarks. Manufacturers are thus allowed opportunity to contest proposed names that are either identical to or similar to their own proprietary names. In contrast, trademark applications are disallowed, in accordance with present procedure, only when they are identical to an INN. A case for increased protection of INNs is now apparent, particularly as a result of competitive promotion of products no longer protected by patents. Rather than market these products under the generic name, many companies apply for trademarks manifestly derived from INNs.

48. This practice undermines the principle that INNs are public property; it could well frustrate the rational selection of further INNs for related substances; and it may ultimately compromise the safety of patients by promoting confusion in drug nomenclature.

#### Classification of drugs and their adverse reactions

49. Emphasis was accorded, in the introductory section of this paper, to the importance of continued assessment of the performance of marketed drugs. Manufacturers are now commonly required to notify regulatory authorities of all presumed adverse reactions to licensed products that are subsequently brought to their notice, wherever they may have occurred.

50. These reports are of value for comparative purposes only if their terminology is adequately standardized. Over the past decade WHO has developed a therapeutic classification of drugs and a comprehensive dictionary of adverse drug reactions within the context of its International Drug Monitoring Scheme. These normative activities seem destined to acquire more formal significance and wider recognition with the introduction and further development of national statutory reporting obligations.

#### The International Pharmacopoeia

51. The Third World Health Assembly, in according to WHO the responsibility of producing the International Pharmacopoeia (WHA3.10), envisaged that it would provide a set of global standards, or specifications, for assuring the quality of all pharmaceutical products moving in international commerce. The Assembly was not in a position to predict the unprecedented scale of new drug development over the ensuing thirty years. Nor could it anticipate that obligatory national drug registration systems, and the subsequent understandings on confidentiality developed between manufacturers and governments, would for a while create some uncertainty about the continued general publication of pharmacopoeial specifications.

52. In the event, the case for maintaining published compendia of pharmaceutical specifications has prevailed, though the task of compiling monographs for new drug substances has devolved, not upon WHO, but upon national or regional pharmacopoeial commissions which operate within - or in close liaison with - the competent drug regulatory authorities.

53. These developments have led to a reappraisal of the International Pharmacopoeia. Opportunity has arisen, in particular, to consider the needs of developing countries, which are particularly vulnerable to substandard, spurious or degraded drugs, but which frequently lack any means to check at first hand the quality of imported or locally manufactured products.

54. As a result, the International Pharmacopoeia is now being radically revised with a view to bringing an effective measure of quality control within the grasp of virtually every country. Priority has been accorded to developing monographs for substances contained within the WHO Model List of Essential Drugs; efforts are now directed to the compilation of monographs for final dosage forms; and, as far as is practicable, reliance is vested in classical methods of analysis that can be performed in a small, modestly equipped laboratory which is recommended as a cost-effective investment in virtually any country where no provisions for quality control as yet exist.<sup>(1)</sup>

55. The reorientation of the pharmacopoeia has recently inspired a number of complementary projects. Accelerated stability studies have been commissioned to identify essential drug substances liable to degrade readily under adverse conditions. Stability data are rarely published and singularly little precise information was previously available on the degradation characteristics of the longest established substances. The results obtained have created a data base that has been used to develop simplified tests for detecting gross degradation in these substances. The tests have been devised and verified in a collaborative study involving many national quality control laboratories and they will shortly be published,<sup>(2)</sup> together with a series of basic (or simplified) tests for confirming the identity of these substances.<sup>(3)</sup> These tests offer no substitute for the full chemical analysis required to assure the compliance of a product with a pharmacopoeial monograph. They hold advantage, however, in that they can be performed outside the laboratory to provide reassurance on the identity of products and to exclude gross degradation at any point in the distribution chain.

#### Good manufacturing practices

56. Proof that marketed pharmaceuticals are of adequate quality cannot be vested solely in the sampling and testing of finished products in independent laboratories. Evidence must also be available that every care has been taken throughout their manufacture to assure the requisite standards. In major drug exporting countries periodic inspection of manufacturing premises and practices by an officially-appointed inspectorate is regarded as a vital component of quality assurance.

57. The scope of these inspections is comprehensive. They involve consideration of the qualifications and post-specifications of personnel; the adequacy of

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(1) WHO Technical Report Series, No. 704, 1984. (Twenty-ninth report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations). Annex 1. pp. 21-31.

(2) Accelerated stability studies of widely used pharmaceutical substances. WHO, Geneva, 1985.

(3) Basic tests for pharmaceutical substances. WHO, Geneva, 1985.

premises, sanitary standards and equipment; the standards of record-keeping and manufacturing operations; labelling and packaging procedures; arrangements for self-inspection and quality control; maintenance of batch distribution records and procedures for handling and notification of complaints.

58. A number of regulatory authorities reserve the right to inspect the premises of manufacturers of imported products. Some countries have entered into bilateral or multilateral agreements to recognize and accept each others' inspection provisions. WHO, in establishing global standards for Good Practices in the Manufacture and Quality Control of Drugs, which are now recognized by 110 Member States, has created a basis for extending mutual recognition of inspection procedures to all countries. This is the essence of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.

#### Harmonization of regulatory requirements

59. In the late 1960s, when many countries were first instituting statutory systems of drug regulation, WHO frequently provided a forum for the discussion and elaboration of norms employed in the technical assessment of drugs. Many basic recommendations on the pharmaceutical, toxicological and clinical aspects of drug evaluation were issued under the auspices of the Organization at that time. This tradition is now continued from within the WHO Regional Office for Europe which is issuing an extensive series of guidelines for the clinical evaluation of specific classes of drugs.

60. Overall, however, WHO is now less involved than formerly in the provision of didactic technical guidance for drug regulators. The broad scientific principles of drug assessment have long been established insofar as contemporary knowledge allows. Until this knowledge is further advanced, the divergences now apparent in national policies and practices are unlikely to yield to attempts to forge an international consensus. WHO's harmonizing role has gradually become adapted to these changed circumstances and now takes several forms.

61. Within a purely scientific context it now promotes collaborative approaches to the validation of the methodological basis of drug control. The multicentre validation of analytical techniques described in the International Pharmacopoeia has recently been complemented in the toxicological field by a collaborative study on mutagenicity testing performed under the auspices of the International Programme on Chemical Safety.<sup>(1)</sup> As practical experience of toxicological testing develops, and as more evidence becomes available to correlate the results obtained with the subsequent performance of drugs in man, the scope for internationally-based evaluations of toxicological practice will undoubtedly increase.

62. In one specific area, however, WHO has retained the initiative to develop and update guidelines relevant to drug assessment that are of unquestioned global relevance. They concern the need to safeguard the basic human rights, the safety and the welfare of human subjects involved in biomedical research. Clinical research is undertaken in many countries. If, in particular, the conquest of tropical disease is to be advanced, drug performance must be assessed in endemic areas, and even in countries that have not previously had cause to develop relevant regulations.

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(1) Evaluation of short-term tests for carcinogenesis. Progress in Mutation Research Volume 5. Published on behalf of the International Programme on Chemical Safety (WHO, ILO, UNEP), Elsevier, 1985.

63. WHO is, itself, a sponsor of such research. It has, therefore, collaborated with the Council for International Organizations of Medical Sciences in broadly-based consultations that have resulted in the publication of two sets of guidelines: Proposed International Guidelines for Biomedical Research Involving Human Subjects, and Safety Requirements for the First Use of New Drugs and Diagnostic Agents to Man. These guidelines provide terms of reference for WHO in the implementation of its own research programmes; they provide models for analogous national regulatory mechanisms and they remain addressed to all individuals and institutions that assume responsibilities connected with the study of drugs in man.

64. Promotion of international collaboration and harmonization also underlies the concept of the biennial International Conferences of Drug Regulatory Authorities, which are planned by a regionally representative organizing committee convened under the auspices of WHO, and organized by the host country. The conferences were originally devised to offer drug regulators from all WHO Member States opportunity to exchange views and experience on the administrative and technical aspects of their responsibilities and to advance interagency communication. The first, which was jointly sponsored by WHO and the United States Food and Drug Administration, was held in Annapolis, Maryland, USA, in 1980,<sup>(1)</sup> and subsequent meetings have been convened, firstly in Rome (1982)<sup>(2)</sup> and most recently in Stockholm (1984).<sup>(3)</sup> Attendance has risen progressively: representatives from 57 countries, and mostly from the developing world, gathered together in Stockholm.

65. A prime concern at all of these meetings has been to improve the flow of information between regulatory agencies and to promote the effective utilization of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce. Each of these issues is discussed more extensively in subsequent sections. However, regulatory policy and administration also raise issues for discussion. At the next conference, which will be held in Tokyo in 1986, conceptual approaches to the registration of "orphan drugs", (or drugs developed for indications that provide little commercial incentive), and to traditional medicines, are prominently featured in the programme. Without mutual understanding of administrative systems, and without a collective will to approximate methods of work, international exchange of technical information between regulatory authorities will remain inadequate and unacceptably vulnerable to misinterpretation.

#### THE ADVISORY FUNCTIONS OF WHO

##### Technical reports and other publications

66. Many of WHO's technical reports bear upon the management and treatment of conditions of prime importance to community health standards. They reflect an internationally-based consensus of expert opinion and, as such, they influence the formulation of relevant national health policy in many countries. De facto, and as

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(1) Proceedings of the International Conference of Drug Regulatory Authorities. 28-31 October 1980, Annapolis, Maryland, United States, FDA/WHO, Geneva, 1981.

(2) Second International Conference of Drug Regulatory Authorities. Ed., D. Poggiolini. Ministry of Health, Italy/WHO, Geneva. Raven Press, 1983.

(3) Proceedings of the Third International Conference of Drug Regulatory Authorities, 11-15 July 1984, Stockholm, Sweden, Swedish National Board of Health & Welfare/WHO, Geneva (In press).

a direct consequence of its constitutional mandate, the Organization is cast in an advisory role on issues that impinge directly on drug marketing and the regulatory process.

67. Typically, these issues relate to the major health problems of the developing world. They are exemplified by the promotion of oral rehydration therapy in the treatment of infantile diarrhoea; the advocacy of combination chemotherapy in leprosy in the face of increasing dapsone resistance; and proposed constraints on the use of the newly-introduced antimalarial, mefloquine, to impede the emergence of resistant falciparum malaria.

68. However, its ability to inspire collaborative effort at international level places the Organization in a favoured position to contribute to the rationalization of drug use in other domains. In 1978, the publication of an internationally-based WHO-sponsored collaborative clinical study on the long-term use of clofibrate resulted in immediate, worldwide reappraisal of the safety of hypolipidaemic agents.<sup>(1)</sup> An ongoing multinational case-control study on the long-term effects of steroid contraceptives<sup>(2)</sup> may well exert similar influence, and the ascendancy of epidemiological approaches to drug assessment seems destined to provide opportunity for international collaborative research on a considerably broader basis.

#### Studies in drug utilization

69. The importance of applying quantitative methods and epidemiological techniques to the assessment of drug performance under routine conditions of use was anticipated fifteen years ago when a Drug Utilization Research Group, in which scientists from 14 countries are now participating, was founded under the aegis of the WHO Regional Office for Europe, following a Symposium on the Consumption of Drugs held in Oslo in 1969. The group was formed to examine striking documented differences in prescribing habits between physicians in neighbouring countries of Europe, and the extent to which drug use - which was acknowledged at that time to be increasing - was medically justified.

70. Ten years later, in a publication summarizing the activities of the members of the group from the time of its foundation,<sup>(3)</sup> optimism was expressed that, although a series of problems had been identified that remained without adequate explanation, studies of drug usage and its correlates would eventually provide the basis for improving the cost-effectiveness of drug treatment with the least possible impairment of the quality of medical care.

#### The concept of essential drugs

71. In 1975 the Organization's mandate to provide advice on the socioeconomic aspects of drug use was considerably strengthened. In the light of a report submitted by the Director-General calling for rationalization and extension of

(1) Committee of Principal Investigators. A co-operative trial in the primary prevention of ischaemic heart disease using clofibrate. British Heart Journal, 1978; 40: 1069-1119.

(2) WHO Collaborative Study of Neoplasia and Steroid Contraceptives. Invasive cervical cancer and combined oral contraceptives. British Medical Journal 1985; 290: 961-965.

(3) WHO Regional Publications European Series No. 8. Studies in Drug Utilization: Methods & Applications. Eds., U. Bergmann, A. Grimsson, A.H.W. Wahba, B. Westerholm. WHO, Copenhagen, 1979.

primary health care services, particularly in rural communities, the World Health Assembly adopted a series of resolutions requesting WHO, inter alia, to cooperate with Member States in formulating drug policies and management programmes relevant to the health needs of populations, and to identify drugs and vaccines which, in the light of scientific knowledge, are indispensable for primary health care and control of diseases prevalent in the population at large.

72. Following wide consultation, an initial model list of essential drugs was issued in 1977 within the first report of the WHO Expert Committee on the Selection of Essential Drugs. This has subsequently been revised and updated in three further reports. The objective has been to retain under review a comprehensive yet limited array of drugs of proven value in the prophylaxis and treatment of commonly occurring conditions and to demonstrate that rationalization of procurement can hold advantage in terms of both economy and efficiency in any health care setting.

73. The criteria for selection are broad, since the parameters that would determine decisions within a national context - including disease prevalence; the nature of primary care and referral facilities; the training and experience of available personnel; financial resources; and genetic, demographic and environmental factors - are undefined. A list that is consonant with local needs and policies must be compiled, as appropriate, at national, or even institutional level. Nonetheless, the WHO list has exerted considerable influence in several respects:

It has served as a stimulus to all countries to consider the available options for establishing cost-effective drug policies in the public sector.

It has provided a systematized approach to drug selection that is applicable in a wide variety of situations.

It has highlighted the outstanding yet discriminatory nature of therapeutic innovation. Whereas disorders of affluent society, including hypertension, arthritis and psychiatric disorders, have attracted the development of large numbers of compounds, several of the major endemic tropical diseases including filariasis, onchocerciasis and trypanosomiasis have engaged virtually no attention. The emergence of the essential drugs philosophy and of effective primary health care programmes within developing countries offers a renewed challenge and an incentive to pharmaceutical companies disposed to remain vigilant to global health issues.

74. The WHO Model List is comprehensive in its scope. Some of the listed drugs are intended exclusively for use in specialised hospital departments. Some can be prescribed safely only within a relatively sophisticated system of medical care, and many others can be used effectively only when continuity of treatment and availability of experienced supervision can be assured. Special attention is accorded, nonetheless, to drugs required in a primary health care setting that can be used safely and effectively by individuals with little formal medical knowledge.

75. The Committee, however, emphasises that the range of drugs supplied to community health workers must be determined at national level having regard, not least, to force of circumstance. In an ideal situation antibiotics, for instance, should be used only by individuals with advanced diagnostic skills with access to appropriate microbiological facilities. In practice, the lives of many children now dying from pneumonia in the developing world could be saved if injectable procaine penicillin were available at the time of their initial presentation. The skills and resources that can be developed at the most peripheral health care level to meet such contingencies depend on the management offered from the first referral

level as well as the accessibility of these facilities. Achievement is also heightened by the availability of accurate and objective information understandable to each category of prescriber.

76. The generation of information that is attuned to local needs and circumstances is, inherently, a national responsibility. WHO, however, has given priority in several of its programmes to the development of resource material included for local adaptation. Training material on case management and on control strategies that has been generated within several of the specialized technical units of the Organization is now being collated and extended to provide the basis of a model formulary consonant with advice already promulgated in various ways by the Organization.

77. This material is intended to supplement and eventually to replace model information sheets prepared within the WHO Secretariat and commended to governments within the reports of the Expert Committee on the Use of Essential Drugs. It is anticipated that the more flexible format of a formulary will avert two problems encountered in the preparation of drug information sheets:

- the difficulty of ensuring that the WHO material is consonant with the officially approved product information already settled between manufacturers and national drug regulatory authorities
- the need to focus attention on practical aspects of case management in different clinical settings rather than on the innate properties of individual drugs.

78. It is vital that such information be available to complement governmental efforts to develop and improve primary health care services. It is also vital that advice on case management within the restrictive perspective of primary health care be based, wherever possible, on practical experience and rigorous assessment. Rational drug use is dependent, in every setting, on controlled, comparative evaluation of therapeutic options.

#### INTERGOVERNMENTAL EXCHANGE OF INFORMATION

##### Mechanisms for collaboration

79. Resolution WHA37.33, in addressing the need for rational use of drugs, assigns a key role to the Organization in developing activities at national, regional and global levels that will improve the provision of unbiased and complete information about drugs to the health profession and the public. At the same time, the United Nations General Assembly, in a series of resolutions relating to the export of hazardous products (37/137) and to consumer protection (39/248), has recently emphasized the continued importance of the intergovernmental systems of information long established by WHO within the pharmaceutical field.

80. The broader charge now placed upon the Organization to provide technical information on drug use directly to the end-users must devolve from its existing intergovernmental remit if its message is to remain aligned with and responsive to nationally-determined policies and decisions. These functions, which are broadly-based, have been defined within a large number of resolutions adopted by the governing bodies of WHO over a period of more than two decades. In general terms they call upon the Director-General:

- to support national drug regulatory authorities by arranging for interchange of information on the registration of new products, and the withdrawal or restriction of existing products on grounds of safety

- to collaborate with these authorities in the collation, analysis and interpretation of reports of suspected adverse drug reactions.

81. National drug regulatory authorities operate within a rigid statutory framework constructed to control the domestic drug market. Much of their work is undertaken in camera since it demands access to privileged, commercially valuable information submitted by pharmaceutical manufacturers specifically and exclusively for regulatory purposes. Many of these authorities have no formal intergovernmental obligations and, where these do exist, they are directed to harmonization of administrative procedures and mutual acceptance of technical decisions among closely-associated trading partners.

82. The need to maintain confidentiality, however, is counter-balanced by an underlying commitment to safeguard health and, in particular, to ensure that sufficient information enters the public domain to permit the safe and effective use of registered drugs. Regulatory authorities, moreover, now find themselves publicly accountable in terms of their own performance. Drug regulation inevitably captures public attention and media coverage whenever drugs are withdrawn from use unexpectedly on grounds of safety.

83. In response to these factors and also, in some cases, to relaxation of governmental policy on classification of confidential data, several more highly evolved authorities have consciously expanded their informational role. This extends not only to the provision of officially-approved prescribing information but, in some cases, to summaries of the evidence on which licences are granted. Many authorities now regularly publish news sheets and bulletins on matters of current therapeutic concern; and some collaborate with national poison control centres, health councils and other nationally appointed bodies charged to develop public awareness of health-related issues.

84. These changes have not only promoted a flow of information into the public domain, they have fostered discussion and collaboration between regulatory authorities which has operated to the benefit of all countries. From WHO's standpoint these trends are reflected in:

- the recognition and support accorded to the biennial International Conferences of Drug Regulatory Authorities (ICDRA) planned and co-sponsored by WHO
- the large number of authorities that, at the request of the Director-General,<sup>(1)</sup> have designated information officers formally responsible for assuring efficient lines of communication with the Organization
- the sustained impetus accorded to the WHO International Drug Monitoring Scheme by the collectivity of the participating countries
- increasing usage and discussion of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.

#### Exchange of information on regulatory decisions

85. In 1963, the World Health Assembly, in Resolution WHA16.36, requested Member States to communicate immediately to WHO any decision to prohibit or limit the availability of a drug already in use; any decision to refuse the approval of a new

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(1) Director-General's Circular Letter, 30 December 1981 (C.L.27, 1981).

drug; and any approval for general use of a new drug accompanied by important restrictions, whenever these decisions are taken as a result of serious adverse reactions.

86. The Assembly has reaffirmed the importance it places on the efficient exchange of this information in several subsequent resolutions which additionally call for the inclusion of:

- decisions to withdraw or restrict the availability of a drug already in use on grounds of lack of effectiveness (WHA23.48)
- data on the scientific basis and the conditions of registration of individual drugs (WHA25.61).

87. Effective implementation of the open-ended collaborative effort that these resolutions require has proven to be dependent upon the creation of an organizational infrastructure. This is now provided through the network of designated information officers and the biennial ICDRA conferences. Nonetheless, logistic difficulties and considerations of confidentiality have frustrated the full implementation of the Assembly's aspirations.

88. Initially, governments were simply invited by the Organization to notify restrictive regulatory decisions of international relevance. These were then transmitted to all Member States in WHO Drug Circulars. For many years this scheme fell short of its potential, partly through default and partly because the removal of drugs from national markets by voluntary agreement with manufacturers rather than by enforcement of statutory controls were rarely reported, even when safety was at issue. Over a period of some 16 years extending up to 1979 a total of only 199 notifications was received by WHO, of which about one half was provided by the United States Food and Drug Administration.

89. The situation has since been greatly improved, both because national authorities have become more perceptive of the need to exchange information and because of intensified promotion of this need by WHO. In 1984 alone, WHO transmitted information on 622 regulatory decisions received from 37 countries. These are conveyed in monthly mailings to information officers in every Member State. The flexibility and informality of this channel of communication has, on several occasions, also proven its value as a means of canvassing opinion on a broad international basis on regulatory issues of immediate concern.

90. However, formal understandings on confidentiality between manufacturers and regulatory authorities still impose an important constraint on exchange of information. Very few regulatory authorities are prepared to disclose information on rejected marketing applications, even when approval is withheld on grounds of safety.

91. Similarly, with the notable exception of the material published by the US Food and Drug Administration, little information has become available internationally on the systematic reviews of efficacy that many authorities are committed to undertake on all currently marketed products. A recommendation adopted by consensus at the Third ICDRA, 1984 noted that:

"Effective international exchange of this information will directly assist regulatory authorities in their responsibility of removing products from national markets that do not conform with prevailing standards of efficacy and safety. It will also substantially reduce the technical and administrative burden on national administrations that derives from this responsibility, since it will reduce the need for independent and repetitive national assessments".

92. Immediately the proceedings of this Conference are published, information officers will be requested to communicate the following additional information to WHO for inclusion in the monthly mailing system:

- results of ongoing review procedures
- a summarized listing of categories of drugs already subjected to review together with a relevant bibliography
- a provisional timetable of projected review procedures.

93. Although information on newly registered drugs is more readily available, its presentation in an international communications system raises both logistic and policy issues. In particular, there is a strong case for selectivity since:

- the same product is frequently licensed in many countries under virtually identical conditions
- many newly registered products are not innovative, since they include new brands or new dosage forms of existing drugs
- the information is already generally available to importing countries as an adjunct to the WHO Certification Scheme.

94. Nonetheless, the assessment of new products accounts for a high proportion of the total work load with many regulatory authorities, and many countries appreciate sight of a three-monthly updating of new products registered elsewhere. Some twenty highly developed countries regularly offer this information to WHO and a selective annotated listing is included in the quarterly WHO Drug Information Bulletin. The process of selection is directed exclusively to avoiding undue repetition and to eliminating non-innovative and combination products that do not accord with criteria of rationality proposed by the WHO Expert Committee on the Selection of Essential Drugs. It is emphasized that annotation does not in any way indicate approval of the product by WHO, and each entry is limited to a brief description of the pharmacological class of the active component together with the licenced indications, contraindications, warnings, precautions and serious known adverse effects.

95. Arrangements have also been made within the past two years to provide every competent national authority with comprehensive independent and authenticated information in the English language on marketed drugs. Through the good offices and generosity of several governments, of the International Federation of Pharmaceutical Manufacturers Associations, and of various national organizations within these countries, the following material is distributed on a complementary basis to all Member States:

Belgium:

Répertoire commenté des médicaments. Centre Belge d'Information  
Pharmacothérapeutique

Folia Pharmacotherapeutica. Centre Belge d'Information Pharmacothérapeutique

France:

Dictionnaire Vidal. OVP Paris (information approved by the Ministry of  
Health is clearly designated)

United Kingdom:

British National Formulary. British Medical Association/Pharmaceutical Society of Great Britain

Data sheet compendium. Association of the British Pharmaceutical Industry (information in compliance with regulations of the UK Department of Health and Social Security)

Martindale's Extra Pharmacopoeia. Pharmaceutical Society of Great Britain.

United States of America:

Drug Evaluations. American Medical Association

Drug Information. American Hospital Formulary Service

Physicians Desk Reference. Medical Economics Co. (information in compliance with regulations of the US Food and Drug Administration)

Summary Bases for Approval. US Food and Drug Administration

96. Negotiations are now in hand to explore whether this service can be extended to material published in other widely used languages. Meanwhile a compendium of publications and documents prepared by national drug regulatory authorities, and by professional and consumerist organizations is issued at six-monthly intervals to information officers. In addition, relevant statutory instruments and regulations are either translated into the working languages of WHO in the quarterly Digest of Health Legislation or indexed by the WHO Collaborating Centre on Drug Information, Hungary.

Monitoring of adverse drug reactions

97. The governing bodies of WHO have identified a need not only for international exchange of information on regulatory decisions but also for central collation of the reports of suspected adverse reactions from which many restrictive decisions devolve. Accordingly, the Director-General was requested in Resolution WHA19.35 to establish an international system of monitoring reports of adverse reactions to drugs using information derived from national centres.

98. This was inspired by an expectation that infrequent and unanticipated drug-related hazards could be identified with greater efficiency by pooling case-reports submitted to individual national centres. Over 20 countries have contributed consistently to the scheme virtually from its inception in 1968, and the data bank, which is now housed in a WHO Collaborating Centre located within the Swedish Department of Drugs, currently contains some 400 000 case reports of suspected adverse reactions to drugs notified spontaneously by clinicians.

99. Spontaneous monitoring systems have an inherent flexibility in that all doctors notionally contribute and all patients are notionally included. They have provided a wealth of material for investigation and the signals they have generated have resulted in many labelling changes and in several withdrawals of marketed drugs. Nonetheless, the data need to be interpreted with caution: probably only a small proportion of drug-induced adverse reactions are reported to national centres and there is no assurance that these are reliably representative of the true hazards of treatment. In most instances spontaneous reports merely provide an alert to the possible existence of a hazard that requires independent investigation for its confirmation. It is for this reason that information in the data base is,

as yet, confidential to the national centres participating in the scheme. Nonetheless, summarized data of reactions within the Nordic Group of countries are now published without restriction and the question of access to the WHO data base will doubtless be reappraised in the light of experience with this initiative

100. Whereas the long adherence of the participating countries to the WHO monitoring system attests to its importance, drug reactions are protean in their manifestations and no single system of surveillance is adaptable to every potential need. Spontaneous monitoring systems, in particular, are inappropriate to the detection and investigation of long-range effects of drugs, and especially of reactions that simulate naturally occurring disease. The emergence of epidemiologically-based approaches to drug monitoring has created possibilities for new approaches to post-marketing surveillance and the feasibility of developing a comprehensive array of surveillance mechanisms adequate for drug regulatory purposes is an issue that has preoccupied drug regulatory authorities and manufacturers for some years.

101. An ideal solution is possibly unattainable, but without a stimulus for international consultation and collaboration involving research-based pharmaceutical companies, university departments of epidemiology, toxicological centres and responsible government agencies, practicable possibilities of utilizing the diverse facilities that already exist to best advantage will remain unrealized. WHO, working together with the Council for International Organizations of Medical Sciences, is already engaged in promoting this dialogue and in exploring the extent to which various forms of surveillance might be feasible and cost-effective in generating information on drug-related hazards in developing as well as developed countries.

#### Evaluated information on regulatory decisions

102. In 1975 the World Health Assembly requested the Director-General to disseminate evaluated information on drugs to Member States. This brief has now been broadened and given a different focus with the adoption, in 1984, of Resolution WHA37.33 which requests the Director-General "to continue to develop activities at national, regional and global levels aiming at the improvement of use of drugs and of prescription practices and the provision of unbiased and complete information to the health profession and the public".

103. Since there is little prospect, having regard to prevailing economic circumstances, that a substantial increase in technical resources can be accorded either at national or international level to subserve this function, fulfilment of the need demands a reanalysis of priorities in drug control. At present, the norm in many countries is to place greater emphasis on the pre-marketing assessment of new products than on the information that will subsequently assure their responsible use.

104. Given that interagency communications are improving, that more effective use might be made of the WHO Certification Scheme, and that adoption of the essential drugs concept offers a basis for rationalizing registration policies, many regulatory authorities, particularly in developing countries, might now review the balance of their activities. Whereas they might reasonably, for the most part, rely on pharmaceutical or toxicological assessments undertaken by other national authorities or by WHO, they are uniquely placed to determine the form and content of the information required both by health professionals and by patients to assure the effective use of the drug under prevailing national conditions.

105. WHO, with a view to supporting national authorities in their informational responsibilities, has already embarked upon a threefold strategy:

- production of a WHO Model Formulary based upon the model list of essential drugs
- preparation of discursive commentaries on regulatory policies and decisions within the WHO Drug Information Bulletin
- renewed promotion of the WHO Certification Scheme, and consideration of its possible extension to provide for exchange of all nationally authenticated product information.

106. The Formulary and the Drug Bulletin are proposed as the main vehicles for WHO's contribution to an integrated drug information system because the Organization can use its constitutional mandate, its technical competence and its working relationships with national drug regulatory authorities, non-governmental organizations and individual experts to best advantage within these contexts.

107. Work in developing the Formulary is already in hand. It is envisaged as a handbook of treatment relevant to the first referral level of medical care. It will also embody teaching material for primary health care workers and the public that can readily be adapted to local educational standards and cultural precepts. Although it will place greatest emphasis on drug treatment, the information will be organized having regard to practical case management. To the greatest possible extent the information will be drawn from advice already issued within the technical reports of the Organization. Completed drafts will be submitted in consultative form, section by section, to designated national information officers, members of relevant WHO expert advisory panels, interested pharmaceutical manufacturers and non-governmental organizations.

108. Having regard to the wide circulation of the WHO Drug Information Bulletin, the many requests that have been received from Member States for permission to translate its contents, and the supportive references made within the governing bodies of WHO, its preparation will retain high priority. Efforts will be made to assure its timely production. Its presentation will be changed to lend it greater appeal and it will be forcefully promoted. Emphasis will be accorded, as in the past, to discursive comparative commentaries on the regulatory status of essential drugs and other important products in various countries, and the present consultative procedures will be maintained to ensure that interested regulatory authorities and manufacturers receive sight of material in draft.

109. In order that these documents remain responsive to the needs of Member States the designated information officers will be asked to arrange that they be kept under review and to indicate how they are used and with what effect. This information will be submitted to the ICDRA which regularly receives a status report from WHO detailing progress in all aspects of the Organization's collaboration with national drug regulatory authorities. In turn, a short report of the proceedings of each Conference highlighting the adopted recommendations will subsequently be made available to the governing bodies of WHO.



RESOLUTIONS OF THE WORLD HEALTH ASSEMBLY  
RELATED TO THE TRANSFER AND DISSEMINATION  
OF INFORMATION ON DRUG QUALITY, SAFETY AND  
EFFICACY

[WHA1.27] The First World Health Assembly accepted the programme on the International Pharmacopoeia and the organization for its implementation as proposed by the Interim Commission.<sup>1</sup> It also adopted the following resolution:

The First World Health Assembly

RESOLVES

(1) that the Executive Board be instructed to establish during its first session an expert committee to be called "The Expert Committee on the Unification of Pharmacopoeias of the World Health Organization", with the following terms of reference:

to act as an advisory body to the World Health Organization;

(2) that the World Health Organization set up within its Secretariat a section on the unification of pharmacopoeias.

July 1948 13,307

WHA3.10 The Third World Health Assembly

1. APPROVES the publication of the *Pharmacopoea Internationalis*, and

2. RECOMMENDS the eventual inclusion of its provisions in the national pharmacopoeias after the adoption of the said provisions by the authorities responsible for the pharmacopoeias.

May 1950 28,19

WHA3.11 The Third World Health Assembly,

Recognizing the desirability that a system of non-proprietary names be established internationally for such new pharmaceutical products as might be contemplated for later insertion in the *Pharmacopoea Internationalis*,

1. APPROVES the general principles enumerated by the Expert Committee on the Unification of Pharmacopoeias at its fifth session,<sup>2</sup> and

2. RESOLVES as follows:

(1) the Expert Committee on the Unification of Pharmacopoeias should undertake the selection and approval of non-proprietary names for drugs which might be described in later editions of the *Pharmacopoea Internationalis*;

(2) such names as are from time to time selected and approved by the expert committee should be communicated by the Director-General to national pharmacopoeial authorities, together with a recommendation that these names be officially recognized and approved, and, if the substances are eventually included in the national pharmacopoeia, adopted as pharmacopoeial names;

(3) such recommendations shall further include a request that such measures as may be deemed appropriate by Member States be taken with a view to preventing the use of the names selected for unauthorized purposes, and in particular to prevent the granting of exclusive proprietary rights in these names to the manufacturer.

May 1950 28,19

WHA15.41 The Fifteenth World Health Assembly,

Considering that

(1) new pharmaceutical preparations appear in a steadily increasing number on the market;

(2) in many of these preparations a great therapeutic activity may be combined with serious side-effects demanding particular care in administration;

(3) recent experience has shown certain defects in existing safety control measures;

(4) these defects are especially related to insufficient clinical trials;

<sup>1</sup> *Off. Rec. Wld Hlth Org.* 10, 17.

<sup>2</sup> *Wld Hlth Org. techn. Rep. Ser.* 1950, 12. See also *Off. Rec. Wld Hlth Org.* 25, Annex 7.

(5) clinical evaluation represents the final assessment of pharmaceutical preparations and is the principal means of detecting harmful side-effects following long-term use;

(6) clinical trials are highly time-consuming, need very large numbers of patients to be observed according to generally accepted principles, and would often be facilitated by international co-operation;

(7) it should be the responsibility of national health authorities to ensure that the pharmaceutical preparations available to the medical profession are therapeutically efficient and that their potential dangers are fully recognized,

1. REQUESTS the Director-General to pursue, with the assistance of the Advisory Committee on Medical Research, the study of the scientific aspects of the clinical and pharmacological evaluation of pharmaceutical preparations;

2. REQUESTS the Executive Board and the Director-General to study the feasibility or otherwise, on the part of WHO, of

(a) establishing minimum basic requirements and recommending standard methods for the clinical and pharmacological evaluation of pharmaceutical preparations;

(b) securing regular exchange of information on the safety and efficacy of pharmaceutical preparations; and, in particular,

(c) securing prompt transmission to national health authorities of new information on serious side-effects of pharmaceutical preparations,

and to report to the Sixteenth World Health Assembly on the progress of this study.

May 1962 118,18

WHA16.36 The Sixteenth World Health Assembly,

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

Having examined the report by the Director-General on the clinical and pharmacological evaluation of drugs;<sup>1</sup>

Considering that international co-operation is essential for the achievement of the best possible protection against hazards for man arising out of the use of drugs;

Agreeing to the definition of a "drug" as any substance, or mixture of substances, destined for use in the diagnosis, treatment, mitigation or prevention of disease in man, as set out in the report of the Study Group on the Use of Specifications for Pharmaceutical Preparations;<sup>2</sup>

Realizing the technical and administrative difficulties of securing regular exchange of information on all drugs,

1. REAFFIRMS the need for early action in regard to rapid dissemination of information on adverse drug reactions;

2. REQUESTS Member States

(a) to communicate immediately to WHO

(i) any decision to prohibit or limit the availability of a drug already in use,

(ii) any decision to refuse the approval of a new drug,

(iii) any approval for general use of a new drug when accompanied by restrictive provisions,

if these decisions are taken as a result of serious adverse reactions; and

(b) to include in this communication as far as possible the reasons for the action taken and the non-proprietary and other names, and the chemical formula or the definition;

3. (a) RECOGNIZES the importance of accurate appraisal, at the national level, of the toxic effects of drugs; and

<sup>1</sup> *Off. Rec. Wld Hlth Org.* 127, Annex 12.

<sup>2</sup> *Wld Hlth Org. techn. Rep. Ser.* 1957, 138, 14.

(b) INVITES Member States to arrange for a systematic collection of information on serious adverse drug reactions observed during the development of a drug and, in particular, after its release for general use;

4. REQUESTS the Director-General

(a) to transmit immediately to Member States the information received under paragraph 2;

(b) to study the value and feasibility, including the administrative and financial implications, of WHO collecting from and disseminating to Member States

(i) the non-proprietary and other names, chemical formulae and definitions of new drugs released or approved,

(ii) the information contained in 3(b) above;

(c) 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; and

(d) to pursue action in the matter and report to the Executive Board and to the Seventeenth World Health Assembly.

May 1963 127,18

WHA18.36 The Eighteenth World Health Assembly,

Recalling resolution WHA17.41 on the compliance of exported pharmaceutical preparations with the requirements applying to pharmaceutical preparations for domestic use;

Having examined the report of the Director-General on the quality control of pharmaceutical preparations,<sup>1</sup> setting out an unsatisfactory situation in regard to the quality control of pharmaceutical preparations moving in international commerce;

Noting that large parts of the world population make use of pharmaceutical preparations without having in their countries adequate facilities for prior quality control; and

Recalling the provisions of Articles 2 and 21 of the Constitution,

1. INVITES governments to take the necessary measures to subject pharmaceutical preparations, imported or locally manufactured, to adequate quality control;

2. REQUESTS the Director-General:

(a) to continue to assist Member States to develop their own laboratory facilities or to secure access to such facilities elsewhere;

(b) to continue to study methods of securing, in the countries of origin, control of the quality of pharmaceutical preparations intended for export; and

(c) to pursue the establishment of internationally accepted principles and specifications for the control of the quality of pharmaceutical preparations; and further

3. REQUESTS the Director-General to report to the Executive Board and to the Nineteenth World Health Assembly on the possibilities of the Organization's playing an even more active role in the quality control of pharmaceutical preparations.

May 1965 143,22

WHA18.42 The Eighteenth World Health Assembly,

Considering resolutions WHA15.41, WHA16.36 and WHA17.39 of the Fifteenth, Sixteenth and Seventeenth World Health Assemblies on the importance of systematic collection, evaluation, and dissemination of information on adverse drug reactions;

Recalling the reports of the several groups of experts convened to consider and study the feasibility and desirability of instituting an adverse drug reaction monitoring programme on an international basis;

Convinced of the urgent need for the international collection and distribution of information on adverse drug reactions; and

Looking with favour upon the offer of the Government of the United States of America to provide facilities for the processing of information on adverse drug reactions, under the auspices of the World Health Organization,

1. REQUESTS the Director-General to study further the requirements of an international programme for the collection, analysis, and dissemination to Member States of information on adverse drug reactions;

2. INVITES Member States to develop as soon as possible national monitoring systems for adverse drug reactions, with a view to taking part in an international system under the aegis of WHO;

3. REQUESTS the Director-General to examine the offer of the United States of America and of any other governments of data processing facilities as a part of an international monitoring system for adverse drug reactions, and to report on the matter to the Nineteenth World Health Assembly; and

4. THANKS the Government of the United States of America for its offer.

May 1965 143,25

WHA19.35 The Nineteenth World Health Assembly,

Having examined the reports of the Director-General<sup>1</sup> on the international monitoring of adverse reactions to drugs;

Recalling resolutions WHA15.41, WHA16.36, WHA17.39 and WHA18.42 of the Fifteenth, Sixteenth, Seventeenth and Eighteenth World Health Assemblies on the importance of systematic collection, evaluation and dissemination of information on adverse reactions to drugs;

Considering resolution EB37.R14 of the Executive Board on the international monitoring of adverse reactions to drugs;

Convinced of the urgent need to collect and disseminate at the international level information on adverse reactions to drugs; and

Taking into account that co-operation with national centres for monitoring adverse reactions to drugs and the utilization of the data-processing facilities available in the United States of America would facilitate the international monitoring envisaged,

1. REQUESTS the Director-General to initiate a pilot research project, along the lines indicated in his report<sup>1</sup>, with the aim of establishing an international system of monitoring adverse reactions to drugs using information derived from national centres; and

2. ACCEPTS the generous offer of the Government of the United States of America of data-processing facilities for this purpose.

May 1966 151,16

WHA22.41 The Twenty-second World Health Assembly,

Emphasizing that, in addition to the pharmaceutical quality control of drugs, it is essential to evaluate their therapeutic safety and efficacy so as to prevent their unsuitable use involving, *inter alia*, excessive expenditures for the individual as well as the public;

Considering that the increasing variety of drugs renders their selection by the prescribing physician difficult; and

Recalling resolution WHA17.39 requesting *inter alia* the formulation by the World Health Organization of generally acceptable principles for the evaluation of the safety and efficacy of drugs,

REQUESTS the Director-General to examine possible ways of providing advice to governments in developing machinery for evaluating the therapeutic safety and efficacy of drugs and to report to the Executive Board and the Twenty-fourth World Health Assembly.

July 1969 176,20

<sup>1</sup> Published, in slightly abridged form, in *Wld Hlth Org. Regn. Rep. Ser.*, 1965, 307, Annex 1.

<sup>1</sup> *Off. Rec. Wld Hlth Org.* 148, Annex 11.

**WHA22.50** The Twenty-second World Health Assembly,

Recalling resolution WHA21.37;

Having considered the report of the Director-General on the quality control of drugs;

Noting with satisfaction the formulation of the "Principles of Pharmaceutical Quality Control"<sup>1</sup> and "Good Practices in the Manufacture and Quality Control of Drugs"<sup>2</sup> as presented in the report of the Director-General;

Recognizing that general observance of such principles and practices is essential and, in particular, a prerequisite for a system of certification for drugs in international commerce; and

Considering that general acceptance of such a certification system would be an important first step toward ensuring the desired level of quality control of drugs in international commerce,

## 1. RECOMMENDS that Member States adopt and apply

(1) the requirements for "Good Practices in the Manufacture and Quality Control of Drugs" as formulated in the report of the Director-General,<sup>2</sup>

(2) the certification scheme on the quality of pharmaceutical products moving in international commerce as formulated in the report of the Director-General as amended,<sup>3</sup>

## 2. REQUESTS the Director-General to report to the Twenty-third World Health Assembly

(1) on those improvements in the requirements for good manufacturing practice and in the certification scheme which may appear to be necessary; and

(2) on further progress with regard to the certification scheme and the implementation thereof.

July 1969 176,24

**WHA23.48** The Twenty-third World Health Assembly,

Recalling resolutions WHA15.41, WHA16.36 and WHA17.39 of the Fifteenth, Sixteenth and Seventeenth World Health Assemblies on the importance of communicating to WHO any decision to refuse the approval of a new drug, or to withdraw or restrict the availability of a drug already in use if such decision is taken as a result of serious adverse reactions, and requesting the Director-General to transmit immediately to Member States the information received;

Acknowledging the value of information distributed through this intergovernmental information system so far;

Noting that it is not only the serious adverse reactions caused by drugs that must be taken into consideration as factors detrimental to the health of the individual, but also their inefficacy; and

Noting also that ineffective drugs are wasteful of individual and public economic resources,

1. INVITES all Member States to communicate to WHO any final decision made by national health authorities to withdraw or restrict the availability of a drug already in use if the decision is taken because of lack of substantial evidence of effectiveness in relation to its toxicity and the purpose for which it is used; and

2. REQUESTS the Director-General to disseminate these decisions in addition to decisions taken as a result of serious adverse reactions, as specified in resolution WHA16.36.

May 1970 184,25

**WHA24.56** The Twenty-fourth World Health Assembly,

Recalling previous Assembly resolutions dealing with pharmacology and the control of drugs, and in particular resolutions WHA16.36, WHA17.39, WHA20.34,<sup>1</sup> WHA21.37,<sup>2</sup> WHA22.50,<sup>3</sup> WHA23.13, WHA23.42<sup>3</sup> and WHA23.48;

Convinced that matters relating to the discovery, production and distribution of drugs, to the control of drug quality, safety and efficacy and to the monitoring of adverse reactions, including dependence-producing properties, should be looked upon as a whole;

Realizing that the continuous development of medical science and of the pharmaceutical industry leads to the appearance of new and more effective drugs;

Being aware of the increasing need for the prescribing physician to know and fully understand the effects, side-reactions and possible interactions of drugs;

Considering the responsibility of the World Health Organization to assist in keeping the national health authorities and the medical profession abreast of such developments through expanded facilities for information on pharmacotherapy and for continuing education in clinical pharmacology; and

Further considering the necessity of devising the most efficient ways for the Organization to carry out this responsibility,

1. COMMENTS the increased emphasis in the programme of the Organization, and the work being done, on pharmacology and on the control of drugs;

2. REQUESTS the Director-General, keeping in mind the need for an overall approach to such matters, to study how best the Organization can cope with its obligations in this domain and expand its activities as required, and to report thereon to the Executive Board at its forty-ninth session and to the Twenty-fifth World Health Assembly;

3. REQUESTS the Director-General to consider the creation of a system of collection and dissemination of information on results of safety and effectiveness trials of new drugs and on their registration in countries having the necessary facilities, for possible use of these data by the health authorities of countries importing pharmaceutical products; and to report on the feasibility and financial implications of such a system to the forty-ninth session of the Executive Board and to the Twenty-fifth World Health Assembly; and

4. FURTHER REQUESTS the Director-General to publish a list of countries where the State authorities responsible for the quality control of drugs recognize and implement the requirements for "Good Practices in the Manufacture and Quality Control of Drugs" and the certification scheme on the quality of pharmaceutical products moving in international commerce as recommended by the Twenty-second World Health Assembly in its resolution WHA22.50.<sup>4</sup>

May 1971 193,31

<sup>1</sup> *Wld Hlth Org. Techn. Rep. Ser.*, 1969, 418, Annex 1.

<sup>2</sup> *Sec. Off. Rec. Wld Hlth Org.*, 176, Annex 12, part 1.

<sup>3</sup> *Sec. Off. Rec. Wld Hlth Org.*, 176, Annex 12, part 2.

<sup>1</sup> *Sec. p.* 132.

<sup>2</sup> *Sec. p.* 133.

<sup>3</sup> *Sec. p.* 123.

<sup>4</sup> *Sec. p.* 133.

**WHA25.61** The Twenty-fifth World Health Assembly,

Having examined the report of the Director-General on the quality, safety and efficacy of drugs;

Mindful of the importance of developing a comprehensive approach to ensuring drug quality, safety and efficacy, monitoring adverse reactions, and developing and disseminating accurate information about drugs;

Convinced of the need to assist national health authorities to meet their responsibilities in relation to drug quality, safety and efficacy,

1. NOTES with appreciation the activities that have been undertaken in accordance with resolution WHA24.56;

2. RECOMMENDS that governments, if they deem it necessary, take suitable measures for giving the public appropriate information about the use, hazards and limitations of drugs;

3. REQUESTS the Director-General to report to the fifty-first session of the Executive Board and the Twenty-sixth World Health Assembly:

(a) on the feasibility of an international information system providing data on the scientific basis and the conditions of registration of individual drugs;

(b) on practicable minimum requirements and on other efforts to develop a comprehensive approach to ensuring the quality, safety and efficacy of drugs, including the feasibility of implementing Article 21 (d) and (e) of the WHO Constitution; and

(c) on the cost of any action foreseen;

4. URGES all countries participating in the monitoring scheme to ensure that reports of adverse reactions after validation are forwarded regularly and with the minimum delay to the Organization; and

5. REQUESTS the Director-General to undertake a study of the most feasible means of indicating by a uniform system of marking the limits of shelf life of pharmaceutical products under the conditions of their storage, as well as the date of manufacture and batch number, and the maintenance of records which facilitate tracing of distribution, and to report thereon to a future World Health Assembly.

May 1972 201,33

**WHA26.30** The Twenty-sixth World Health Assembly,

Recalling resolutions WHA24.56 and WHA25.61;

Having examined the report of the Director-General on the feasibility of an international information system on drugs,

1. THANKS the Director-General for his report;

2. CONSIDERS that the implementation of an international information system providing data on the scientific basis and the conditions of registration and withdrawal of individual drugs would be of considerable importance in the development of a more comprehensive approach to ensuring drug quality, safety and efficacy;

3. BELIEVES that the proposed feasibility study would provide the basis for assessing the potential value of such a system; and

4. REQUESTS the Director-General to develop the proposed feasibility study and to report to a future World Health Assembly on the findings of this study and on their financial implications.

May 1973 209, 14

**WHA26.31** The Twenty-sixth World Health Assembly,

Recalling resolutions WHA16.36 and WHA23.48; and

Reiterating that all drugs made available to consumers should comply with adequate standards of quality, safety and efficacy, and that the World Health Organization has a major role to play in the collection and dissemination of information on drugs,

1. INVITES Member countries to continue to communicate to the World Health Organization any decisions by the national control authority resulting in the withdrawal from the market of any pharmaceutical product, and to indicate in the communication the name of the product, its composition, its dosage form, the name of the manufacturer and the findings of the studies which resulted in the withdrawal; and

2. REQUESTS the Director-General to continue to disseminate information concerning such decisions without delay and to make this information activity part of the proposed feasibility study on the international information system on drugs.<sup>1</sup>

May 1973 209, 15

**WHA28.66** The Twenty-eighth World Health Assembly,

Having considered the report of the Director-General on prophylactic and therapeutic substances;<sup>2</sup>

Recognizing the importance of further development of international standards and requirements for prophylactic and therapeutic substances;

Convinced of the necessity of developing drug policies linking drug research, production and distribution with the real health needs,

1. THANKS the Director-General for his comprehensive report;

2. URGES governments and professional bodies to ensure that the health personnel and the public are adequately educated and kept informed as to the proper use of prophylactic and therapeutic substances; and

3. REQUESTS the Director-General:

(1) to continue to develop activities related to the establishment and revision of international standards, requirements and guidelines for prophylactic and therapeutic substances in consultation, as appropriate, with relevant governmental and nongovernmental organizations in official relations with WHO;

(2) to develop means by which the Organization can be of greater direct assistance to Member States in:

(a) the implementation of national programmes in research, regulatory control, management and monitoring of drugs and, in so doing, also in the formulation of national drug policies;

(b) advising on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs;

(c) the education and training of scientific and technical manpower for research, production, evaluation, control and management of prophylactic and therapeutic substances;

(3) to study ways and means of optimizing inputs and outputs of the international system for drug monitoring so that it will be useful for both developed and developing countries;

(4) to disseminate to Member States evaluated information on drugs; and

(5) to report on the above matters to the Executive Board and a future World Health Assembly.

May 1975 226, 35

<sup>1</sup> See resolution WHA26.30

<sup>2</sup> WHO Official Records, No. 226, 1975, p. 96.