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THE RATIONAL USE OF DRUGS

MEXICO: A CASE STUDY<sup>1</sup>

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## THE RATIONAL USE OF DRUGS

### MEXICO: A CASE STUDY<sup>1</sup>

1. The following account of the experience and activity of Mexico up to June 1985 in the field of drugs attempts to describe the control and distribution of drugs.

#### BACKGROUND

2. As a developing country in Latin America, Mexico has a pharmaceutical industry which must be placed in group 5 of those defined by Gerefi, Morrison, Fefer & Antezana in various documents published by the Pan American Health Organization.<sup>1</sup> In a few particular respects, however, its situation differs from that described for the years 1977-1980 in those documents.

3. The present population of Mexico is already almost 80 million, 65% in urban areas and the remainder scattered throughout the country in communities of less than 2500 people. The annual population increase, which was 3.23%, has fallen to 2.6% in the decade 1975-1985. Notwithstanding this fall and optimistic assumptions concerning family planning, Mexico will have a population of 110 million by the year 2010. The morbidity and mortality rates are beginning to show the familiar dual trend of the more advanced developing countries; while mortality rates for respiratory and gastrointestinal infections and malnutrition continue to be high, chronic degenerative diseases and accidents are now among the 10 leading causes of death in the relevant age groups.

4. Although Mexico is at present in the fifteenth place in the world economy, the financial and economic crisis of the last three years has revealed structural weaknesses in the pharmaceutical industry in the country: a serious dependence on foreign imports of basic intermediates; control by the multinational industry extending from parent companies down to national subsidiaries; difficulty in obtaining appropriate technology for the Mexican industry; lack of coordination in research and development in the pharmaceutical field; all compounded by an unreasonably large and chaotic market for pharmaceuticals in the private sector.

5. In December 1982 and the first quarter of 1983 the country suffered severe shortages of drugs and intermediates, partly because of the chronic scarcity of foreign exchange. At that point the President, the Treasury and the Ministry of Health launched an emergency plan for the import or production of vital drugs during the crisis. Although the shortages no longer exist, the Federal Government has subsequently undertaken a series of measures in the health, economic, financial, and structural fields as part of a national development programme to strengthen, stimulate, and regulate the pharmaceutical industry on a rational basis.

6. Fortunately a number of earlier developments helped the country to overcome the emergency by serving as an infrastructure on the basis of which new systems and mechanisms could be created. Briefly, they were as follows.

- From 1958 to 1960, when the Mexican Social Security Institute was rapidly developing into an organization able to provide health care of a high quality for its beneficiaries and the National Medical Centre was founded,

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<sup>1</sup> For example, PAHO/AMRO document CD29-DT-4, 1983.

Dr Bernardo Sepúlveda, whose death this year is deeply regretted, and a group of expert advisers in pharmacology and other related fields drew up the first list of essential drugs and the first National Drug Formulary. These two policy instruments were compulsory only for the Mexican Social Security Institute since at that time there was no real health sector in the sense in which we now understand it and as it operates today.

- In 1977 the National Formulary (Cuadro Básico) for Drugs in the Public Sector, containing 444 generic drugs and 636 presentations or dosage forms, was drawn up, with the aim of introducing it in all health care establishments. The same year saw the establishment of the Interministerial Commission on the Pharmaceutical Industry, which was composed of representatives of the Ministries of Trade, Finance, Health, National Heritage and Industrial Development, and Agriculture, and of the Mexican Social Security Institute (IMSS) and the State Workers' Institute of Social Security and Services (ISSSTE). This Commission proposed a set of minimum standards to be met for the facilities and equipment of the pharmaceutical industry, registration or authorization being accorded to the industries that complied with them.
- Since 1980 consolidated tendering for the procurement of drugs by the health sector has also become official practice, although this system is still being strengthened and perfected.

7. The above developments not only paved the way for the emergency to be surmounted but also led to the decision to establish and strengthen systems and mechanisms for the present and future development of the Mexican pharmaceutical industry.

#### STRUCTURE OF THE MEXICAN NATIONAL HEALTH PROGRAMME

8. The health sector in Mexico is headed by the Ministry of Health and also comprises the IMSS, the ISSSTE, the National System for Integrated Family Development, and the Medical Services of the Federal District.

- The IMSS provides health care and other labour-related benefits and is made up of three major groups: (i) the Federal Government, (ii) employers, and (iii) industrial workers and other employees in commerce and services. All members and their families receive social benefits, which include the preventive, curative, and rehabilitative health care they require. The IMSS, which has been operational since 1944, covers the health care needs of about 30 million Mexicans and provides the drugs needed for the preventive care or treatment of the insured population at no additional cost over and above the general contributions paid by workers, employers, and the Federal Government to finance the Institute's total budget.
- The ISSSTE comprises the Federal Government and the employees who work in the various departments and ministries that make up the Federal Government. Its activities are similar to those of the IMSS and it provides white-collar workers with health care and the drugs this involves. The ISSSTE provides services to about seven million people.
- The Ministry of Health, financed solely by the Federal Government, is responsible for the provision of health services for the general population, i.e., those who have no social security cover. To this end hospital services are being decentralized to the States and the Federal District, so that they will be able to run hospital establishments and provide health

care for deprived urban and rural populations. The Ministry of Health also has authority over the national health institutes, which are high-level teaching and research institutions. It provides health services for about 10 million Mexicans through its decentralized establishments and the national health institutes.

- The other establishments that form part of the health sector cover a population of about 2-3 million.

9. About 50 million Mexicans thus have some kind of access to institutions that provide health care services and procure drugs for them. These 50 million Mexicans represent 65% of the total population of the Mexican republic. This is the majority of the population and therefore the main target of the Government's health programme.

10. The national health programme also includes activities in the field of environmental sanitation that must be carried out on an intersectoral basis throughout the country and activities to promote primary health care in accordance with the Alma-Ata Declaration.

#### NATIONAL FORMULARY FOR DRUGS IN THE HEALTH SECTOR

11. When the health sector was formally constituted by virtue of a resolution published in the Official Gazette of the United Mexican States on 9 June 1983 the President of the Republic, taking as a basis the experience of the IMSS and the official health system with the National Drug Formulary as described above, established the National Formulary for Drugs and Other Inputs for the Health Sector. This new Formulary is considerably wider in scope, covering not only drugs but also laboratory reagents and medical instruments and equipment, dressings and other medical supplies, and relevant scientific information.

12. Under the provisions of the same resolution the Interinstitutional Commission on the National Formulary was set up as a working group of the Council for Public Health, a collegiate body under the authority of the President of the Republic and chaired by the Minister of Health. The resolution entrusted the Commission with the task of keeping the National Formulary under permanent review and making adjustments as necessary.

13. The Commission immediately established its own rules and proceeded in accordance with its mandate to set up special committees composed of representatives from the institutions of the health sector to deal with each section of the National Formulary. It also established relations with the various existing committees and internal commissions in each of those institutions.

14. A procedure was thus set up that would ensure the involvement of the component institutions of the sector in successive stages of the work, as well as providing for participation by experts in the various fields concerned, who were required to reach consensus on the final form of the various sections of the National Formulary.

#### Formulation of the list of essential drugs

15. Once the procedure described above had been established, the next step was to select the products that should be included in the list of essential drugs for the health sector. This was done on the basis of the following criteria:

- (1) selection of drugs with the greatest efficacy and the lowest risk

- (2) elimination of drugs superseded by others of better quality, and inclusion of new products of proven therapeutic value
- (3) deletion of duplicate drugs with the same pharmacological action
- (4) exclusion of unjustified combinations of drugs.

16. The above criteria are in line with the norms established by WHO and a number of other international agencies and follow the precedent established by the previous National Formulary for the public sector in that generic drugs and, whenever possible, single-component drugs are used, in accordance with modern pharmacological practice. The most authoritative recent publications on the subject were also consulted and the views of specialists heard before conclusions were reached on a number of points under discussion.

17. A variety of opinions were expressed and, although there were certain differences, which are only to be expected in matters of this complexity, consensus was achieved. This resulted in a list of essential drugs consisting of 329 generic drugs in 485 presentations or dosage forms. The list included 20 new generic drugs with 34 codes, while 148 generic drugs from the older National Formulary were excluded without in any way detracting from the therapeutic efficacy of the new list, since the drugs excluded were duplications and associations of drugs for which there was thought to be no justification and which were therefore considered unnecessary.

#### Preparation of the National Formulary for Drugs in the health sector

18. After careful selection of the products to be included in the list of essential drugs, the next step was to draw up the National Formulary for Drugs. This process took into account the established condition that the National Formulary should be an instrument to give clear, precise, and concise guidance to doctors in one of their most important activities, namely the prescribing of drugs. Consequently the Formulary was divided into 24 groups, in which drugs were mostly classified in alphabetical order according to their use in different specialties such as anaesthesiology, cardioangiology, and dermatology, or according to their use for specific diseases such as immuno-allergic, infectious, or parasitic conditions. In some cases classification is based on the main indication, such as analgesia or family planning; or on the composition of the drug, e.g. electrolyte solutions or plasma substitutes; or lastly, on the nature of biological agents, such as vaccines, antitoxins, and immunoglobulins.

19. Again following the established pattern, each of these groups was in turn divided into subgroups according to the specific therapeutic action of the drugs, so as to ensure to the greatest extent possible a systematic presentation of their pharmacological effects. The number of subgroups in each group obviously varies in accordance with the particular composition of the different groups.

#### The National Formulary as a guide to therapy

20. The new National Formulary has various important features that provide guidance for treatment. One is the informative text that precedes the subgroups and summarizes the therapeutic indications, undesirable effects, and contraindications. This material has been updated and arranged in a uniform manner to serve as a useful introduction to each chapter for rapid reference.

21. Another feature is the summary tables, in which a description is given of each individual drug. Generally speaking the format used in the earlier version of the National Formulary has been followed, so that it contains a series of columns for the initials of the family doctor, general practitioner, or specialist or the hospital, as required for prescription at different levels. It also includes the generic name of the drug, its code, its dosage form and packaging, the dose and route of administration, and the indications for adults or children. Some changes have been made to these columns in order to make them consistent with the modifications to the National Formulary.

22. The next two columns are of particular interest and contain first of all the indications, carefully revised, followed by the contraindications and undesirable effects. In the light of our better understanding of the risks and hazards of the indiscriminate use of drugs, the contents of this latter column are especially relevant. In the drafting process the contraindications have been reviewed and updated and the list of undesirable effects considerably extended; these effects are enumerated but no attempt is made to rank them according to frequency of occurrence, and the list is not exhaustive. Two further items, entitled "Cautions" and "Pharmacological Interactions", have been added. The "Cautions" point to the particular care with which the drugs should be used in certain specific circumstances, while the "Pharmacological Interactions" indicate, to the extent that this is known, the reciprocal effects of drugs within the body, which sometimes enhance their activity and sometimes do the opposite, with all the concomitant dangers and drawbacks.

23. In general, the old rule that the wrong dose of the right drug is just as likely to result in failure as the administration of the wrong drug should be accepted. The usual doses for the vast majority of cases have therefore been indicated. However, in extreme situations and in other special circumstances doctors must use their judgement and take account of their colleagues' opinion to determine the appropriate use of drugs for the particular needs of individual cases.

#### Exclusive packaging for the health sector

24. The institutions that make up the health sector have decided to adopt an exclusive form of packaging for all drugs included in the National Formulary. This is another distinctive feature of the Formulary and a sign of cohesion among the institutions of the sector. In addition to the practical advantages for the identification of drugs and their use by patients, the intention is to stress the quality of the products selected for the National Formulary. The institutions of the health sector have published a Manual of standards for health sector packaging, which contains all the relevant specifications so as to facilitate their uniform application by suppliers.

25. Advances in pharmaceutical science, scientific innovations leading to the development of therapeutically significant new drugs, and scope for improvement of the list of essential drugs as contained in the National Formulary result in the need for its continuous review and updating. Hence, following the WHO recommendation that models should be used but adapted to the particular needs and requirements of individual countries, the Council for Public Health in 1985 published a supplement updating the National Formulary for Drugs and incorporating the amendments and suggestions made by the country's scientific community, doctors, pharmacists, and chemists, the analytical quality control system of the health sector, and the pharmaceutical industry. Some 95% of the modifications concern points of detail relating to international nonproprietary names, specific salts and their active ingredients and, in some cases, dosages and dosage forms. Two further generic drugs have also been included and two excluded on the ground of their long-term toxicity.

26. The National Formulary for Drugs is now in use in 90% of the sector's institutions.

#### LEGISLATION ON DRUGS AND ON THE PHARMACOCHEMICAL AND PHARMACEUTICAL INDUSTRY

27. All the measures described are aimed at obtaining the best, most effective, safest, and least expensive drugs so as to benefit both the final consumer and the intermediary, i.e., the physician. It has therefore become very important to update and adapt the legislation to make it into an adequate and reasonable framework for activities.

28. The right to health protection has been embodied in the Constitution.

29. Two invaluable legislative and scientific/technical documents closely concerned with drugs were published on 23 February 1984: the Comprehensive Programme for the Development of the Pharmaceutical Industry 1984-1988, and the derivative Presidential Decree for the Promotion and Regulation of the Pharmaceutical Industry.

30. This legislation takes into account the history of the industrial infrastructure up to 1982, the critical drug shortage that occurred during the first quarter of 1983, and procedures and mechanisms for enabling Mexico, following a thorough analysis, to produce and regulate its own drugs rationally without neglecting the complex and expensive research and development work on genuine therapeutic innovations, including the biotechnical pharmacological revolution. Advances resulting from this work will be incorporated into the National Formulary for Drugs whenever justified, bearing in mind the need to encourage the national industry financed mainly with Mexican capital, but without discriminating against international industry insofar as it complies with general industrial, commercial, and health promotion policies.

31. The General Health Law that came into force on 10 July 1984 contains legislative provisions governing both the setting-up of pharmaceutical enterprises and their products, i.e., drugs as finished products made available to the public.

32. In order to make the legislation on the Comprehensive Programme and on the Pharmaceuticals Decree clear and comprehensible, rules for implementing the legislative measures were published, following negotiations and hearings, in October 1984. The Government encountered opposition, as provided for under the country's democratic system: 38 pharmaceutical companies established within the country, all of them branches of multinational concerns, challenged the three legislative measures enacted. It should be pointed out that 38 other multinational companies and 308 national companies financed mainly with Mexican capital did not take any legal steps to challenge the measures. The four main points in the legislation that led to the objections were as follows:

(1) An inaccurate interpretation of the Programme and Decree as totally protectionist measures favouring the Mexican industry, which is to make greater efforts to bring about vertical integration in the national production of starting materials and active intermediates for the preparation of essential drugs in accordance with the health requirements of the Mexican people. This measure does not exclude or discriminate against multinational companies in regard to the manufacture of new pharmaceutical products.

(2) The use of generic names without the registered trademarks on all products on sale to the health sector in accordance with the National Formulary, and addition of the generic name to the registered trademark of

products in the private sector that contain the same generic substances, formulae, and dosage forms as those in the National Formulary. In such cases the rules stipulate that the dosage forms of private sector drugs, like those in the National Formulary, must be adjusted to contain the same number of units as stated in the National Formulary and include on their labels the code number for the drug given in the National Formulary.

(3) Following the inclusion of a drug of therapeutic importance in the National Formulary, the rules provide for a period of three years' grace before the generic name must be added to the label and the dosage form adjusted.

(4) The elimination of drugs from the register - the provision that approved therapeutic novelties must be genuinely important advances, the refusal to register a large number of duplicate formulae (there are 68 trade names for the generic drug ampicillin, 112 registered trademarks for vitamin preparations and similar products, etc.), and the ban on irrational combinations of drugs that lead to large numbers of toxic reactions and to dosages that are not appropriate for individual therapeutic needs.

33. All these objections, which led to the challenge by 38 multinational companies, were the subject of negotiations with the Departments of Trade and Industrial Promotion and the Department of Health. The objections were given a full hearing and, after some minor concessions, they were approved in the Resolution establishing Rules for Implementing the Decree on Promotion and Regulation of the Pharmaceutical Industry, which was published on 2 April 1985 and annulled the previous resolution. The Comprehensive Development Programme and the Decree on the Promotion and Regulation of the Pharmaceutical Industry remained unchanged.

34. The present Resolution on Rules for Implementing the Pharmaceuticals Decree, which makes new national procedures for vertical in-depth integration compulsory, is consistent with the implementation of Mexican and international joint investments and has led to 30 new tenders for the manufacture of pharmaceutical preparations and active intermediate substances included among the 70 listed as priorities, so that 40% of these substances are now being manufactured in the country as compared with 20% in 1982.

35. The practical implementation of the rule that the registered trademark must be accompanied by the generic or international nonproprietary name produced some opposition from the international pharmaceutical industry, which argued that the generic substances are not bioequivalent with the national products. Studies of the bioavailability and dissolution of some of these products have already been made, and show that some drugs from the international market present serious problems of absorption, pharmacokinetics, and pharmacodynamics as compared with similar products manufactured within the country (IMSS, 1984). Strictly speaking, this has created greater requirements in regard to the pharmacokinetics of the drugs, regardless of whether they are manufactured by multinational or by national companies, and the origin is not taken into account when conducting the analytical tests. Fortunately the quality control system of the health sector exercises strict control in this respect, only giving approval to optimum batches.

36. The Resolution also lays down the terms of reference and purposes of the semi-State drug companies Vitrium and Proquivemex, the only two semi-State pharmaceutical companies run by the Mexican Government, in respect of fundamental aspects that are also covered by the 1984 Decree on the Promotion and Regulation of the Pharmaceutical Industry. Vitrium manufactures starting materials and priority intermediates of drugs and active principles which private industry does not

produce: vaccines, biologicals, oligopoly drugs, "orphan" drugs, and drugs for the health sector that are chronically in short supply. Proquivemex is responsible for the manufacture of some finished products on the list of essential drugs given in the National Formulary.

#### PRESENT STATUS OF THE PHARMACOCHEMICAL AND PHARMACEUTICAL INDUSTRY

37. Sales of drugs in Mexico currently amount to approximately US\$ 1200 million. In 1982 the health sector accounted for 25% and the private sector for the remaining 75%. In 1985 sales to the health sector have increased to about 40% of the total.

38. Consolidated tendering for procurement of drugs and other supplies for the health sector underwent some changes in 1984. For the first time the total sales of Mexican companies to the public sector exceeded those of the multinationals, 53% as against 47% (44% and 56% in 1982), and a Mexican company now occupies first place in terms of sales to the health sector.

39. In 1982 there were 76 pharmaceutical companies in Mexico financed mainly by foreign capital, and their sales in that year accounted for 72% of the total market. The remaining 28% was distributed among the 242 companies financed mainly by Mexican capital. There are at present 380 registered pharmacochemical and pharmaceutical companies, and the total share of sales of those financed mainly with Mexican capital, although still lower than that of the multinational companies, has increased to 38%. In 1981 only 11 Mexican companies were among the 50 pharmaceutical companies with the highest production and sales; in 1985 there were 16 Mexican companies in this group.

40. The pharmaceutical industry established in Mexico is not self-sufficient in active principles and intermediate materials for drugs. In 1982 approximately 80% of active principles and intermediates had to be imported, entailing an annual outflow of some US\$ 250 million. This was the largest item of expenditure on imports in the sector total of US\$ 300 million. Since income from exports was only US\$ 100 million, there was a deficit of US\$ 200 million. At present 40% of starting materials and basic intermediates are produced within the country and the aim is to attain 65% by 1988. In 1984, the trade deficit was US\$ 106 million.

41. In contrast to the sector manufacturing finished drugs, the 60 pharmacochemical companies financed mainly by Mexican capital accounted for 65% of total sales in 1984, as against 46% in 1977, and have thus overtaken the multinational pharmacochemical companies.

42. As is evident throughout this document, the national policy of the pharmaceutical industry has been formulated and guided by the firm political, health, and industrial policy of the country's highest authorities, who despite the difficulties that have been encountered remain determined to achieve the objectives of the programme.

#### RESULTS AND CONCLUSIONS

43. The policy for the registration of new drugs can be seen to have undergone a substantial change: from July 1983 to June 1984 350 products were registered, 90% of them duplicating already existing formulae, but during the corresponding period in 1984-1985 only 57 products were registered, of which 8 were important novelties and the remainder were generic drugs identical with those in the National Formulary and single-component drugs.

44. Similarly, and in compliance with the Rules for Implementing the Decree, 1200 products intended for the private market had the number of units in their dosage forms adjusted by June 1985, and already display the generic name or international nonproprietary name together with the trademark. These 1200 private sector products represent 245 generic drugs contained in the National Formulary, i.e., progress has been made on about 75% of the process initiated in February 1985. The 1200 adjusted drugs are manufactured by 122 pharmaceutical companies, including 16 multinationals that have expressed reservations but have already complied with this provision under the new Resolution on Rules after lengthy talks and negotiations with the Departments of Health, Trade, and Industrial Promotion. It should be pointed out that these multinational companies explicitly consider that the step they have taken of their own accord will facilitate settlement of the legal process instituted against the Federal Government so that the reservations can be withdrawn.

45. The new regulations concerning the General Health Law will enable the national health authorities to carry out the process of purging the registers by eliminating ineffective and obsolete products and, above all, by reformulating the numerous multi-component drugs or associations of drugs (50% of the total) that have been a feature of the irrational proliferation of trademarks in the private market.

46. The section of the National Formulary dealing with drugs has already been introduced in 90% of the health sector, and the section dealing with curative and prosthetic equipment in 100%. This has made it possible to strengthen bulk purchasing within the health sector by building up a grading system for suppliers, cutting costs, putting an end to discretionary expenditure and purchases, rationalizing the procurement of supplies and equipment, facilitating distribution and transport and, a very important point, genuinely promoting the industries manufacturing supplies and equipment, for the National Formulary is an instrument for and a guideline to the priority activities of the health sector.

47. These last three points give greater relevance to the measures taken to ensure the rational use of drugs in both prescribing and retailing and supply to the public. Even self-medication is becoming less chaotic. The measures also enable the trade authorities to fix equal prices for equal products, thus rationalizing the process and ensuring greater savings for the final consumer.

48. A programme of basic drugs derived from the list of essential drugs has been initiated. These drugs may be retailed freely at preferential prices on account of their high level of consumption.

49. Mechanisms for research and technological development in Mexico have since 1984 been effectively integrated and coordinated under the sponsorship of the State departments involved, higher education establishments, and groups of research workers in pharmacology and pharmacy, under the guidance of the Health Department and the National Council for Science and Technology. Industry has joined in this work, and 30 projects concerning new active pharmaceutical substances are already in progress. The research and development function within the companies has likewise been strengthened through a commitment to invest at least 4% of their sales of starting materials in this activity.

50. In September 1984 a standing committee for updating the Pharmacopoeia of the United Mexican States was officially set up. It has completed about 40% of its work.

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51. An endeavour has been made to summarize what Mexico has been doing to ensure the rational use of drugs. Although much still remains to be done, it is believed that the steps initiated and now in progress will provide a more rational basis for the control and distribution of drugs.

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