

## BIBLIOGRAPHIC DATA SHEET

1. CONTROL NUMBER  
PN-AAH-5952. SUBJECT CLASSIFICATION (695)  
NCOO-0000-0000

## 3. TITLE AND SUBTITLE (240)

Planning pharmaceuticals for primary health care; the supply and utilization of drugs in the Third World

## 4. PERSONAL AUTHORS (100)

Gish, Oscar; Feller, L. L.

## 5. CORPORATE AUTHORS (101)

Am. Public Health Assn.

## 6. DOCUMENT DATE (110)

1979

## 7. NUMBER OF PAGES (120)

147p.

## 8. ARC NUMBER (170)

615.19.G532

## 9. REFERENCE ORGANIZATION (130)

APHA

## 10. SUPPLEMENTARY NOTES (500)

(In APHA International Health Programs monograph series no. 2)

## 11. ABSTRACT (950)

## 12. DESCRIPTORS (920)

Drugs	Health planning
Medical services	Delivery systems
Supply	Pharmaceutical industry

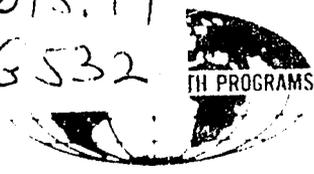
## 13. PROJECT NUMBER (150)

931097100

14. CONTRACT NO.(140)  
AID/ta-C-132015. CONTRACT  
TYPE (140)

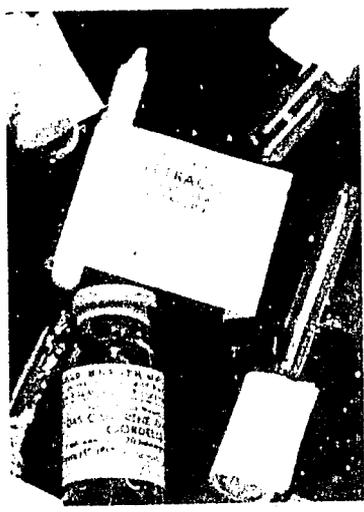
## 16. TYPE OF DOCUMENT (160)

615.19  
G532



# PLANNING PHARMACEUTICALS FOR PRIMARY HEALTH CARE: THE SUPPLY AND UTILIZATION OF DRUGS IN THE THIRD WORLD

Oscar Gish, M.S.S., M. Phil.  
Loretta Lee Feller, M.P.H.



MONOGRAPH SERIES

**PLANNING PHARMACEUTICALS  
FOR PRIMARY HEALTH CARE:  
THE SUPPLY AND  
UTILIZATION OF DRUGS IN  
THE THIRD WORLD**

by

**Oscar Gish, M.S.S., M. Phil.  
Loretta Lee Feller, M.P.H.**

**AMERICAN PUBLIC HEALTH ASSOCIATION  
INTERNATIONAL HEALTH PROGRAMS  
MONOGRAPH SERIES  
NO. 2**

**Herbert T. Dalmat, Ph.D.  
Project Director**

Funded by  
The Agency for International Development  
Contract AID ta-C-1320

1979

**Views expressed by authors do not necessarily reflect those of APHA or AID.**

**Cover photos: WHO 12041 by Almasy, 9137 by Spooner, 17207 by Abcede, and 11803.  
UNICEF 5065 by Tardio and 4363 by Ling.**

**American Public Health Association  
International Health Programs  
1015 Fifteenth Street, N.W.  
Washington, D.C. 20005, U.S.A.**

## PREFACE

The place of pharmaceuticals in primary health care, while of self-evident importance, has been relatively neglected in the general health care literature. As attention is directed towards elements within health care systems, and to the problem of what works, what does not work and why, issues of selection, procurement, and distribution of pharmaceuticals quickly come to the attention of all concerned.

In the total budgets of health ministries of developing countries, sometimes as much as 40 percent of available funds are expended for medications and biologicals. When even closer attention is paid to the activities and specifics surrounding the selection, procurement, supply, and distribution of pharmaceuticals, it becomes even more evident that opportunities exist for improving performance, and for achieving economies through thoughtful examination of practices and policies by LDC officials and cooperating countries. This monograph has been commissioned to stimulate debate, raise the level of consciousness, and promote thinking about the pharmaceutical subsector within health care. It is not meant to be a "how-to" manual, but does bring together in a single source information for decision-makers who have neither time nor easy access to widely scattered literature on the subject.

Donald C.E. Ferguson, Ph.D., M.P.H.  
Chief, Health Delivery Systems  
Office of Health  
Development Support Bureau  
Agency for International Development

# FOREWORD

As the thrust for achieving more adequate levels of "health for all by the year 2000" gains momentum, increasing attention is focused on finding appropriate solutions to the complex problems of expanding and extending health care.

Given the heavy burden of illness, the scarcity of resources, and the lack of adequate input of previous systems, it is increasingly apparent that new approaches must be found. With the recognition that the conventional patterns of curative, hospital-based, high technology medicine do not offer adequate solutions, a growing emphasis is being placed on promotion of health through more integrated actions of health care, sanitation, education, agriculture, transportation, and a renewed emphasis on participation by individuals and communities stressing the need for utilizing previously untapped resources.

Numerous challenges are posed by this effort, pointing up the many unanswered questions, unsolved problems, inadequate information sources and unexplored issues.

In addressing this, the American Public Health Association has established a Health Information Exchange through which it generates, collects, analyzes, and disseminates information on issues in health care delivery. As a part of this effort, a monograph series will review some of the critical subjects of concern such as comprehensive planning, manpower development, financing, environmental aspects of health programs and mobilization of the private sector. These reviews strive to synthesize available knowledge in a format of interest and use to individuals concerned with the planning and implementation of health care programs.

Problems of pharmaceutical supply and utilization are fundamental to extending health care, but have received relatively little attention. In this monograph, Mr. Gish and Ms. Feller provide an overview of basic issues regarding pharmaceuticals, in terms easily understandable to non-economists. The authors look at important questions relating to the availability of medicaments, and alternative ways of providing them. We hope that the volume will increase understanding of these issues and assist in the complex search for appropriate methods of improving health around the world.

Herbert T. Dalmat, M.S., Ph.D.  
Project Coordinator  
International Health Programs  
APHA

Susi Kessler, M.D.  
Director  
International Health Programs  
APHA

## AUTHORS' NOTE

This volume does not pretend to offer instant, "cookbook" solutions to what are very complex problems. Rather, its purpose is to offer to the reader an introduction to the variety of issues involved in the "supply and utilization of drugs in developing countries." Virtually all of the material now available in this area tends to concentrate upon only one or another of the several aspects of supply or distribution. This monograph is an attempt to put together within one set of covers a discussion of many, if not most, of the issues involved in the planning of pharmaceuticals, especially in the less developed market economies.

Two basic assumptions of this work are that, other things being equal, it is desirable for Third World countries to move towards increased self-reliance in drug production, and that this goal will be more quickly achieved in the context of drug policies directed in the first place toward widespread coverage of the population with basic primary health care services.

Many people have provided direct assistance to the preparation of this volume. These include staff members of such international agencies as UNCTAD, UNIDO, UNICEF and WHO, civil servants from several Third World countries, and many university and other scholars working in the United States, Great Britain and other parts of the world.

In fact, the number of helpful people has been so large as to preclude individual mention; here, we can only express gratitude for their collective assistance. However, special mention must be made of the help given by Professor Brian Abel-Smith (U.K.), Professor Pierre Chaulet (Algeria) and Professor Robert Grosse (U.S.). We also must thank Dr. S. Kessler of the International Division of the American Public Health Association for her support, and Dr. H. Dalmat of the same organization for his often painstaking efforts in helping to see this project through to a successful conclusion.

Oscar Gish  
Lee Feller  
School of Public Health  
The University of Michigan

## AUTHORS' PROFILES

**Oscar Gish** is teaching at the Department of Health Planning and Administration in the School of Public Health, The University of Michigan. From 1973 to 1976 he was a Research Fellow of the Institute of Development Studies at the University of Sussex, England. From 1971 through 1973 he was *de facto* head of the Planning and Analysis Unit of the Ministry of Health in Tanzania. Prior to this Mr. Gish was briefly attached to the Netherlands Economic Institute, after spending four years with the Science Policy Research Unit at Sussex University. He has studied in the United States, the Netherlands, and Great Britain, where he received degrees in history, the social sciences, and economics; his final degree was an M. Phil. Mr. Gish has written numerous articles, edited *Health Manpower and the Medical Auxiliary*, and published a volume titled *Doctor Migration and World Health*. His most recent books are *Planning the Health Sector*, published in 1975 and reissued in 1978 by Croom Helm (London), *Guidelines for Health Planners*, published in 1977 by Tri-Med (London) and with Godfrey Walker, *Mobile Health Services*, also published by Tri-Med in 1977.

**Ms. Lee Feller** received her Master's degree from the School of Public Health at the University of Michigan in 1977. Prior to that time she traveled extensively throughout Latin America and was employed in the areas of family planning and rural health services in the United States. Ms. Feller is currently Research Coordinator at PRETERM, Inc., a center for reproductive health in Washington, D.C.

# TABLE OF CONTENTS

	<i>Page Number</i>
I. INTRODUCTION .....	1
1.2 International Trade in Pharmaceuticals.....	1
1.2 The Need for Drugs .....	3
II. THE TRANSNATIONAL PHARMACEUTICAL INDUSTRY	7
2.1 History .....	7
2.2 The Structure of the Pharmaceutical Industry.....	9
2.3 Research and Development (R&D) and the Patent System	14
i. R & D	
ii. The Patent System	
2.4 Promotion .....	20
2.5 Pricing and Profitability .....	22
III. PHARMACEUTICAL PRODUCTION IN DEVELOPING COUNTRIES .....	35
3.1 Production by Subsidiaries .....	35
3.2 Issues in Technology Transfer .....	37
i. Licensing Agreements	
ii. Appropriate Technology	
3.3 Stages of Drug Production .....	44
3.4 The Pharmaceutical Industry and the Public Health Service .....	46
IV. PURCHASING .....	51
4.1 The Formulary System of Drug Procurement .....	51
i. Therapeutic Need	
ii. Evaluation of Safety and Effectiveness	
iii. Nomenclature	
iv. Criteria for Selecting Cost-effective Drugs	
4.2 Centralized Procurement .....	67
4.3 The Organization of the Drug Supply System.....	70

V. UTILIZATION.....	77
5.1 Drug Prices.....	77
5.2 Drug Prescribing .....	79
5.3 Pharmacy Workers .....	86
VI. DISTRIBUTION .....	93
6.1 National Patterns of Drug Distribution .....	93
6.2 Delivery Systems .....	94
VII. SUMMARY CONCLUSION .....	98
7.1 Summary, Recommendations, and Research Needs .....	98
i. Supply Conditions	
ii. Procurement Planning	
iii. Planning the Drug Utilization System	
7.2 Regional and International Cooperation .....	105
ANNEXES	
A. Patent Abuse .....	108
B. WHO Model List of Essential Drugs .....	121
C. Glossary of Terms .....	135
D. Selected Bibliography .....	138

# I.

## INTRODUCTION

### 1.1 *International Trade in Pharmaceuticals*

The figures shown in Table 1.11 are only roughly indicative of average per capita demand for pharmaceutical products, but the relatively low estimates for the less developed countries listed, particularly India and Nigeria, suggest that a large segment of the world's population does not

Table 1.11

ESTIMATED GLOBAL PURCHASES OF HUMAN  
PHARMACEUTICALS BY MAJOR WORLD REGION AND COUNTRY,  
1975

(U.S. Dollars, Manufacturers' Prices)

	<u>Regional Total</u> (millions)	<u>Country Total</u> (millions)	<u>Per Capita</u> <u>Averages</u>
World Total	\$37,500		\$ 9.60
North America (incl. Caribbean)	9,000		
U.S.A.		\$7,500	35.05
Mexico		800	13.70
South America	2,400		
Brazil		1,000	9.30
Argentina		600	26.10
Western Europe	12,750		
France		2,750	51.90
West Germany		3,350	53.35
U.K.		1,100	19.50
Sweden		300	36.60
Eastern Europe	5,250		
USSR		3,500	13.70
Asia	6,800		
Japan		4,250	38.45
India		450	0.75
Africa	825		
South Africa		275	11.10
Nigeria		75	1.20
Oceania	475		
Australia		400	29.65

*Note:* Because of definitional uncertainties, lack of comparable statistics, possible double counting, currency fluctuations, and differences in inflation rates, the data in this table reflect rough estimates only.

Source: L. Schaumann, Pharmaceutical Industry Dynamics and Outlook, Stanford Research Institute, Menlo Park, California, 1976, p. 16.

TABLE 1.12  
INTERNATIONAL TRADE IN MEDICINAL PRODUCTS, 1969 AND 1974  
(Value as percentage of World Market Economy Countries)

	IMPORTS		EXPORTS	
	1969	1974	1969	1974
<u>Developed Market Economy Countries</u>	62.4	67.1	94.2	92.8
American	6.3	6.2	17.1	14.6
Asian	7.1	8.0	2.4	2.5
European	45.0	48.6	73.5	74.6
<u>Developing Market Economy Countries</u>	37.6	32.2 (1973)	5.8	7.2
<u>10 Principal Trading Market Economies</u>	41.7	46.7 <sup>a</sup>	86.8	84.4 <sup>b</sup>

<sup>a</sup>Includes FRG, Japan, Italy, Belgium/Luxembourg, France, Netherlands, USA/PR, UK, Spain, Sweden (in order of magnitude).

<sup>b</sup>Includes FRG, USA/PR, Switzerland, UK, France, Italy, Netherlands, Belgium/Luxembourg, Denmark, Japan (in order of magnitude).

Source: United Nations Yearbook of International Trade Statistics, 1976, Volume II, p. 103.

have access to modern drugs.\* Considering that only the more significant drug producing countries are listed in this table, and that India, Mexico, Brazil and Argentina account for a large proportion of total drug production accomplished by the developing group of countries, the estimated percentages of drug imports into developing countries shown in Table 1.12 reflect very low average consumption levels among a

\*The literature about 'drugs' or 'pharmaceutical products,' etc. is not always clear with regard to the usage of the terms within specific contexts. Sometimes 'drugs' refers to pharmaceuticals expected to be available only on prescription, but often all medicaments intended for human consumption are so designated. The authors have tried to be consistent in the use of these terms, at least in so far as allowed by available sources of information. Except when specifically indicated, herbal and other traditional medicaments are not included in the discussion.

substantial number of countries having little or no nationally based industry. Accurate figures are not available, but market surveys indicate that developing countries account for less than 20 percent of world pharmaceutical consumption. Table 1.13 shows some 1976 estimates of continental drug consumption.<sup>1</sup>

Table 1.13

World Drug Consumption, 1976 (%)

Europe	45.8
Americas	26.9
Asia	23.7
Africa	2.4
Oceania	1.1

Table 1.14

Production of Pharmaceuticals in Selected Developed Market Economy Countries, 1963 and 1970  
(U.S.\$ million)

Country	Value of output		Percentage of total		Average annual growth rate (1963-70)
	1963	1970	1963	1970	
Canada	222	457	2.9	2.8	10.9
France	755	1372	9.9	8.4	8.9
Germany, Fed. Rep.	643	1643	8.4	10.0	14.4
Italy	492	1104	6.4	6.7	12.2
Japan	942	2825	12.3	17.2	17.0
Netherlands	96	242	1.3	1.5	14.1
Switzerland	(n.a.)	450(est.)	-	2.7	-
United Kingdom	450	700	5.9	4.3	6.6
United States	3716	7000	48.7	42.6	9.4
Sub-total	7316 <sup>a/</sup>	15793	95.8	96.2	11.6
Other <sup>b/</sup>	312	622	4.2	3.8	10.3
TOTAL	7628 <sup>a/</sup>	16415	100.0	100.0	11.6

<sup>a/</sup> Excluding Switzerland

<sup>b/</sup> Australia, Austria, Belgium, Denmark, Finland, Norway and Sweden

Source: UNCTAD, A case study of the pharmaceutical industry (TD/B/C.6/4) 1975, p. 7.

The great bulk of drug production has been centered in a very few countries. About 80 percent of total output in 1963 and 1970 was accounted for by France, the Federal Republic of Germany, Italy, Japan, and the United States (Table 1.14). According to United Nations trade figures for 1974, these countries exported about 60 percent of the total value of medicinal products moving in international commerce. When another major producing country, Switzerland, is included, six countries accounted for about 75 percent of the total value. One of the most important aspects of this concentration is that poor countries have very little control over the production of drugs, and therefore the final prices. Of particular importance is the fact that all countries purchasing from private firms heavily engaged in export production must bear the costs that these firms devote to competitive international marketing activities. The extensive expenditures of the leading firms on competitive technological development (R & D) and promotion will be discussed further with special reference to the oligopolistic market conditions and pricing practices that have been observed in recent studies of the transnational pharmaceutical industry.

## *1.2 The Need for Drugs*

The price of drugs, however, is not the only issue at hand. The search for relief from painful or unwanted physical symptoms is probably as long and varied as human history. The most ancient records of human civilization throughout the world carry references to herbal concoctions, extracts, charms, mineral powders and special words or ceremonies designed to prolong life or at least make it more pleasant.

Traditionally, the creation of "cures" was not repetitive in the sense of mass production techniques. The conscious activity of developing a cure involved not only the practitioner's knowledge of the materials used, but also an understanding of individual patients within the context of their shared community environment. The medical practitioner generally was regarded as a respected member of the community, and it may be assumed that the strong belief of patients in the therapies of traditional practitioners added significantly to their actual effect.<sup>2</sup>

Certain forms of medicine practiced today involve a similar emphasis on an understanding that extends beyond specific physical symptoms. In ayurvedic medicine the practitioner classifies individual patients according to their general physical condition as well as their mental disposition, and this classification is used in conjunction with a clinical diagnosis of the disease in choosing a treatment.<sup>3</sup> A shared community environment is an important element in many traditional treatments for "nonspecific" or psychosomatic symptoms, in that traditional psychotherapy requires that the practitioners grasp the broad social meaning of patients' symptoms.

Symptoms are often interpreted as “manifestations of a conflict between the patient and other individuals, dead or alive, spirits and the non-material forces that pervade society.” In order to devise a treatment the practitioner must discover the disruption in the patient’s interaction with the social, economic, and cultural fabric of society.<sup>4</sup>

Modern Western medicine took a sharp turn away from traditional therapeutics in the first decades of the twentieth century. During the period when biomedical research led to a series of breakthroughs in curative drug therapy, initially the sulfa drugs, the foundation of scientific laboratory based research upon which modern medical practice is based came to be viewed as increasingly important relative to practitioners’ broad social knowledge of individual patients.

Scientific research on the fundamental structures and operations of living organisms is undoubtedly related to extraordinary gains in human capability to resist and cure disease. At the same time it appears that the reduction of therapy to pills and potions has contributed to the neglect of the social and environmental aspects of human health. As Rene Dubos wrote in *Mirage of Health* (1959):

The belief that disease can be conquered through the use of drugs fails to take into account the difficulties arising from the ecological complexity of human problems . . . the accounts of miraculous cures rarely make clear that arresting an acute episode does not solve the problem of disease in the social body—nor even in the individual concerned.<sup>5</sup>

Despite the limited value of drug treatment, those populations financially capable of procuring drugs have been highly receptive to the therapeutic methods used by modern medical practitioners. In part this is due to an entirely valid recognition of the immediate life-saving effects of drugs such as the penicillins and quinine. However, it is also representative of the assumption implicit in the organization of modern Western scientific medicine—that people can purchase health passively.<sup>6</sup> The spread of uniform consumption patterns and aspirations among the world market economies has brought this same type of organizational relationship between patients, medical practitioners and pharmaceutical technology to poor societies whose health needs are more related to a cleaner environment, improved sanitation facilities and the production of more food for local consumption. As such, health resources have been drawn toward a form of technology which is *at once* divorced from the complex reality of human illness, and which has focused on the development of an increasing number of new drugs at the expense of the efficient production of drugs already proven supportive to preventive and curative health services at the primary care level.

The comments about drug utilization made by Dubos many years ago are still relevant today, considering the continuing virulence of many contagious diseases for which successful curative treatments have long

been established. In the face of rising public expenditures on pharmaceutical products, health resource planners must begin to examine the effectiveness of drugs *in terms of the elimination of diseases from the social body*, rather than only the individual patient or experimental group. In many countries this type of analysis would require an additional grouping (e.g., a national "formulary committee") within the division of the public health sector that is responsible for the registration of drugs. Such divisions are not primarily responsible for weighing the scientific evidence supporting the safety and effectiveness of specific pharmaceutical products in the treatment of individual cases of disease, and this is a major regulatory task in itself.

An analysis of the broad effectiveness of drug consumption by such a committee would primarily involve the determination of nationwide therapeutic need and related studies of the social, economic, and technological influences affecting the supply of drugs and their utilization by the population. One of the most significant influences in this regard has been the transnational pharmaceutical industry, and the discussion that follows outlines some of the unique characteristics of the industry with special reference to the Third World.

## FOOTNOTES

1. Figures appearing in the WHO Background Document for reference and use at the Technical Discussion on "National Policies and Practices in Regard to Medicinal Products; and Related International Problems" (A31 Technical Discussion 1), 6 March, 1976.
2. Cousins, N. The Mysterious Placebo: How Mind Helps Medicine Work, *SR* 10:9-16 (1977).
3. Traditional Medicine: some examples of its use, *WHO Chronicle* 31:428-432 (1977).
4. Harding, T. Traditional Reading Methods for Mental Disorders, *WHO Chronicle* 31:436-440 (1977).
5. Dubos, Rene. *Mirage of Health* (New York: Harper and Row, 1959) pp. 161-162.
6. For an interesting discussion of this and related concepts, see Titmuss, R.M. Sociological Aspects of Therapeutics, in P. Talalay (ed.), *Drugs in Our Society* (Baltimore: Johns Hopkins, 1964).

## II.

# THE TRANSNATIONAL PHARMACEUTICAL INDUSTRY

### 2.1 *History*

The relatively recent expansion of the modern pharmaceutical industry in the developed market economies is integrally related to the discovery of sulfa drugs by academic laboratories, particularly the initial isolation of sulfanilamide by scientists at the Pasteur Institute in 1935.<sup>1</sup> Prior to these discoveries pharmaceutical technology was considered to be more or less stable and, as with most commodity businesses, the costs of labor, materials and administrative expenses accounted for most of the sales returns on drugs. Research expenditures during this early period were minimal (2-4 percent of sales) compared to current levels.<sup>2</sup> Scientific breakthroughs are often put forward as the primary stimulus for the increasingly research-intensive character of the pharmaceutical industry, i.e., the readily acquired basic research discoveries permitted new entrants to the market, established firms perceived a threat to their sales position, and a new era of competition through product differentiation began.<sup>3</sup> This view certainly has some basis in the history of events, but before describing the particular structure and operations of the transnational pharmaceutical industry a broader historical framework will be outlined which takes into consideration additional factors which have added impetus to its development.

Modern Western drugs are mostly chemical substances derived from the petrochemical or fermentation industries. The earliest technological innovations in the field of chemically based drugs took place within the German chemicals industry, which was the only major international supplier before World War I. The problems associated with reliance on one supplier of materials critical to national welfare was perceived during the war, when the German chemical industry temporarily withdrew from the world market.<sup>4</sup> The British government, among others, included chemicals in its policy of key industry duties on imports, which allowed local firms to achieve substantial growth within their home markets.<sup>5</sup>

Such direct government support during the early stages of development of the fine chemical industry was an important determinant of later developments in the modern pharmaceutical industry. This was particularly true in Europe, where the leading pharmaceutical firms were created as subsidiaries of chemical companies. In a report to the International Social Security Association it was pointed out that because the pharmaceutical industry is closely connected with the chemical industry, which as a whole involves a powerful concentration of capital, the growth of the pharmaceutical sector has been strongly influenced by the expansionary

trends of its parent firms. Because the intensive research efforts involved in pharmaceutical development raise manufacturing costs considerably and capital outlays have to be recouped more quickly than drug sales allow, this sort of vertical integration has become a very important component in the market power of many leading firms.<sup>6</sup>

Perhaps of equal importance has been the role of governments in developed countries in directing public funds toward the training of scientific professionals, as the process of research-intensive industrialization called for an increasingly specialized division of labor. In fact, the early supremacy of the German chemical industry has been explained by its extensive employment of chemists and engineers in the first decade of the twentieth century and its initial integration of universities, industrial laboratories, professional societies and trade unions into industrial research efforts.<sup>7</sup>

During roughly the same period, an organizational movement by Western medical professionals resulted in the transformation of medical schools from training centers for primary care practitioners into more scientifically specialized institutions.<sup>8</sup> Physician orientation thus shifted toward more highly specialized forms of curative medicine, which led to greater support for the pharmaceutical industry's search for new drugs having relatively narrow potential therapeutic value to society. In turn, the availability of these highly effective new drugs increased the market for physicians' services, at least in the countries in which the most potent drugs could only be bought after medical consultation. As the pharmaceutical industry expanded, the links between industrial promotion and medical education strengthened to the point where the industry became the primary source of physician information on new drugs, and the number of drugs prescribed increased substantially.

In summary, several interacting trends fueled the research and development function of the modern pharmaceutical industry. Because pharmaceutical firms in the major drug producing countries of today were initially linked to industries with large amounts of surplus capital, new ideas emanating from public support of scientific education could rapidly be transformed into marketable drugs.<sup>9</sup> The shift in medical education toward greater specialization in curative medicine broadened the potential market for new drugs, and pharmaceutical firms were able to make enormous gains in a relatively brief period. An additional point that should be stressed here is that although the profitability of the transnational pharmaceutical industry has received a growing volume of attention in recent years, the substance of the issue is better understood in terms of a much broader pattern of industrialization involving the progressive accumulation of available capital and technical expertise by the leading firms and an orientation toward extensive promotion of new products. In this sense the relationship between the highly profitable pharmaceutical industry and the state has become increasingly complex in all of the market economies, as the state must act as "facilitator" in the

process of industrial growth and as mediator between the interests of the industry, the medical profession, and the consuming public.<sup>10</sup>

## 2.2 *The Structure of the Pharmaceutical Industry*

Structural indices of competition in the pharmaceutical industry, the number and size distribution of firms in the market, show the concentration of drug production into the hands of a few transnational pharmaceutical companies (TNCs) to have been increasing over time.<sup>11</sup> For example, a recent study estimates that of the 2,000 to 3,000 companies that could be considered "broadly competent dose-form pharmaceutical operations," only about 100 supply 90 percent of total world shipments. The leading 25 firms account for over 50 percent of the total and the major 14 about 30 percent.<sup>12</sup> An earlier study indicated that by 1990 world pharmaceutical production and marketing will be mostly divided among one to two dozen companies.<sup>13</sup> Table 2.21 shows some of the recent sales figures provided by the leading TNCs. A comparison of these data with earlier sales figures leads to the conclusion that the top five TNCs have retained their leading positions in recent years and perhaps have pulled ahead even further.

Regarding the market power of the TNCs within the major producing countries, twenty pharmaceutical companies accounted for more than 80 percent of all U.S. drug sales (prescription and "over the counter") in 1976.<sup>14</sup> In the United Kingdom, 51 companies supplied about 95 percent of the market, and the ten largest of these accounted for over 50 percent of drug sales in 1974.<sup>15</sup> Tables 2.22 and 2.23 show some earlier estimates of concentration of drug production and sales in these and other developed market economies. It has been argued that these figures do not signify an unusually high level of market power when compared with other industries because individual firms rarely account for more than 10 percent of total sales in any given country.<sup>16</sup> However, the market for drugs is divided into different therapeutic categories (e.g., antibiotics, hormones), and it is generally agreed that there is a much greater degree of concentration of firms within each category, or sub-market. For example, Table 2.24 lists patents issued in the different product categories between 1965 and 1970, and shows that the number of firms involved in new drug production is very small even in such widely utilized product categories as antiparasitics and antibiotics.<sup>17</sup> A 1975 study estimated that about three-fourths of all ethical drugs can be obtained from only a single producing firm.<sup>18</sup> This situation is not necessarily due to the difficulty of the production process, but rather to the concentration within a few firms of the financial and technological capability to develop new drugs. When one of these firms develops a new drug, in all but a few special situations, it is immediately put under patent, and the developing firm then retains the right to control the production and sale of that drug for a specified time period. The number of firms engaged in selling drugs is much larger

TABLE 2.21

Sales, 14 Leading Pharmaceutical Manufacturers, 1974 (U.S. \$million)

Company (nationality)	Estimated Drug Sales	% of Companies' Total Sales
1. Hoffman-LaRoche (Swiss)	\$1112	56%
2. Hoechst (FRG)	1100*	13%
3. Ciba-Geigy (Swiss)	974	26%
4. American Home Products (U.S.)	950	44%
5. Merck and Co. (U.S.)	890	67%
6. Sandoz (Swiss)	808	51%
7. Bayer (FRG)	750	10%
8. Watner Lambert (U.S.)	675	35%
9. Eli Lilly (U.S.)	634	57%
10. Pfizer (U.S.)	575	37%
11. Bristol-Meyers (U.S.)	550	35%
12. Boehringer-Ingelheim (FRG)	535	74%
13. Takeda (Japan)	511**	57%**
14. Shering-Plough (U.S.)	500	71%

\* Including Roussel-Uclaf

\*\* Excluding deAngeli and Sturge

Source: Annual Reports, trade journals and industry reports. In L. Schaumann, Pharmaceutical Industry Dynamics and Outlook to 1985, Menlo Park, California, Health Industries Research Department, Stanford Research Institute, 1976, p. 18.

than the number of firms involved in all stages of drug production, but marketing firms must purchase materials and the right to sell patented drugs from the major producing firms: thus, indicators of concentration of production are generally most important in explaining the market power of the TNCs. Economic analyses of the pharmaceutical industry have often concluded that the few firms in each therapeutic sub-market are likely to behave like an interdependent group (a "therapeutic oligopoly") and refuse to compete with each other on a price basis.<sup>19</sup> Investigation into such relationships between the leading firms have been carried out by several governmental groups as well as the United Nations.<sup>20</sup>

As mentioned earlier, in most countries the pharmaceutical sector represents a broadening of operations by the chemicals industry. Although many of the leading TNCs developed as subsidiaries of manufacturers of popular early medicinal substances and toiletries, a strong chemicals industry has been a necessary concomitant to the substantial growth of the pharmaceutical sector in all of the major drug producing countries, and the market power of the TNCs is closely related to the concentration of chemical production in the developed market economies. In fact, the chemicals industry was so central to the early industrialization process in these countries, involving as it did the accumulation and reinvestment of massive amounts of capital, that the economies of scale which they have achieved in basic production processes would be difficult to accomplish in any country now beginning production. Even those countries with sufficient petroleum (one of the principal resources needed for chemical production) will require a lengthy period of capital investment and technological development to build up a fine chemicals industry, and during the developmental stages the costs of producing intermediate pharmaceutical chemicals may significantly exceed the costs of importing them.<sup>21</sup> To a great extent the cost picture could be altered if investments in industrial plants were coordinated by

TABLE 2.22

CONCENTRATION IN THE PHARMACEUTICAL MARKET, 1970\*

Country	Data Source	Percentage of Total National Market		
		Top 10 Firms	Top 20 Firms	Top 50 Firms
U.S.	Pharmaceutical Manufacturers Association	52.6	76.2	95.6
Holland	Neprochem	50.0	75.0	95.0
U.K.	Estimate	45.0	68.0	96.0
France	Estimate (1969)	37.4	51.8	74.8
West Germany	Bundesverband der Pharmazeutischer Industrie	35.0	50.0	73.0
Belgium	Association générale de l'industrie de Médicament	29.0	45.0	65.0
Italy	Estimate	25.0	39.0	62.0

\* Source: C. Levinson, *The Multinational Pharmaceutical Industry*, International Chemical Federation, Switzerland, (n.d.), P. 12.

TABLE 2.23

Number of Companies Obtaining Ten or More Patents  
in Each Therapeutic Class Between 1965 and 1970

Therapeutic Field	Number of Companies
Anti-infectives:	
Antibiotics	9
Antiparasitic	11
Antibacterial	15
Antiviral	6
Cardiovascular:	
Vasoactive	1
Hypotensive	7
Antianginal	1
Cardiotonic	0
Antiarrhythmic	2
Blood:	
Coagulants and anticoagulants	1
Hypolipemic	6
Hypoglycemic	3
Neurological:	
Tranquilizers and sedatives	13
Stimulants and antidepressants	10
Anticonvulsants	3
Anesthetics	0
Analgesics	9
Hormones:	
Prostaglandins	1
Corticosteroids	1
Estrogens, androgens, progesterones	15
Other hormones	0
Others:	
Antihistamines	1
Bronchodilators	0
Anti-inflammatory and antipyretic	15
Immunosuppressants	1
Anti-cancer	2
Vaccines	0
Gastrointestinal	3
Anorexic	1
Diuretic	2
Muscle Relaxants	0

Source: Derwent Central Patent Index, prepared by Derwent Information Service, England. Patents are listed the first time they are granted in one of the following countries: U.S., Great Britain, Netherlands, Belgium, France, South Africa, Canada, West Germany, East Germany, Japan, Switzerland, and the Soviet Union. Patents are for pharmaceutical compounds and processes primarily. Each patent is counted only once and listed in the first therapeutic category given.

In D. Schwartzman, Innovation in the Pharmaceutical Industry, (Baltimore and London: Johns Hopkins Press), 1976.

means of regional agreements between countries, and technological development also involved joint contributions from participating countries. The difficulty lies in the extent to which industrial ventures involving scarce energy resources can be planned to the equal advantage of countries with varying national resources, capabilities for productive use of chemicals, and market situations. Also, the synthesis of active

ingredients from basic chemicals involves the entire evolution of technology in the transnational pharmaceutical industry, and TNCs have proved to be extremely recalcitrant about divulging their "trade secrets" despite pressure from host countries.

The leading transnational pharmaceutical companies have not attained their sales positions primarily by increasing the efficiency of finished drug manufacture. Once the active ingredients are synthesized, the manufacturing process is relatively simple. Furthermore, the market for the great majority of drugs is very narrow, and further economies of scale at the final stages are not probable. Competition in the pharmaceutical industry is based, rather, on the continuing discovery of new drugs and intensive promotional campaigns, i.e. creating new markets. The expense involved in competing in this type of modern, high technology industry is extremely high, and firms tend to meet the strains of competition by merging. In fact, the concentration of drug production into a relatively small number of TNCs has proceeded by a lengthy series of mergers between the leading firms and the acquisition of smaller marketing firms. As a result of this process, very high rates of profitability have been increasingly limited to a few broadly based firms with sufficient capital to continue expanding. Two giant firms in the Federal Republic of Germany are probably most representative of this trend. Hoescht, which ranked second in world drug sales in 1974 (Table 2.21) was the eighth largest company in the world in terms of overall net sales in 1976. Bayer, which was among the top fifteen TNCs in total drug sales in 1974, was also one of the most successful firms in the world according to overall net sales figures published in 1976.<sup>22</sup> The far more extensive interests of these companies in chemicals are shown by the relatively low proportion of total sales they accomplish in their pharmaceutical divisions, 13 percent and 10 percent respectively. Most of the leading TNCs now have widely diversified interests—fertilizers, foodstuffs, and animal health care products represent some of their other important sources of income.<sup>23</sup> It is also the case that many of the firms involved in drug production are linked with other industrial sectors equally significant to health on an international scale.

Mergers within the pharmaceutical sector have been subject to governmental inquiries in some of the major drug-producing countries, primarily because of the noncompetitive nature of certain patented drugs. The ParkeDavis/ Warner Lambert merger, for example, was reported as possibly resulting in the elimination of competition in 52 drug lines.<sup>24</sup> The Monopolies Commission in the United Kingdom examined the proposed acquisition of Glaxo by the Beecham and Boots groups and concluded that the benefits of economies of scale in research which might be gained would probably be exceeded by the resultant problems of market power.<sup>25</sup> Regarding international mergers between companies, the leading European companies have recently made several acquisitions of U.S. firms, presumably because the U.S. market is still growing, while in recent years

an increasing number of European countries have placed tighter cost-price controls on drug production and sales.<sup>26</sup> As a result, the share of foreign drug firms in total U.S. sales volume has increased from 25 percent in 1975 to 35 percent in 1977.<sup>27</sup> This is still a relatively small foreign share in international terms. For example, in the U.K., a major producing nation, foreign owned companies supply about 66 percent of the market for National Health Service medicines.<sup>28</sup> In fact, the only market economy in which nationally based firms account for the great majority of their home sales (87 percent) is Japan, which continues to maintain an unusually restrictive policy of industrial protectionism.<sup>29</sup>

The pharmaceutical industry of today is truly transnational, and the leading TNCs are represented throughout the world. The development of TNCs as subsidiaries of large companies with transferable resources and relatively stable capital inflows has enabled them to assume the risk of investing heavily in the expansion of their research capabilities. As their research and promotional activities have become increasingly expensive, the firms have sought to reduce the risks of competition as well as strengthen their overall position in the market by merging and acquiring smaller firms throughout the world. While their control of such a vast percentage of the world market for drugs has allowed them to increase their expenditures for new drug development, the value of their function as innovators has been increasingly offset by the extent of their power to determine the product mix and cost of international drug supplies. Market power in the drug sector is derived mainly from the ownership of the great majority of patents on finished drugs and pharmaceutical production processes (technological "know-how") and from the powerful demand-creating influence of extensive information and advertising activities promoting new drug products.

## 2.3 *Research and Development (R & D) and the Patent System*

### *i. R & D*

The content of modern research efforts in the field of pharmaceuticals reflects the progressive concentration of industrial R & D activities into perhaps two dozen firms, as well as a division of labor between researchers supported by the public sector and research groups within the industry.<sup>30</sup> Since the discovery of sulfa drugs in the 1930's, the public sectors of the developed market economies have provided funds for basic research activities (which are considered to be pure science and therefore not legitimate areas for the restriction of knowledge imposed on patented discoveries), while the pharmaceutical industry has financed the development of final drug products and techniques for their wide-scale production.<sup>31</sup> Legislative actions by most producing countries have resulted in the requirement that the industry also include in its developmental activities procedures for proof of safety and efficacy.

Some primary questions relating to industrial drug development activities are (a) does the profit motivation in industry based research lead to the *omission* of potential areas of benefit to groups with the least available resources for drug purchases, particularly the populations of the poorest countries, and (b) how has the application of biomedical knowledge for commercial gain affected the *content* of industrial research?<sup>32</sup> Both of these questions involve the direction of industrial research and its potential responsiveness to health needs. Industrial research is charged against sales, so that current customers in all countries dealing with the TNCs pay for benefits which may be enjoyed by future consumers.<sup>33</sup> At the same time, worldwide purchasing patterns have little influence on the direction of industrial research, which is oriented toward market forecasts based on epidemiological findings primarily in the industry's countries of origin. Along with Western biomedical research in general, pharmaceutical technology has been highly responsive to the social conditions engendered by the expansion of the industrialized market economies, particularly changes in prevalent disease patterns from communicable and parasitic illnesses to chronic ailments such as heart disease, cancers of an industrial origin, and various stress-related diseases.<sup>34</sup>

This technological bias is intensified by the concentration of research and development activities into a relatively smaller number of firms. As an example, in the U.K., the four largest firms were reported as accounting for over 70 percent of the total amount of research expenditure.<sup>35</sup> Very few chemically based drugs have been discovered in the developing market economies, even in those having a relatively significant pharmaceutical industry. However, the geographical distribution of industry research has been shifting recently, primarily because certain development costs, particularly for research personnel, are lower in developing countries, requirements for testing human subjects are less formidable, and delays in registration of new drugs are shorter. Nonetheless, evidence indicates that this change in the geographical distribution of research activities has not affected the industrialized country disease orientation of the TNCs.<sup>36</sup> The industry term for its R & D activities is "consumer oriented research," meaning the discovery of products and styles of presentation which will expand the sales of drugs to those populations with already proven high utilization rates. Thus, the low purchasing power of populations in developing countries has significantly lowered their potential impact on the direction of new drug development, even when such development is being carried out within low income countries.

Hoffman-La Roche is the only major firm presently maintaining a very extensive research effort aimed at developing treatments for the types of parasitic and mycological diseases prevalent in developing countries. Recently, other leading TNCs have submitted proposals to the WHO for research in the field of tropical diseases, apparently with the anticipation

of reducing their R & D overhead expenditures by developing important new drugs with United Nations funds.<sup>37</sup> With regard to consumers in developed countries, even if they receive more future benefits from the research activities they help support with their current purchases, they must continue to face the same issues of the high cost of the curative drugs produced by the transnational pharmaceutical firms relative to the amount of disease reduction likely to result from their development and utilization. Because the principal illnesses (communicable and parasitic diseases) of poor countries are associated with lack of adequate food and unhygienic conditions, they can only be eliminated by systematic efforts at disease prevention which take place within the context of egalitarian socioeconomic development.<sup>38</sup>

The second issue relating to the direction of industrial research is the tendency of the firms to capitalize on existing technology by creating new drugs which are primarily molecular modifications of existing therapies (me-too drugs), or new fixed-ratio combinations of chemical entities which have been found to be individually effective.<sup>39</sup> Some of these modifications have been found to be of great importance to treatment, but the combination drugs have been determined to be largely unnecessary and often are not included in formularies prepared by clinical pharmacologists and medical experts.<sup>40</sup> Development of new combination drugs dropped sharply in the 1960s, but it appears that the problem of new chemical modifications that are of no additional benefit to drug therapy continues, and when these drugs are successfully promoted they often do not offer the purchaser any reduction in costs.<sup>41</sup> The greatest problem they represent is the confusion involved in purchasing, because the information provided by the pharmaceutical firm does not include reference to the costs and benefits of new drugs relative to similar, established drugs; or when it does, the information is likely to stress very minor improvements in safety and efficacy.

The risk element in high expenditures on research and development (the average for R & D among the large firms is 10 percent of sales) is often put forward as a counter to the charge that the high rates of profitability enjoyed by the multinational pharmaceutical industry are a source of economic loss to society. During the R & D process, thousands of compounds are investigated, and the great majority are eliminated before testing on animals is begun. Only a small percentage of the discoveries are actually marketed.<sup>42</sup> The time required to develop a product has been estimated at up to twelve years, depending on the regulatory requirements of the country in which it is introduced. The industry's economists assert that it is increasingly difficult and expensive to achieve results from R & D in the form of a successful product and point to the apparent slowdown in the rate of new drug discoveries.<sup>43</sup> Therefore, from the standpoint of the firms, a successful drug must pay for itself as well as the lines of research that were embarked upon without any (marketable) end product.<sup>44</sup>

TABLE 2.31  
NEW DRUGS ACCORDING TO COUNTRY OF DISCOVERY<sup>a</sup>

Year	United States	West Germany	France	Switzerland	England	Japan	Benelux <sup>b</sup>	Italy	Scandinavia <sup>c</sup>	Others <sup>d</sup>	Total	Percent
1961	32.5	10	10	10	5.5	2	1	3	1	7	82	10.8
1962	17	15	23	6	3	2	7	4	5	2	86	11.4
1963	25	19	18	7	9	13	1	2	3	1	98	13.0
1964	15	11	8	3	3	8	2	4	1	7	62	8.2
1965	12	9	14	5	3	11	1	6	-	3	62	8.5
1966	20	7	23	3	4	8	2	2	2	9	80	10.6
1967	16	9	19	8	6	6	-	8	1	10	83	11.0
1968	15.5	10.5	17	4.5	4	5	4	1.5	2	6	70	9.3
1969	13.5	12	22	3	3.5	6	2	5	1	2	70	9.3
1970	17	5	16	6	2	6	1	1	3	3	60	7.9
Total	183.5	107.5	170	57.5	43	67	21	36.5	19	50	755	
Percent	24.3	14.2	22.5	7.6	5.7	8.9	2.8	4.9	2.5	6.6		100

a Source, *Drugs Made in Germany*, Vol. 15, Editio Cantor KG, Aulendorf, West Germany, 1972.

b Includes Belgium, the Netherlands, and Luxembourg.

c Includes Norway, Denmark, and Sweden.

d Includes Argentina, Czechoslovakia, East Germany, Canada, Austria, Portugal, Spain, USSR, and Hungary.

Source: H. E. Simmons, *The Drug Regulatory System of the FDA: A Defense of Current Requirements for Safety and Efficacy*. International Journal of Health Services, Vol. 4, No. 1, (1974) Table 2, p. 100.

Table 2.31 shows that over time the number of new drugs has been decreasing slightly. While some economists attribute this decrease to time consuming regulatory requirements for new drug approval, it appears that the central reason for the slowdown is a deficiency of basic biologic knowledge in several industrial target areas for research, e.g., cancer and stroke.<sup>45</sup> As one pharmaceutical expert has argued, the decrease in new drugs may actually be beneficial for consumers as it is representative of a

decline in the development of unimportant or duplicate drugs which account for most of the thousands of drugs now available.<sup>46</sup>

One analysis of the transnational pharmaceutical industry included the observation that expensive industrial research activities, in effect, have pulled away available resources from basic to applied research.<sup>47</sup> This may prove to be an increasing problem in developing countries with limited public funds for research, as the movement of research funds into the subsidiaries of the TNCs may tend to attract scientific talent toward the industry and away from the more basic research areas.

## ii. *The Patent System*

In order to maintain its past record of high profitability, the pharmaceutical industry must ensure that its products continue to enter the market at a regular rate. There is little doubt that patents have been a key element in the expansion of the TNCs. Patents afford firms the legal right to exclude others from certain acts relating to the inventions they describe, and grant temporary monopoly privileges on the sale of a new product for a specified time period. Those firms which have had several successful patented products in past years are assured a fairly high rate of return on R & D investment until the expiration of the patents, allowing them to absorb the time lag and risk involved in further new product development. It has been argued that competition within the industry lessens this assurance, but as has been noted previously, the number of firms involved in a particular therapeutic category are limited. Furthermore, due to the heavy expenditures on sales that accompany each new drug, many duplicative drugs have proven to be extremely profitable for all of the firms involved in their production. Currently, in some countries, a large number of patents taken out on drugs discovered in the 1960's are about to expire. Recently this situation was brought to public attention in the United Kingdom, when the pharmaceutical industry approached the government with an amendment to the new Patents Act, which extends a new patent's life from the present 16 years to 20. The industry's amendment would extend the Act to cover existing patents expiring during the next five years.<sup>48</sup>

The patent system has received considerable attention in connection with the transfer of technology to the developing market economies. Detailed documentation of the international patent system has been provided by the United Nations Conference on Trade and Development (UNCTAD).<sup>49</sup> Table 2.23 showed the ownership of patents on therapeutic substances to be highly skewed toward the developed countries. The UNCTAD report examined all patents granted in 1972 and reported that nationals within the group of developing countries owned only six percent of the total number, and less than one percent of all patents granted to foreigners. This study also found that the greatest concentration of patents registered in developing countries is in the chemical sector and

that among these patents the great majority concern drug products.<sup>50</sup>

The encouragement of invention and the promotion of economic development are the principal intents of patent legislation, but critics have charged that the misuse of patent privileges, either through refusing to utilize patented technology in the countries to which it is registered, or through attaching restrictive clauses to license agreements involving patent privileges (see section 3.2), actually interferes with economic growth and innovation.

Penrose (1973) described both sides of the issue of whether or not patents assist in the transfer of technology.<sup>51</sup> She states the argument supporting the concept that patenting assists technology transfer (and therefore economic development) as follows:

The disclosure of the technology which is contained in the patent grant and is public knowledge is rarely sufficient to permit its full application without the know-how and the technical help of the patentee. Business firms will not give this know-how and this help in conditions which might rob them of the protection their patents provide and where consequently anyone could use the technology made available . . . It is also argued that in addition to the transfer of technology through the licensing of patents to local firms and the provision of technical know-how, foreign patenting promotes foreign investment. Direct foreign investment tends to enter the more modern industries where technology is likely to be patented.

Counter-arguments point out that few patents registered by foreigners are actually worked in the developing countries, and that their basic function has been to reduce the competition that might otherwise have taken place among various international sellers of technology. For example, the knowledge required to produce a certain ingredient in a drug may be developed in a number of countries by several firms, but the first firm to arrive at that piece of knowledge can claim the right to patent it and exclude others from using it in the country granting the patent privilege even though other firms are willing to provide that know-how at a much lower price. A patent holder may exploit a patent, decide not to use it, or may license to a third party some or all of the rights granted by the patent. Evidence that patents granted to foreigners in developing countries are not extensively utilized has been provided by Vaitos (1972), Katz (1972) and Grundmann (1976).<sup>53</sup> Vaitos found in Colombia that 2,534 of the total of 3,513 patented processes or products belonged to the pharmaceutical industry, and that of these only ten were actually being developed within the country. Katz examined patent utilization in Argentina over a period of ten years and found that no more than 5 percent of the patents were being worked at any one time. Regarding the industry rationale for patent registration, Grundmann carried out a sample survey of foreign patent holders in 17 African countries and also concluded that patents are taken out in developing countries primarily to

protect the firms against imitators, either by enforcing patent monopolies or by preventing local production. There appears to be a strong national interest in protecting local inventions in most of the market economies, and at least some legal provisions are made for patent holders. The denial or withdrawal of these privileges from non-nationals only could cause serious difficulties with foreign investors. Production on the basis of licensing agreements with patent holders has sometimes led to the exportation of the locally produced goods, earning countries foreign exchange which would not have been possible in the absence of the license agreement. However, territorial restrictions on exports, which have been imposed on licensee firms in many developing countries, remove most of this potential benefit.

Earlier, the risk-reducing effects of vertical integration in the pharmaceutical industry and mergers between leading firms were discussed. One of the other great remaining risks to TNCs with regard to their large R & D investments is the possibility that they will face an increasing number of legal constraints on the promotion and pricing of their new patented products.<sup>54</sup>

#### 2.4 *Promotion*

An early Organization for Economic Development (OECD) study of the pharmaceutical industry in Europe examined size distribution of firms and problems of scale and found that production costs are not greatly reduced as size increases, i.e., economies of scale in the final phase of drug production are negligible. However, the advantages of the large firms become apparent in advertising and promotion. The extensive promotional activities of the leading firms are far beyond the expectations of smaller firms.<sup>55</sup>

Several forms of promotion are practiced by the multinational pharmaceutical firms, and much of it is related to their use of trademark names.<sup>56</sup> Because most drugs are created in their final form by industrial laboratories, the industry creates a generic name (usually long, and thus difficult to pronounce and remember) and then chooses a simpler name to be associated with the product—the trademark, or brand name. These brand names have two functions: the initial promotion of a new drug and the differentiation of a drug that is made by several different firms.

The promotion of a new drug by its brand name is most effective in the context of medical education and the continuing education of doctors. Promotion and its relation to medical education will be discussed later, in the section on utilization; here it is sufficient to point out that when doctors become accustomed to knowing a drug by its brand name they will generally prescribe it by that name. Furthermore, the habit creating effect resulting from the use of brand name products by prescribing physicians extends to patients and even to manufacturing firms producing drugs which are no longer under patents or license. The

patent continues to retain the memory of the brand name product and will ask for it again if the same condition appears. Realizing the habits of doctors and their patients, instead of using generic names local firms will choose names very similar to the original brand names of drugs promoted by the transnational pharmaceutical firms.<sup>57</sup>

When small firms create their own modifications of brand names, they add to an already confusing situation. Aside from their role in the promotion of new drugs, brand names are also used for product differentiation. Several of the major firms sell the same drug under different brand names, resulting in a situation in which one drug may be known by as many as 25 different names. Most of the countries which do not have a national formulary specifying that purchases must be made by generic name have seen a rapid rate of growth in the number of preparations available: in Belgium there were 9,000 preparations on the market; in Spain, 12,400; in India and Colombia, at least 15,000; in the Federal Republic of Germany 24,000; in Brazil, around 30,000; in the U.S. the number may be over 35,000; and in Mexico, possibly as many as 80,000. Obviously, many of these are duplicate products.<sup>58</sup>

The amount of money invested in the promotion of this staggering array of therapeutic preparations represents a considerable investment on the part of the multinational drug firms. The Task Force on Prescription Drugs (U.S.) calculated that marketing expenses, including all aspects of promotion, were equivalent to about 15-35 percent of sales among the leading companies (roughly three times the volume of expenditures on R & D).<sup>59</sup> It has been estimated that *in 1970 the value of industry expenditures on promotion was approximately equal to the total value of drug production by the developing and Southern European territories.*<sup>60</sup>

Advertisement and promotion by TNCs is directed toward physicians by means of a variety of programs and publications funded by the industry, including: medical conferences apparently unrelated to pharmaceutical products; the establishment of study fellowships, especially in developing countries; paid advertising in medical journals (to the extent that most of them could not continue to publish without it); direct mailings to doctors; free samples; help with ordering; and the publication of information for pharmaceutical reference books such as the Physicians Desk Reference (P.D.R.) and the Monthly Index of Medical Specialties (M.I.M.S.). In addition, the use of company representatives, "detail men," to inform physicians and other purchasers of the merits of new drugs is extremely widespread. It has been calculated that there is one detail man for every ten physicians in the United States; in Colombia, one for every five physicians; in Tanzania, one for every four; and in Guatemala, Mexico, and Brazil, one for about every three physicians.<sup>61</sup> Contributing to the "hard sell" approach in developing countries is the fact that detail men often have higher incomes than the doctors they seek to influence.<sup>62</sup>

Comparative international studies of information provided by TNCs

for pharmaceutical reference volumes, medical journals and drug labels have shown important international variations in the quantity and content of information. A study of reference volumes publishing information from industry sources for physicians in the United States and several Latin American countries pointed out that warnings and contraindications for use were minimized in the information provided in the Latin American volumes when compared to the United States publication, while indications for use were far more numerous. Similar discrepancies have been found in a comparison of the African M.I.M.S. and its British equivalent.<sup>63</sup> Although the full disclosure of hazards in published drug information was not required by some of the countries involved in these comparisons, the findings reflected poorly on the ethical behavior of the firms involved. Hearings in the U.S. Senate in connection with this topic revealed resistance within the industry to the international disclosure of data resulting from clinical testing legally required by the U.S. Food and Drug Administration (FDA).<sup>64</sup> Since the FDA has relatively detailed regulations concerning the application and final approval for new drugs, this information could be valuable in restricting the flow of ineffective drugs into countries where facilities and personnel for testing drugs are limited.

There appears to be an international movement among the developing market economies toward the creation of legislation in the area of drug information that is similar to that of the U.S. However, professional reliance on biased promotional literature for drug information already may have been a contributing factor to the rise of resistant strains of bacteria due to excessive use of antibiotics, heightened fatality rates from aplastic anemia as a result of the irrational use of antipsychotic tranquilizers, and numerous other drug related ills.<sup>65</sup> The emergence of drug-resistant strains of the bacteria responsible for pneumonia and gonorrhea is also related to the incorrect utilization of antibiotic drugs, but because self-medication is so common in developing countries these problems cannot be traced directly to the information available to physicians.<sup>66</sup> One account of pharmaceutical promotion in Latin America found that 75 percent of all drugs sold in one South American country were purchased by consumers for self-medication. Access to ethical drugs in some of the poorest countries was found to be related more to the retail cost of the medications than to health needs or legal restrictions on sales.<sup>67</sup> Unfortunately, when a large proportion of a country's population does not have access to the services of qualified health care practitioners, the promotion of modern chemical drugs becomes directed, in effect, toward consumers who are unlikely to be able to comprehend their potential dangers.

## 2.5 *Pricing and Profitability*

Competition in the transnational pharmaceutical industry is based on

innovation and the promotion of brand name products rather than price, and among the leading firms only a small proportion of the selling prices of drugs represents direct costs of production. However, the drug industry in many countries also includes a large number of smaller firms, usually selling only to their home markets, which do not have R & D divisions or extensive promotional expenditures. These companies concentrate on bulk manufacture of "commodity generics," i.e., widely used drugs which are no longer under patent and thus can be offered at much lower prices. Despite the rising costs of modern health care, these lower priced drugs are usually passed over in favor of newer, patented drugs which are advertised as being of "higher quality." Recently, in view of cost containment efforts by the United Kingdom and several other developed countries to encourage physicians to prescribe drugs by their generic names, the major producing firms have also begun to promote drugs with generic labels. These drugs are called "branded generics," and their higher price levels are also defended as being a necessary consequence of superior quality control procedures.

Evidence submitted by the American Public Health Association supporting the repeal of antisubstitution laws (laws requiring a pharmacist not to substitute a generic equivalent for a product named in a prescription) included the data presented in Table 2.51. This table is of particular interest in that the costs vary between the distributors, yet all of the products in each of the three categories were produced by one company. These kinds of data strongly contradict the argument that there are significant differences in quality between brand name drugs, "branded generics," and "commodity generics," as very often these are produced by the very same firm. A comparison of brand name and generic label drugs in Costa Rica (Table 2.52) resulted in similar findings. The fact that the great majority of drugs purchased in Costa Rica are brand name products (84 percent over a one year period, 1970-1971) emphasizes the social costs of the highly successful marketing activities of the leading TNCs.

The case of tetracycline deserves special attention due to the extensive documentation of over-pricing and oligopolistic practices with regard to this drug that has appeared over the past twenty years. The U.S. Trade Commission concluded that the first company to patent this drug, Pfizer, was directly responsible for "procurement by misrepresentation" of monopoly control over tetracycline. An agreement between Pfizer and Cyanimid was uncovered showing that Cyanimid had withdrawn its own application for the tetracycline patent after accepting an offer from Pfizer to divide up the American market for the drug. This agreement enabled the two firms to establish noncompetitive prices from 1949 to 1953.<sup>68</sup>

Later, five companies marketing tetracycline under separate brand names were subject to around 150 civil action suits started by various groups on the basis of similar charges of oligopolistic over-pricing.<sup>69</sup> Today, with regard to tetracycline, there appears to be a more competitive

TABLE 2.51

CHLORAL HYDRATE 500 MILLIGRAM CAPSULES

<u>Manufacturer</u>	<u>Distributor</u>	<u>Average Wholesale Price per hundred</u>
T. F. Scherer	H. B. Cenci Labs	\$ 1.60
	ICN Pharmaceuticals	1.60
	Invex Pharmacy	na
	Ladco Labs	na
	Life Labs	na
	MSD	4.04
	Progress	na
	Rexall	na
	Squibb	5.00
	Stanlabs	2.15
	Stayner	1.60
	Towne, Paulsen and Co.	1.60
	United Pharmacy	na
	Alliance Labs	na
	Hoack Labs	na
	McEesson Labs	1.75
Purepak Pharmacy	1.48	

ERYTHROCYCIN STEARATE 250 MILLIGRAM TABLETS

<u>Manufacturer</u>	<u>Distributor</u>	<u>Average Wholesale Price per hundred</u>
Mylan Labs.	Towne, Paulsen, and Co.	\$ 8.83
	Syeth	9.35
	Progress Labs	na
	Rexall Drug	na
	Mallinkrodt	9.95
	Cherry Pharmacy	5.70
	SKF	10.15
	Alliance	na

TETRACYCLINE HCl 250 MILLIGRAM CAPSULES

<u>Manufacturer</u>	<u>Distributor</u>	<u>Average Wholesale Price per hundred</u>
Mylan Labs.	A. H. Robins	\$ 3.25
	Towne, Paulsen and Co.	1.50
	Molins	1.92
	Syeth	2.06
	Invenex	na
	Rexall	na
	American Pharmacy	na
	Central Pharmacy	na
	Hoack Labs	na

Source: Hearings before the Subcommittee on Monopoly of the Select Committee on Small Business, U.S. Senate, Ninety-Third Congress, second session, on Present Status of Competition in the Pharmaceutical Industry, Part 24: 10168-10172.

environment in the United States; four firms produce it in bulk form and about seventy companies distribute it. However, the concentration in the earlier phase of production continues to be reflected in purchase patterns. An investigation carried out by the Council on Economic Priorities revealed that price differentials in the U.S. antibiotics market are now quite broad, e.g., in 1974 the price to the pharmacist of 1,000 250 mg. capsules of tetracycline varied from U.S. \$4.12 to U.S. \$50.00.<sup>70</sup> More importantly, however, in another survey it was found that *more prescriptions were written for one of the most expensive preparations available*, an older brand name tetracycline distributed by one of the leading firms, than for any of the less costly preparations.<sup>71</sup> Oxtetracycline, a modification of tetracycline, was supplied by 21 distributors in 1975, seven of which were large firms selling it under well known brand names. Here again it was found that the most expensive product, one manufactured by Pfizer, had the greatest sales, approximately 99 percent of the market.<sup>72</sup> This is one example of a common occurrence in pharmaceutical purchase patterns. Long periods of monopoly control over the production of various drugs, augmented by heavy promotion, result in habit creation among prescribers that appears to defy economic rationality totally.

Similar variations in drug prices have been disclosed on an international scale. The transnational pharmaceutical industry has never published information explaining its pricing practices, but at one point it was argued that prices in developed countries were higher than in others because of their greater degree of purchasing power. This assertion has been proven to be invalid repeatedly in comparisons of international prices. In fact, figures such as those shown in Table 2.53 are not uncommon in comparisons of this kind: per capita income levels in Costa Rica and Mexico are much lower than in the other countries cited. Returning to the case of tetracycline pricing, 13 years of legal action in the U.S. against five drug firms were followed by several suits filed in 1978 by developing countries, charging the firms with conspiring to eliminate competition and fix prices on an international basis.<sup>73</sup> The only general conclusion that can be drawn on this issue is that TNCs have charged whatever national markets would bear, and the market power of the leading firms has enabled them to limit the sales of many important drugs to that part of the population which could afford the going price—a part which, in many countries, is very small indeed.

It is important to emphasize here that the vertically integrated character of the transnational pharmaceutical industry affects not only the prices of finished drug exports, but also the prices of intermediate chemicals required for the production of drugs. TNCs have been repeatedly criticized for manipulating the prices of imports to their subsidiaries or joint operations in developing countries ("transfer pricing"). An investigation in one Latin American country found that the prices local subsidiaries were paying for intermediate chemical products

TABLE 2.52

## COMPARISON OF CONSUMER PRICES OF TRADEMARK AND GENERIC LABEL CAPSULES OF CHLORAMPHENICOL 250 MG., APRIL, 1976 IN COSTA RICA

<u>Trademark</u>	<u>Manufacturer</u>	<u>Price per capsule in colones</u>	<u>Multiple of the lowest price</u>
Clor Gutis	Gutis Products	0.60	1.00
Cloramfenicol	Lab. McKesson	0.86	1.43
Sintomicetina	Grupo Lepetit SPA	1.15	1.92
Clorosuk	Laboratorios Sukia	1.23	2.05
Chloramex	Durex	1.65	2.75
Quemicetina	Carlo Erba SPA	2.00	3.32
Chloromycetin	Boehringer Mannheim, GmbH	2.75	4.58
Paraxin	Parke Davis	2.77	4.62

Source: Lara, J.A., Rodriguez, C.F., and Lara, J.A., Las Transnacionales y el costo de los medicamentos in Costa Rica, Comercio Exterior, Banco Nacional de Comercio Exterior, S.A., Vol. 27, No. 8 (August, 1977), p. 247.

were, *on average*, 155 percent higher than if those products had been purchased on the world market.<sup>74</sup> Individual examples of chemical import prices ranged up to 5,000-6,000 percent over prices available elsewhere.<sup>75</sup> Similar evidence about such transfer pricing has been uncovered in Brazil, Egypt, Iran, India, and other countries.<sup>76</sup>

A detailed study was carried out by the United Kingdom's Monopolies Commission into the prices of Hoffman-LaRoche's leading products, Librium and Valium. The United Kingdom has a rather unique system of negotiating profits with pharmaceutical firms based upon audited accounts of their costs. Statements provided by Hoffman-LaRoche included costs of the active ingredients for Librium and Valium at £437 and £979 respectively per kilo. When operations and overhead costs in the United Kingdom were deducted, prices were set at a level that showed a profit of less than 5 percent. However, the Monopolies Commission found that the costs of the active ingredients for the drugs were listed elsewhere in Europe at £9 and £20 respectively per kilo and concluded that Roche was using artificially high transfer prices to mask the actual profit level, which may have exceeded 80 percent.<sup>77</sup> After negotiations with the U.K. government concerning the Commission report, Roche agreed to repay £3.75 million in excess profits, and later agreed to a price-fixing order cutting the prices of Valium and Librium to half the 1970 level.

An empirical study of European pharmaceutical prices between 1964 and 1974 attempted to explain price variations within the European Economic Community. Two of the principal conclusions were: a drug will tend to be higher priced in countries where it is not widely used; and "the age composition of the products on the market and the speed of their replacement may well influence the overall average price in different markets." In other words, a greater acceptance of unpatented, standard

TABLE 2.53  
HIGHEST PRICES OF LIBRUM AND VALIUM<sup>®</sup> IN FIVE COUNTRIES  
(March 1976, in U.S. dollars)

Country	Librium 100 tablets 10.37	Valium 100 tablets 5.55	Multiple of the lowest price of Librium	Multiple of the lowest price of Valium
U.K.	8.33	6.63	1.00	1.00
F.R.G.	4.38	5.35	5.28	8.49
Switzerland	4.75	5.44	5.72	9.08
Mexico	4.42	6.03	5.33	9.57
U.S.A.	5.80	6.89	6.99	10.38
Costa Rica	7.03	9.13	8.47	14.49

Source: Lara, C.A., Rodriguez, C.C., and Lara, S.A., *Las Transnacionales y el costo de los medicamentos en Costa Rica*, p. 246, and *La industria farmacéutica en México*, p. 699.

Comercio Exterior, Banco Nacional de Comercio Exterior, S.A., Vol. 27, No. 8, (August, 1977).

TABLE 2.54

THE COST OF 'BASE-LINE' TUBERCULOSIS DRUGS IN  
SOME AFRICAN COUNTRIES IN 1973

<u>Country</u>	<u>Isoniazid/150 mg 1,000 tablets</u>	<u>Streptomycin/100 g</u>	<u>Isoniazid/300 mg + Thiacetazone/150 mg 1,000 tablets</u>
Algeria	5.75	12.50	--
Cameron	1.32	6.72	6.83
Ivory Coast	1.98	6.78	--
Congo	2.42	6.98	5.50
Dahomey	2.84	11.02	--
Egypt	1.48	2.97	1.48
Gabon	2.63	6.49	7.02
Guinea	5.20	30.83	--
Upper Volta	1.54	8.09	9.49
Kenya	1.67	3.97	2.38
Madagascar	3.06	7.55	1.15
Mali	3.96	11.45	--
Morocco	1.33	6.44	4.44
Niger	12.33	22.02	15.46
Nigeria	1.67	1.46	3.29
Central Africa Rep.	1.54	7.05	--

Source: P. Chaulet and O. Y. Sow, *The Price of Recovery, Tuberculosis*, No. 33, June 1974, p. 17.

drugs produced by firms without heavy R & D overhead costs contributes to lower overall price levels. Chaulet and Sow (1974) examined the cost factors involved in the purchase of drugs for treating tuberculosis in several African countries.<sup>29</sup> They found that the prices varied significantly between the nineteen countries included in the study. The standard base-line drugs for the treatment of tuberculosis, isoniazid and streptomycin, are both widely used throughout Africa, and well over twenty years has passed since their discovery. From the data presented in Table 2.54 it appears that some of the poorest countries, which must import all of their drugs from TNCs and pay for them with scarce foreign currency, have had difficulty in taking advantage of a market situation which should have driven prices downward at a relatively equal pace. Mention was made of the Third Regional Tuberculosis Conference in Africa, where it was suggested that concerted action be taken in that continent to obtain better purchase conditions. Initially such regional bodies could facilitate

the gathering of comparative cost data on the drugs or intermediate chemical products that are currently being purchased, an enterprise already embarked upon by some developing countries on an independent basis.

Information on the profitability of TNCs is difficult to interpret, as they are widely diversified companies and the specific profit figures arising from the sale of pharmaceuticals are not readily available. Declared profits of the leading TNCs which could be considered primarily as pharmaceutical firms show them to be among the most profitable industrial operations in their home countries. For example, the average return on capital employed for the industry as a whole during the years 1960-1973 was about 18 percent in the U.S., compared with a figure of about 11 percent for all other types of manufacturing industry in that country. However, the figures which have been published cannot be taken to be a completely valid assessment of true net gains because the transnational character of these companies allows them to declare profits in various countries depending on the tax situation, restrictions on repatriation of profits, and legislative requirements.<sup>80</sup> Switzerland, for example, allows TNCs an unusual degree of secrecy in financial matters so that the real level of drug profits gained by the leading Swiss firms, Hoffman-LaRoche, Sandoz, and Ciba-Geigy, is known only to their top executives. Some other countries without a domestic drug industry show significant international trade in pharmaceuticals only because they offer very advantageous tax opportunities, e.g., the Bahamas, Hong Kong, and Singapore.

## FOOTNOTES

1. For further information on the history of the industry in the developed market economy countries see, for example, Davies, W., *The Pharmaceutical Industry* (Oxford: Pergamon Press, 1967) and OECD, *Gaps in Technology: Pharmaceuticals* (Paris, 1969).
2. See Clymer, H.A. The Economic and Regulatory Climate, U.S. and Overseas Trends. In Helms, R.B. (ed.), *Drug Development and Marketing* (Wash., D.C.: American Enterprise Institute for Public Policy Research, 1975), p. 138.
3. See for example, Cooper, M.H. *Prices and Profits in the Pharmaceutical Industry* (Oxford: Pergamon Press, 1966), p. 1, and J.F., *The U.S. Ethical Drug Industry, Science for the People* (July, 1972), p. 13.
4. Silverman, M. and Lee, P.R. *Pills, Profits and Politics* (Berkeley and Los Angeles: University of California Press, 1974), p. 4.
5. Cooper, M.H., *op cit.*, p. 4.
6. Kastner, F. *Volume and Cost of the Supply of Medicaments* (Geneva: General Secretariat of the ISSA, 1974), p. 32.
7. Braverman, H. *Labor and Monopoly Capital* (New York: Monthly Review, 1974), p. 138.

8. The transition in United States medical schools came about as a result of the Flexner Report, sponsored by the American Medical Association, which led to a reduction in the number of medical schools and a reorientation of the profession toward a dynamic technology base. For a brief account of this transition and its effects on the U.S. medical system, see S. Kelman, *Toward the Political Economy of Medical Care*, *Inquiry* VIII, No. 3, pp. 30-38.
9. See, for example, Clymer, H.A., *op cit.*, p. 138.
10. The U.S. Senate Hearings, *Competitive Problems in the Drug Industry* (Wash., D.C.: Government Printing Office), now include over thirty volumes of testimony and evidence from public officials, industry spokesmen, health professionals and consumer advocates, and are one of the most comprehensive sources of information on the issues of profitability, consumer costs, health and safety.
11. One of the most detailed reviews in this area is UNCTAD, *Major Issues in Transfer of Technology to Developing Countries. A Case Study of the Pharmaceutical Industry*, UNCTAD TD B C.6 4 (8 Oct., 1975). Study prepared by S. Lall.
12. Schaumann, L. *Pharmaceutical Industry Dynamics and Outlook to 1985* (Menlo Park, CA: Health Industries Research Dept., Stanford Research Institute, 1976), p. 17.
13. Noyes Data Corporation, *European Pharmaceutical Market Report* (New Jersey: NOC, 1971), pp. 148-149.
14. The total number of drug producing establishments in the U.S. in 1976 was 1,078, but of these only 140 were involved in research. See the U.S. Department of Commerce, *U.S. Industrial Outlook 1977*, pp. 146.
15. *The Pharmaceutical Industry*, *op cit.*, pp. 14-15.
16. UNCTAD, *op cit.*, pp. 14-16.
17. Schwartzman, D. *Innovation in the Pharmaceutical Industry* (Baltimore and London: Johns Hopkins University Press, 1976).
18. *FDA Consumer* (December, 1975 January, 1976), p. 9.
19. Markham, J. Economic Incentives and Progress in the Drug Industry in Talalay, P. (ed.), *Drugs in Our Society* (Baltimore: Johns Hopkins University Press, 1964), pp. 169-170. See also Comanor, Research and Competitive Product Differentiation: The Drug Industry and Medical Research, *Journal of Business* (Jan., 1966) and Jadlow, J. Competition and Quality in the Drug Industry: The 1962 Kefauver-Harris Amendments as Barriers to Entry, *Antitrust Law and Economics Review* (Winter 1971-72).
20. For example, The U.S. Senate Hearings, *Competitive Problems in the Drug Industry and Restrictive Business Practices*, Studies of the United Kingdom of Great Britain and Northern Ireland, and the United States of America and Japan (New York: United Nations, 1973).
21. UNCTAD, *op cit.*, p. 57.
22. *Business Week* (25 July 1977), p. 80.
23. Murray, M. The Pharmaceutical Industry: A Study in Corporate Power, *Inter. J. of Health Services*, 4, No. 4 (1974), pp. 625-640.
24. *The Economist* (24 April, 1971), p. 99.
25. Monopolies Commission, *Beecham Group Ltd. and Glaxo Group Ltd., The Book Company, Ltd., and Glaxo Groups, Ltd.* (London: HMSO, 1972).
26. Holhe, P.G., European Drug Companies on a U.S. Buying Spree, *New York Times* (Jan. 22, 1978), p. F-3. Hoechst and Bayer were two of the firms acquiring further U.S. interests.
27. *Ibid.* 1975 figure calculated by U.S. Department of Commerce, *U.S. Industrial Outlook 1977*.

28. *The Pharmaceutical Industry*. A discussion document for the labour movement (London: The Labour Party, 1976), pp. 11-13.
29. *Japan Economic Yearbook 1977-78*. *The Oriental Economist*, p. 104. Although Japanese firms control roughly 87 percent of the market, more than 60 percent of the drugs sold there are of "more or less foreign origin," due to license agreements.
30. UNCTAD, *op cit.*, p. 35.
31. Two exceptions to the basic applied division of labor are the Wellcome Institution of the Burroughs-Wellcome Company, and the cancer laboratory funded by Hoffman-LaRoche.
32. For a discussion of various aspects of industrial research and the public interest, see Klass, A. *There's Gold in Them Thar Pills: An inquiry into the medical-industrial complex* (Baltimore: Penguin Books, 1975).
33. See, for example, *A Report on the Supply of Chlordiazepoxide and Diazepam*. The Monopolies Commission HCP 197 (11.4.1973).
34. One well-documented account of changing morbidity patterns in Western countries is Eyer, J. and Sterling, P. Stress-Related Mortality and Social Organization. *The Review of Radical Political Economics*, 9, No. 1 (Spring, 1977), pp. 1-44. Another account from a different perspective, utilizing a broader selection of comparative Western health statistics, is Maxwell, R. *Health Care, The Growing Dilemma* (New York: McKinsey and Co., Inc., 1974).
35. UNCTAD, *op cit.*, p. 20.
36. *Ibid.*, p. 21.
37. Muller, M. A Benevolent Face for the Drug Industry? *New Scientist* (21 July, 1977), p. 157.
38. Segall, M. *Pharmaceuticals and Health Planning in Developing Countries* (Brighton: Institute of Development Studies at Sussex, 1975).
39. Task Force on Prescription Drugs, *Final Report* (Wash., D.C.: U.S. DHEW, 1969), pp. 7-9. U.S. Senate testimony included the estimate that 80 percent of all research funds resulted in duplicative drugs.
40. *Ibid.*, p. 8.
41. Silverman, M. and Lee, P. *Pills, Profit and Politics, op cit.*, pp. 39-43.
42. UNCTAD, *op cit.*, p. 32.
43. The differing rates of new drug introduction between the major drug-producing countries have been discussed at length by Wardell, W. and Lasagna, L. *Regulation and Drug Development* (Wash., D.C.: AEI Institute for Public Policy Research, 1975). They and industry economists advance arguments to the effect that the United States has overly restrictive regulatory requirements, causing a new "drug lag."
44. The *U.S. Industrial Outlook 1977* estimated that the cost of developing a new drug from discovery to marketplace was between U.S. \$15-21 million in 1976. For a summary of industry views on this and other issues, as well as a summary of industry criticisms, see Heller, T. *Poor Health, Rich Profits*. Multinational Drug Companies in the Third World (Nottingham: Spokesman Books, 1977) pp. 27-30.
45. Simmon, H.B., Director, Bureau of Drugs, FDA, DHEW, *Competitive Problems in the Drug Industry*. Part 23 (1973), pp. 9421-9433.
46. *Ibid.*, p. 9422.
47. Klass, A., *op cit.*
48. *The Economist* (13 August 1977), p. 83.
49. UNCTAD, *The Role of the Patent System in the Transfer of Technology to Developing Countries* (TD/B/AC.11/19/Rev. 1), 1975.

50. *Ibid.*, Table 7 and Table 8, p. 38.
51. *Ibid.*, p. 41.
52. Penrose, E. International Patenting and the Less Developed Countries, *Economic Journal*, 83:766-786 (September, 1973).
53. Vaitos, C.V. Patents Revisited: Their Function in Developing Countries. *Journal of Development Studies*, 1:71-96 (October, 1972); Katz, J.M., Patentes, corporaciones multinacionales y tecnologia: un examen critico de la legislacion internacional. *Desarrollo Economico: Revista de Ciencias Sociales*, 12, No. 45 (April-June, 1972); Grundmann, H., Foreign Patent Monopolies in Developing Countries: An Empirical Analysis. *Journal of Development Studies*, 12, No. 2:187-196 (Jan., 1976).
54. Hollie, P.G., *op cit.*, noted that in Europe: "National health plans and controlled drug prices have limited the European industry's growth to about half of the 12 percent a year it enjoyed before 1970. Government-controlled companies are becoming formidable rivals. And domestic political uncertainties cloud the outlook. In France, for example, the Communist-Socialist coalition's platform for the spring [1978] elections calls for the nationalization of the pharmaceutical industry."
55. OECD, *op cit.*, pp. 47-64.
56. Trademarks and their impact on the international drug market are examined in O'Brien, P. *Trademarks, the International Pharmaceutical Industry, and the Developing Countries*, ISS Occasional Papers, No. 63 (April, 1977).
57. *Ibid.*, p. 9. Also see Handoussa, H.A., *The Pharmaceutical Industry in Egypt* (Ph.D. Thesis, University of London).
58. *Ibid.*, p. 9; Ledogar, R. *Hungry for Profits* (New York: I.D.O.C., 1975), p. 12. Cuba has moved in the opposite direction, from 40,000 drugs stocked in 1959, to a current list of about 400.
59. Task Force on Prescription Drugs, *Final Report*, *op cit.*, p. 9. Also see Katz, *op cit.*, p. 23.
60. UNCTAD, *A case study of the pharmaceutical industry*, *op cit.*, p. 31.
61. Statement of Milton Silverman, Ph.D.; *Competitive Problems in the Drug Industry*, Part 32: p. 15367 (1976). Also Yudkin, J. To Plan is to Choose, University of Dar es Salaam, mimeo (1977), p. 9.
62. *Ibid.*, p. 15371.
63. Silverman, M. *The Drugging of the Americas* (Berkeley and Los Angeles: University of California Press, 1976); Ledogar, R., *op cit.* Also see their statements in *Competitive Problems in the Drug Industry*, Part 32, and Yudkin, J., *op cit.*, p. 13.
64. *Competitive Problems*, Part 32:15411 (1976).
65. *Competitive Problems*, *Ibid.*, pp. 15366-7.
66. Dixon B. Drug Resistance Spurs Vaccine Research, *New Scientist* (17 November 1977) reports on the "prospect of a return to preantibiotic days" if drug resistant strains become widespread.
67. Ledogar, R., *op cit.*
68. Goodman, L. The Law and Monopoly, The Case of Tetracycline. *New University Thought*, 3, No. 4 (1963), p. 48.
69. Klass, A. *op cit.*, pp. 78-79. In 1975 nearly one million citizens received more than \$20 million in refunds stemming from these suits, the largest class action settlement in U.S. history.
70. Brooke, P.A. *Resistant Prices: A Study of Competitive Strains in the Antibiotics Markets* (New York: CEPI, 1976). See also Graedon, J., *The People's Pharmacy* (New York: Avon Books, 1976), pp. 285-305.

71. Graedon, J., *Ibid.*, p. 291.
72. *Ibid.*, p. 292.
73. A U.S. Supreme Court decision early in 1978 allowing foreign nations to bring antitrust suits to federal courts was, in effect, a legal victory for India, Iran, and the Philippines, three of the first countries to bring suit. In Weaver, W., *Court Allows Suits by Foreign Nationals*, New York Times (12 January 1978).
74. Muller, R. and Barnett, R. *Global Reach* (New York: Simon and Schuster, 1974), p. 158.
75. UNCTAD, *op cit.*, p. 29; Vaitzos, C.V. *Intercountry Income Distribution and Transnational Corporations* (Oxford: Clarendon Press, 1974).
76. For examples from India see, Badami, P.L. *The Pharmaceutical Industry: A Survey, Commerce*, 116 (1968); from Brazil, in Ledogar, *op cit.*, pp. 53-60; from Iran, in Salekhou, G. *Commercialization of Technology in Developing Countries*, Ph.D. Thesis, New School for Social Research (1974).
77. The Monopolies Commission, *op cit.*, and *The Pharmaceutical Industry, op cit.*, pp. 19, 22-23.
78. Cooper, M. *European Pharmaceutical Prices 1964-1974* (London: Croom Helm, 1975), pp. 20-21.
79. Chaulet, P. and Sow, O.Y. *The Price of Recovery, Tuberculosis*, 33 (June 1974), pp. 14-17.
80. UNCTAD, *op cit.*, pp. 28-30.

## III.

# PHARMACEUTICAL PRODUCTION IN DEVELOPING COUNTRIES

### 3.1 *Production by Subsidiaries*

Much of the profitability of the pharmaceutical industry is derived from sales in developing countries. In Colombia, TNC subsidiaries accounted for 90 percent of total output in 1974-75.<sup>1</sup> The twenty largest firms in Brazil are reportedly controlled by foreign capital, and TNCs accounted for 80 percent of all Brazilian drug sales in 1973.<sup>2</sup> In India, sixty firms with significant foreign equity accounted for 70 percent of finished drug sales in 1973-74.<sup>3</sup> Considering that the mentioned countries are relatively advanced in domestically owned and operated pharmaceutical production, it can be assumed that the sale of drugs in developing market economies is accomplished almost entirely by TNCs and their affiliates.

A full explanation of the historical determinants resulting in the movement of the leading drug firms into relatively poor market economies is beyond the purposes of this discussion. However, generally speaking, in many such countries independent industrial entrepreneurship has not been particularly attractive to local investors, who have tended to be primarily involved in agricultural or mineral production oriented toward the world market. Therefore, industries important to modern drug production, such as petrochemicals, have often remained underdeveloped. Small-scale drug production was being carried out in Latin America and elsewhere at roughly the same time as the leading TNCs were entering into their initial expansionary period. However, many such small firms never realized the benefits from ties with publicly supported universities, medical schools, and research institutions that became so important to the discovery of new drugs in the post World War II era.<sup>4</sup> The highly skewed patterns of income distribution common to many of the least developed market economies have also contributed to slowing the growth of certain industries, in that effective demand for mass-produced technological goods has remained low.

Furthermore, modern pharmaceutical technology based on the synthesis of active ingredients led to the production of drugs which were far more potent than previously available medicinal substances. As appreciation of their effectiveness spread, the pharmaceutical industries located in the developed market economies reaped high levels of profit, allowing them to make further advances in their technological and marketing capability and move still more rapidly into the world market. Often firms producing for small foreign markets were eager to enter into joint operations with TNCs, and the extensive resources available to these firms allowed them to out-produce their competition. Firms which attempted to remain independent were unable to expand production

under the competitive strain of the heavy promotional campaigns carried out by the local affiliates of the TNCs.<sup>5</sup> Therefore, indigenous new drug development was constrained by the division of labor between the central operations of the TNCs and their foreign affiliates, which placed the responsibility for long range planning and R & D on the parent company.<sup>6</sup>

Another major aspect of the technology lag in pharmaceuticals experienced by many developing countries has been the continuing widespread use of traditional medicines derived from locally grown vegetable and animal materials. Although the heritage of traditional medicines is rich and varied in many parts of the world, the production of these curative substances never evolved from the stage of a cottage industry. To a significant degree this can be attributed to the low purchasing power of the segments of the population which have been most dependent upon traditional medical care. Traditional practitioners, who tend to have the same basic standard of living as their clients, have not separated their curative services from their production of medicines, and often maintain their economic status by refusing to share information about their curative work. Until recently there have been few national efforts directed toward pooling knowledge about traditional medicines and investing in their production.<sup>7</sup>

The expansion of TNCs to cover the demands of those populations which could afford the high cost of modern drugs typically has been initiated by the location of export sales outlets in foreign markets. When international commerce has become difficult, as during World War II, the acquisition of foreign manufacturing facilities and/or the creation of new facilities for the formulation and packaging of bulk imports of active ingredients has followed.<sup>8</sup> In more recent years state interventions by developing countries aimed at encouraging import substitution and broader legislative regulation of pharmaceuticals have further contributed to the movement of TNCs into foreign based production.

Some TNCs have continued with the vertical integration of drug production in their foreign operations, depending on available raw materials and local industrial development. Pfizer, for example, has built petrochemical plants in Mexico and Colombia.<sup>9</sup> However, the integration of all aspects of drug production in one foreign country is not usually accomplished by TNCs. More often international "product-by-plant" specialization occurs, whereby the location of a manufacturing plant is planned according to varying costs of production factors, e.g., the final stages of production (formulation and packaging) tend to be most labor-intensive and are often located in developing countries where wage levels are lower. The initial and most profitable stage of drug production—synthesis of active ingredients—is primarily carried out in the home countries of the TNCs, where long periods of capital-intensive technological development have yielded significant economies of scale in complex production processes.<sup>10</sup>

Product-by-plant specialization in the pharmaceutical industry often results in raw materials' being exported from a developing country for processing elsewhere, then imported back to the country in finished drug form. This is largely the case with drugs derived from animal and vegetable matters. Plants from Africa, Asia, and other parts of the world are sent to the major drug-producing countries for reduction to an essential active ingredient.<sup>11</sup> In many such cases there is no obvious value in this movement of materials. For example, in 1975, rumors of an insulin shortage in a South American country led to an examination of the supply sources of that country, which were found to be the imports of a single TNC. At the same time the local subsidiary of another TNC was exporting pancreas material from cattle, a basic raw material used in the production of insulin, a process which could have been carried out within the country.<sup>12</sup>

International fragmentation of the production process may be based on sound economic principles from the standpoint of the TNCs, but it is often cited as one of the principal factors impeding the full transfer of pharmaceutical technology to developing countries. Even India, which has undergone a sustained effort directed at developing an indigenous pharmaceutical industry, remains dependent on TNCs for the supply of most active ingredients.<sup>13</sup>

The use of "tied-aid" agreements of TNC subsidiary companies is another issue of importance to the potential transfer of technology. In connection with this, a recent report explained that:

...foreign subsidiaries are (often) privileged beneficiaries of the State-to-State aid granted by the parent company's country of origin. In fact, the parent company influences the policy of the donor country to include intermediary products financed by such aid, while the subsidiary company tries to ensure the import list allows the import of intermediaries. In a period of foreign exchange difficulties, the subsidiary company, being in a position to manufacture, can surpass its competitors and make fruitful profits.<sup>14</sup>

The production and sale of drugs in developing countries can be accomplished by wholly owned foreign subsidiaries, wherein all aspects of control are retained by stockholders in the home country of the TNC; more often, some resident ownership and control is involved in "joint venture" operations. External control has also been exerted over independent firms through the licensing process when the technology involved in production and/or the intermediate materials have been purchased from TNCs.

### *3.2 Issues in Technology Transfer*

The sale of technology by transnational industries, and sometimes by governments, is a complex issue. Even the industrialized market econo-

mies import much of their technology through license agreements, and there is little doubt that poor countries will want to continue purchasing at least some technology from abroad for an indefinite period of time. However, there exists a growing volume of evidence that much of the transfer of technology to developing countries has not been appropriate in terms of local conditions; furthermore, the weak bargaining position of developing countries in relation to the sellers of technology fosters unfair pricing practices and the attachment of disadvantageous conditions to sales agreements.<sup>15</sup>

### *i. Licensing Agreements*

Whereas basic scientific knowledge is considered to be freely available to all who wish to use it, the means for applying concrete scientific knowledge to the production process, i.e., technology, is privately owned and can be bought and sold like any other commodity. One of the most important arguments against the possibility of successful technology transfers from TNCs to independent pharmaceutical firms in developing countries is that when these firms produce drugs under license to TNCs, what follows is not so much a transfer of productive capability as a rental of know-how from TNCs under highly restrictive conditions.<sup>16</sup>

In licensing agreements, holders of patents and or trademark names grant other companies permission to manufacture and market the patented product according to the terms of the agreement. Payment for technology may involve specific bulk sum and or royalty payments based on a given percentage of sales. The license often specifies a package of items, e.g., it may include a trademark, industrial design, the provision of experienced personnel to train workers or advise on technical problems, or various other items associated with the particular technological process.<sup>17</sup> Often when license agreements involve particularly large potential markets, e.g. when the government of a developing country acts as the licensee, two or more TNCs cooperate in a joint licensing venture. Egypt entered into such an agreement with three of the leading TNCs in a move to nationalize the production base of pharmaceuticals in that country. In 1974 about 75 percent of Egypt's total imports of medicinal substances were active ingredients that were manufactured into finished drugs within the country. However, it appears that further agreements involving the "backward integration" of production have been blocked by the licensing firms.<sup>18</sup>

The flow of technology from foreign based TNCs rarely results in a full transfer of productive capability, especially when the conditions of the licensee's environment are not taken into account in the agreement. Typically, changes in the structure of imported machinery or modifications of industrial designs to suit local supplies of raw materials are prohibited by patent protection. In addition, bargaining on the sale of technology tends to be biased to the advantage of the small number of

sellers (licensors), and they can achieve greater financial benefits from package agreements involving their own personnel and intermediate materials.<sup>19</sup> On the other hand, the situation may be very different for firms that are not associated with TNCs. These firms must in some cases face certain difficulties in obtaining intermediate materials from TNCs (e.g., pressure to form an affiliation) and the firm's inability to procure these materials at a reasonable price may effectively inhibit their position as competitors.

The payment of royalties to patent holders is usually tied to agreements concerning the purchase of intermediate chemical products. Apparently royalties are often relatively low, or are not levied, when this type of purchase agreement is in effect. One of the primary reasons TNCs favor this type of agreement is that royalties are subject to taxation and the licensor is liable for payment. Furthermore, the price of imported chemicals can be controlled entirely by TNCs and, as in the cases of transfer-pricing described earlier, outflows of foreign exchange are not as easy to distinguish when they take the form of these hidden costs.<sup>20</sup> In Turkey it was reported that royalty payments as a percentage of sales were significantly lower for firms operating as subsidiaries of TNCs.<sup>21</sup> It is clear that in developing countries the use of transfer-pricing substantially lowers the ability of the public sector to control the costs of imported technology in the pharmaceutical sector.

Restrictive clauses attached to license agreements were discussed at length in the UNCTAD study of the patent system, a portion of which is reproduced in Annex A.<sup>22</sup> The most notable of these restrictive clauses include: obligations to purchase chemical products from the licensor; prohibitions on exports; and other territorial restrictions on distribution. However, more favorable licensing agreements that do not include such restrictive clauses have been offered by a variety of firms and public sector organizations, particularly those based in the Eastern European planned economies and Italy. For example, the Hungarian partner in pharmaceutical technology transfer agreements (MEDIMPEX) has included in its terms of sale the acknowledgement that Hungarian products will be given priority by firms in developing countries only if they are sold on an internationally competitive price basis.<sup>23</sup>

More positive aspects of technology sales agreements are related in part to the policies of the firm or governmental organization acting as licensor, but the bargaining position of the licensee firm (or government) is crucial to the assurance of a full transfer of productive capability by the close of the agreement period and to the creation of a new or improved manufacturing operation that can eventually provide a net economic benefit for its country. One way of improving the bargaining position of firms involves the accumulation of comparative cost information about any ingredients or machinery that are offered by the licensor in connection with the technology involved. Many of the earlier references to alleged over-pricing of imports by TNCs would not have emerged in the

absence of the data collection activities carried out by organizations operating in the public interest. The passage of legislation ensuring licensees the freedom to purchase materials from sources appropriate to local conditions at competitive costs would be especially useful in countries planning to develop a pharmaceutical sector with indigenous capital. Clearly, a TNC subsidiary or affiliate with substantial foreign equity would have little interest in obtaining this type of information.

Legislation controlling several types of abusive practices in licensing agreements (such as "tie-in" clauses and export prohibition) is another option that might lead to an improved bargaining position. Several countries already have laws of this type, e.g., the Andean group of countries of South America, India, and Zambia.<sup>24</sup>

Informed purchasing and legal sanctions against the misuse of patent privileges are two options readily available to developing countries having the need to import pharmaceutical technology. However, regardless of the effectiveness of regulatory control, the more patented products and processes that are licensed to local firms, the higher the probable cost of the final product. Only when there are many potential sellers of technology are prices likely to fall to lower levels. Options available to planning authorities include: (1) a limitation on the purchase of the newest forms of foreign pharmaceutical technology, which are inevitably under patent; and (2) a limitation or withdrawal of all patent privileges in the pharmaceutical sector, which in practice would mean prohibiting the manufacture of some new drugs. Of course, such choices would be strongly related to overall national policy regarding foreign investment.

One other issue of importance to license agreements is the appropriateness of the technology being transferred. The large, relatively unskilled labor force available to industrialization efforts in developing countries is a primary source of value. The neglect of this potential value through the importation of capital intensive technologies may be increasingly costly, both in terms of unemployment and dependency on processes that are too complex for ready adaptation to local use.

## ii. *Appropriate Technology*

### *The Labor Force*

One indicator of the capital intensive nature of modern drug technology as it has evolved in the developed countries is the relatively negligible increase in the number of workers employed in drug manufacturing over recent years. One report estimated that in the transnational pharmaceutical industry labor accounts for only about 3 percent of total costs.<sup>25</sup> A recent United Nations study of the structure of European industry found that in 1970 only about one percent of total employment in manufacturing was accounted for by the pharmaceutical sector in the major drug-producing countries.<sup>26</sup>

Since the pharmaceutical industry is potentially labor intensive at the stage of formulation and packaging and its skill requirements are not high, some stages of production would seem to be well suited to developing countries. However, TNCs have continued to stress further automation in the production process, in effect eliminating more jobs than they create.<sup>27</sup> An examination of all manufacturing in Latin America with a similar capital intensive, high technology emphasis found that while the share of industry in the national product more than doubled in the period 1925-1970, and the work force had grown in absolute terms, the proportion of the work force employed in manufacturing actually fell during that same time period.<sup>28</sup> It appears that personnel working in other capacities, particularly marketing, have accounted for increasing proportions of all persons employed by large drug firms. In Brazil, for example, a study of subsidiary operations in the drug field showed that some firms were employing more detail men than production workers.<sup>29</sup> These trends have serious implications with regard to the transfer of technology to developing countries, as the training of production workers is of significant overall importance to future industrial growth.

The potential for replacing capital (i.e. machinery) with greater numbers of workers has been criticized from the standpoint of improved quality control. This argument points to the possibility of more errors in a production process which requires at certain points careful measurement and control to ensure that the finished drug product will be efficacious and fall within established standards of safety for human use. On the other hand, if workers are not trained to produce drugs in relatively small scale manufacturing facilities that can be distributed throughout countries that are predominantly rural, transporting drugs to distant areas will remain a major problem in countries which lack funds, vehicles and personnel for delivering drugs when and where they are most needed.<sup>30</sup>

### *Raw Materials*

Chemical synthetics, which form the bulk of modern drug supply, are currently derived from raw materials produced by well developed petrochemical industries located in the highly industrialized countries. Since TNCs have had easy access to these products they have had little incentive to focus research on other types of raw materials, particularly vegetable matter which may be foreign to their countries.<sup>31</sup>

Some developing countries, particularly those with known oil reserves such as Argentina and Mexico, are able to plan linkages between the petrochemical and pharmaceutical industries and thereby internalize all aspects of the production of petrochemical based drugs. In most of the world, however, the production of a full range of basic chemicals from petroleum, coal, and alcohol is at present a distant goal that cannot be reasonably linked to plans for drug production. This is one of the reasons that alternative types of raw materials are being considered by countries

in which firms or public sector organizations are actively interested in the national production of at least some basic drugs.

The raw materials for drugs produced by fermentation include several types of low cost carbohydrates. Molasses by-products, for example, are apparently being used as the basis of development in the Cuban organic chemicals industry.<sup>34</sup> A study of Tanzanian potential for indigenous drug production found that hecogenin, a by-product of sisal processing used as a raw material for corticosteroid production, could conceivably be processed within the country instead of being sold abroad in a crude state.<sup>35</sup> This study also pointed out that the routine extraction of by-products from existing wood industry (e.g. eucalyptus for antiseptic purposes, camphor, and gum caraya as a bulk laxative) could be augmented by further extraction processes to yield aliphatic and aromatic chemicals that could be used as intermediates for drug manufacture.<sup>36</sup>

A group of chemicals derived from plants which are still commonly used in modern drug production are the alkaloids. However, countries which might exploit this aspect of their natural resources, e.g., Turkey, have not yet done so to any significant degree.<sup>37</sup> The prospect is particularly appealing in that alkaloids are relatively easy to extract and could be processed by local factories for local needs or exported at a greater value than if they were sold as raw materials.<sup>31</sup>

A survey of medicinal plants in India reported that closer attention to the improvement of cinchona plantations for quinine production is an obvious approach to indigenous drug development in countries where planting is possible. By-products from tea wastes can provide some countries with all of their caffeine requirements, and theophyllin can be extracted from the dust for conversion into an asthma treatment (aminophylline). Some of the more important findings of Indian research on locally grown medicinal plants, notably *Rawvolfia serpentina*, a cure for high blood pressure, are also discussed in the survey.<sup>37</sup> In a WHO Seminar on the Use of Plants in Health Care, it was pointed out that many other valuable drugs such as atrophine, quinine and morphine came into use after the study of corresponding medicinal plants – *beladonna*, *cinchona*, and *opium*.<sup>38</sup>

Drugs produced by the fermentation process, as mentioned earlier, are an attractive option for local production because of their dependence upon readily available and inexpensive raw materials. The preparation of vaccines and the production of antibiotics from micro-organisms by fermentation are being examined in several countries, but as yet such production takes place in very few developing countries. Even if countries choose not to observe patents on associated technology, substantial problems are presented by the sophistication of this process; in particular, the need to obtain special strains which produce high product yields involves unusually precise quality control specifications.<sup>39</sup> Furthermore, industrial fermentation plants are currently operated on a very large scale, and reducing the scale of such facilities to suit national needs may not be an easy task.

In any event, considerations of the rising costs of antibiotics coupled with the increasing amounts being utilized by local populations may result in decisions by some countries to build fermentation and production facilities in order to ensure adequate supplies of this basic therapeutic category. Consulting groups such as the Intermediate Technology Development Group (ITDG) based in London and some international agencies, particularly UNIDO, could prove useful in providing technical advice about the creation of such facilities, especially if they are to be on a small scale.<sup>40</sup> Where capability to begin antibiotic production in the near future is unlikely, this process could still be utilized in simpler form to produce food yeast, which is an excellent source of B vitamins.

The use of organic raw materials that can be locally raised appears to be a rational strategy for less industrialized countries seeking greater self-sufficiency in drug supply. It should be emphasized that the utilization of local agricultural or animal by-products for modern drug production is complementary to the reintegration of traditional herbal medicines into westernized medical systems. Increased acceptance and encouragement of the heritage of popular herbal medicine is occurring throughout the world after a long period of neglect, largely because of the failure of expensive forms of Western medical treatment to cover the basic health care needs of many population groups.<sup>41</sup>

The People's Republic of China has taken the lead in producing both traditional medicines and modern drugs and along with Korea and some countries of Southeast Asia exports herbal mixtures.<sup>42</sup> Most of the traditional herbal mixtures have a mild pharmacological action, and where they are widely accepted by local populations there appears to be no reason to replace them with a supply of more expensive modern drugs of similar low level effectiveness (e.g., cough syrups, mild stimulants or relaxants). UNIDO is capable of assisting the least developed countries with the collection of data on medicinal plants. It also has been involved in establishing a pharmaceutical center in Africa which is intended to assist in the transfer of such simple technologies as those involved in the extraction of herbs and animal by-products. National research efforts aimed at the identification of specific, active ingredients are being carried out in, for example, China, India, and Mexico.<sup>43</sup>

Smaller countries may run some risk in diverting highly trained personnel and public funds into such long-range research projects. In countries where there exist serious shortages of lifesaving basic drugs, an appropriate technology strategy would probably begin with the establishment of a national list of essential drugs and the assurance that firms or public sector producers focus raw material extraction and processing on substances which are known to form the basis of one or more of those essential drugs, for example, some of the alkaloids and the carbohydrates which could be developed from vegetable by-products and thus become the starting materials for a fermentation facility producing antibiotics. In connection with this, a Vietnamese report about their early experiences in

drug production noted that an initial overemphasis on medicinal plants partially hampered the development of a national capacity for producing modern drugs which already are being consumed in considerable quantities.<sup>44</sup>

### *3.3 Stages of Drug Production*

There are four distinguishable stages in modern drug production. First, raw materials must be made available by the production of synthetic chemicals or the fermentation of naturally occurring materials. Secondly, active ingredients must be purified and the desired mix of ingredients for a particular pharmaceutical chemical achieved. This stage involves the most elaborate quality control precautions in order to assure that the finished ingredients have the required chemical properties and are effective and safe for human use. The third stage is more mechanical and the simplest to achieve on a small scale. It involves the formulation of the active ingredients into final dosage form ready for medicinal use. Packaging into containers suitable for immediate medical use may be included in this stage, or this may be relegated to health sector institutions, e.g., hospitals or health centers.<sup>45</sup>

Recent United Nations data showed that only sixteen developing countries have a pharmaceutical sector which is well enough established to plan for the integration of most aspects of drug production in at least some product lines. Only seven of the group of developing countries have already achieved full integration of production in enough therapeutic categories so as to have achieved a reasonable level of pharmaceutical self-sufficiency. The remainder of the developing countries have only a simple formulation and packaging industry (around 45) or else no manufacturing capacity at all (around 43).<sup>46</sup>

The problems involved in carrying out the production of raw materials for chemical synthetic drug production have already been discussed. Some countries are capable of significant progress in this area, however, and cooperative arrangements can be extremely useful for proposed exchanges of technology and achieving economies of scale in a range of basic chemicals. The establishment of Cooperative Pharmaceutical Production and Technology Centres (COPPTeCs) would seem to be a logical step and is being facilitated by the joint efforts of UNIDO, UNCTAD, and WHO. On a regional basis, the experiences of ACDIMA (the Arab Company for Drug Industries and Medical Appliances) and the Andean Pact countries could be of use to other regional groupings. India and China are both capable of offering technical assistance in this complex area. The provision of raw materials from locally available substances, as described earlier, is perhaps a more viable long range option for individual countries. This would require a thorough survey of resources, including vegetable material growing wild or, preferably, widely available as by-products of agricultural and animal production.

Initial investments would involve the systematic collection of agricultural by-products and or the establishment of enterprises which could grow specific species. Considering the difficulties involved in transporting vegetable raw materials, due to their volume/weight ratio and the poor condition of rural roads in most developing countries, processing and storage facilities would have to be planned near the sources. Animal organs may be processed for certain drugs, particularly in countries with extensive cattle resources, but well equipped slaughterhouses and modern, reliable refrigerated storage facilities are necessary.<sup>47</sup> The preparation of drugs from natural raw materials by the industrial fermentation process is the biological equivalent of fine chemicals manufacture, but, again, fermentation is a high technology process and a feasibility study (perhaps with the assistance of UNIDO) should precede the raw material survey if more than simple extraction processes are planned.

The second stage, manufacturing pharmaceuticals from raw materials, is an area in which existing local industry might be put to use. An industrial scale plant would require the transfer of technical know-how, either through licensing agreements or by the acquisition of basic industrial design information from international agencies. The Pharmaceutical Centre in Africa, for example, has been organized with the assistance of UNIDO in order to transfer technology between countries for the local production of medicinal products such as intravenous fluids and extractions from plant and animal materials.

At this stage the problems of quality control are critical because the biological behavior of many preparations can vary greatly as a result of seemingly trivial changes in formulation or physical treatment.<sup>48</sup> In view of the potential risks of "haphazard operations" the Twenty-eighth World Health Assembly recommended that Member States apply the revised requirements for "good practices in the manufacture and quality control of drugs" and participate in the revised "certification scheme on the quality of pharmaceutical products moving in international commerce." The "good practices" requirements specify that every manufacturing establishment should have a quality control department with a laboratory for performing all such tests. There is a real need, particularly in small scale plants just beginning manufacture, for a quality assurance manual with specifications which can be adhered to where expensive laboratory apparatus is not available.<sup>49</sup> Basically, it would describe tests for commonly used medicines that the particular facility was capable of manufacturing and clearly indicate the kinds of equipment required. Much of the testing could be done with fairly inexpensive and simple equipment, but for more sophisticated work regional laboratories would be necessary.<sup>50</sup> Very detailed information on the quality of pharmaceutical products is being provided by the World Health Organization.<sup>51</sup>

The third stage, the formulation of pharmaceuticals, may be accomplished in a small scale manufacturing operation or in a health sector setting (i.e. a hospital, clinic, or pharmacy). Since there are no significant

economies of scale at this stage the investment required would be largely devoted to equipment, which may be more or less labor intensive depending upon the level of technology. The large scale serial production of finished pills and capsules would seem to lend itself to the intensive use of local labor. This stage of production is the starting point for countries without any previous national involvement in drug manufacturing, and even when bulk materials must be purchased from TNCs, experience has shown that large savings to purchasers can be effected.<sup>52</sup> The State Pharmaceuticals Corporation in Sri Lanka estimated that if 34 widely used tablets and capsules were formulated in local factories from imported pharmaceutical chemicals, there would be a foreign exchange saving of almost one-half million U.S. dollars, plus the added benefit of new employment opportunities.<sup>53</sup> In-country formulation also enables manufacturers to respond more appropriately to the needs of their particular national health services (e.g. tropical packaging).

### *3.4 The Pharmaceutical Industry and the Public Health Service*

A report submitted by the Director-General of WHO regarding national drug policies noted that decisions about drugs must be made within the framework of both overall health planning and national planning for economic development. In some developing countries there may be plans to stimulate the growth of a pharmaceutical industry capable of supplying the home market with drugs, thereby reducing imports and saving scarce foreign exchange. Other countries may also be interested in beginning production of some products for international export. A national drug industry can also have considerable strategic value during times of war, trade embargo, epidemic or other natural disaster, when the health of large numbers of people is endangered.<sup>55</sup>

If the health needs of the population are to be served, the pharmaceutical industry and the public health services must achieve a level of cooperation which ensures that drug production reflects the true therapeutic needs of the country, and if there is to be more than one producing plant, that manufacturing operations are geographically distributed throughout the country so as to facilitate the transport of finished products to health care institutions. Without regional planning, plants are likely to be clustered in only one to two large cities. In Turkey and Mexico, for example, more than 80 percent of manufacturing facilities are located in one large urban area.<sup>56</sup> A cooperative relationship also protects the industry from potentially hazardous international competitive conditions in its initial phase which, considering the relatively low level of demand for more than a few basic products, could be devastating.<sup>57</sup> This would be particularly true if the nationally based company was forced to compete with brand name products that were already familiar to prescribing physicians. A reciprocal relationship between the producers and the health sector would also require an effective system of public

accountability, with public participation in planning agreements that include detailed information about costs.

In selecting drugs to be nationally produced it should be accepted that meeting national therapeutic requirements for these drugs will not necessarily be a commercially profitable endeavor. As noted earlier, commercial considerations have biased industrial research (therefore, the array of available drugs) toward the needs of wealthy consumers. In addition it appears that in many developing countries local private sector manufacturers, regardless of the geographical source of their capital, are primarily concerned with making profitable—even if therapeutically unimportant—drugs and cosmetics (e.g. large numbers of vitamin preparations, cough syrups, skin preparations).<sup>58</sup> According to the Director of the Central Drug Research Institute at Lucknow, India, at least 40 percent of Indian national production is of less commonly used drugs not relevant to the vital needs of the population, and some firms have been devoting as much as 80 to 90 percent of their production to common household remedies and vitamins.<sup>59</sup> Total self-sufficiency in drug supply in any but a few developing economies (e.g. China, India) is highly unlikely, but limited resources can be put to good use with careful planning.

Beyond production capability, however, there is a question of necessity. Many countries, among them some of the most developed market economies, prefer to purchase drugs from foreign companies. Efficient large scale purchasing is greatly facilitated in countries such as Norway by the use of a national formulary which limits the number of drugs which may circulate in the health sector. Before turning to a discussion of purchasing, however, it is important to stress that national production of a basic list of drugs in cooperation with the public health services, whether financed by government or private sector capital, should be accompanied by a regulatory structure capable of creating and enforcing policies relating to the public accountability of producers in terms of price, quality, and the kinds of products manufactured.<sup>60</sup> In the developed market economies, where the drug industry flourished without this structure, assuring the public accountability of the industry has taken the form of long and costly legislative procedures involving the difficulties of negotiating with industries already in a strong political position due to their great contributions to the overall economic growth of their home economies.

## FOOTNOTES

1. UNCTAD, *op cit.*, p. 19.

2. *Ibid.*, p. 18 and Ledogar, R., *op cit.*, p. 7.

3. *Ibid.*, p. 18; See also UNCTAD, *The Pharmaceutical Industry in India*. Study prepared by the Jawaharlal Nehru University and the Indian Council of Scientific and Industrial Research (TD B c.6 20), 1977, p. 6.

4. For example, Bertero, C. *Drugs and Dependency in Brazil: An empirical study of dependency theory*, Ph.D. Thesis, Cornell University (1972).
5. Bertero, C. *Ibid.*, see the section on the Brazilian pharmaceutical industry.
6. This pattern is typical of transnational enterprise. Subsidiaries and foreign affiliates carry out activities similar to the parent company, becoming "miniature replicas" of the TNC's home operations, yet the planning of expansion is retained by the parent. In connection with this, see, e.g., Evans, P.B., Direct Investment and Industrial Concentration. *Journal of Development Studies* (1976), pp. 119-136.
7. See Bannerman, R.H. WHO's programme in traditional medicine. *WHO Chronicle* 3, No. 11 (November, 1974), for a summary of recent international efforts in this regard.
8. UNCTAD, *The Pharmaceutical Industry in India, op cit.*, p. 1.
9. Murray, M., *op cit.*, p. 629.
10. The protectionist policies initiated by Western Europe and the United States following World War I resulted in heavily capital-intensive production processes, due in part to the relative shortage of labor, and to the preference for "stable" production factors, i.e., machinery, in lieu of large numbers of workers.
11. Cilingiroglu, A. *Transfer of Technology for Pharmaceutical Chemicals*, (Paris: OECD, 1975), p. 24.
12. Ledogar, R. *op cit.*, pp. 66-67.
13. UNCTAD, *The Pharmaceutical Industry in India, op cit.*, p. 20.
14. Cilingiroglu, A., *op cit.*, p. 28.
15. Cilingiroglu, A., *op cit.*, pp. 54-56. See also UNCTAD, *Guidelines for the study of the transfer of technology to developing countries*.
16. UNCTAD, *A Case Study of Spain*, Report by the UNCTAD. Secretariat (TD B AC.11 17) 1974, pp. 44-45.
17. See for example, Ljunggren, S. *Some Aspects on the Licensing of Contraceptives with Special Regard to the Manufacture, Marketing and Distribution in Developing Countries* (ID WG.116 b), 1971.
18. Handoussa, H.A. *The Pharmaceutical Industry in Egypt*. Ph.D. Thesis, University of London, School of Oriental and African Studies, 1974.
19. For an examination of technology transfer in Africa, see Thomas, D.B., *Importing Technology into Africa* (New York: Praeger, 1976).
20. UNCTAD, *A Case Study of Spain, op cit.*, pp. 28-30.
21. Cilingiroglu, A., *op cit.*, p. 77.
22. UNCTAD, *The role of the patent system in the transfer of technology to developing countries* (TD B AC.11 19 Rev. 1), 1975. See also Cilingiroglu, A., *op cit.*, pp. 65-82, for a report of contract terms found in five Southern European countries.
23. See the description of the IMARSEL Chemicals Co., Ltd., in Nigeria, for example, in UNCTAD, *A case study of Hungary* (TD B AC.11/18), 1974, pp. 31-32.
24. UNCTAD, *The role of the patent system in the transfer of technology to developing countries, op cit.*, p. 25.
25. Heller, T., *op cit.*, p. 15.
26. Table A. 4, *Appendix A. Structure and Change in European Industry* (New York: United Nations, 1977).
27. Cilingiroglu, A. *Transfer of Technology for Pharmaceutical Chemicals* (Paris: OECD, 1975), p. 22-23.
28. Heller, T., *op cit.*, p. 15.

29. Bertero, C. *Ibid.*, pp. 103-105.
30. Dunnill, P. *The Provision of Pharmaceuticals by Appropriate Technology* (London: ITDG, 1975).
31. Barker, C. *Pharmaceutical Production in a Less Developed Country*, IDS Communication 119 (1975), pp. 20-23.
32. Cilingiroglu, A., *op cit.*, p. 24.
33. National Drug Policies, *WHO Chronicle* 29:337-349 (1975).
34. Barker, C., *op cit.*, pp. 20-23.
35. *Ibid.*
36. *Ibid.*
37. Kempanna, C. Prospects for medicinal plants in Indian agriculture, *World Crops* (July August, 1974).
38. Discussed in the *WHO Chronicle* 31:527 (1977).
39. Dunnill, P. The Provision of Drugs by Appropriate Technology, *Appropriate Technology* 4, No. 2:6-7 (August, 1977).
40. For an early UNIDO paper on the use of organic raw materials, see Horvath, G. Active principles, drugs, pharmaceutical intermediates and pharmaceutical preparations extracted or prepared from botanicals, animal organs and agricultural residues (ID/WG.37/15), 1969.
41. Traditional medicine: some examples of its use, *WHO Chronicle* 31:428-432 (1977). See also *World Health*. The magazine of the WHO, special issue on traditional medicine (November, 1977).
42. For a brief description of drug manufacture in China, see Sidel, V. and Sidel, R. *Serve the People* (Boston: Beacon Press, 1973), pp. 187-189.
43. For an overview of Chinese traditional medicines from the standpoint of production and political rationale, see The American Herbal Pharmacology Delegation report, *Herbal Pharmacology in the People's Republic of China* (Washington, D.C.: National Academy of Science, 1975).
44. McMichael, J.K. (ed.) *Health in the Third World: Studies From Vietnam* (Nottingham, U.K.: The Bertrand Russell Peace Foundation, 1976), p. 170.
45. Cilingiroglu, A., *op cit.*, pp. 59-60.
46. Patel, S. Paper presented at the Working Group Meeting on Pharmaceuticals, Georgetown, Guyana (1976).
47. UNIDO, *Establishment of Pharmaceutical Industries in Developing Countries* (ID/35), 1970, pp. 22-23.
48. Binns, T.B. Responsibility for Providing Drugs for Diseases Prevalent Outside the Country of Origin. Paper presented at the Fourth Symposium on *Clinical Pharmacological Evaluation in Drug Control*, Copenhagen: WHO, 1975, pp. 3-5.
49. Deasy, P.B. and Timoney, R.F. (eds.). *The Quality Control of Medicines* (New York: Elsevier Scientific Publishing Co., 1976), see in particular the chapter by C.A. Johnson, International Problems in the Control of Medicine.
50. Binns, T.B., *op cit.*, pp. 4-5.
51. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*, Technical Report Series, No. 567 (Geneva: WHO, 1975); *Specifications for Pharmaceutical Preparations*, Technical Report Series, No. 487 (1972); *Guidelines for Evaluation of Drugs for Use in Man*, Technical Report Series, No. 563 (1975); *Bioavailability of Drugs*, No. 536 (1974).
52. Interview with a Brazilian doctor manufacturing drugs in a hospital laboratory, in Ledogar, R., *op cit.*, pp. 10-12.

53. Bibile, S. Case Studies in the Transfer of Technology: Pharmaceutical Studies in Sri Lanka (TD/B/C.6/21), 1977, pp. 30-31. Due to difficulties of the government in securing agreement to the plan from the local TNC subsidiaries, the "34 drug programme" was drastically scaled down, and the government began to plan a state-run formulation operation.
54. National Drug Policies, *op cit.*
55. Schaumann, L. Pharmaceutical Research: An International Quest for Technology. Paper presented to the Academy of Pharmaceutical Science, New York (1977), p. 5.
56. Lopez, O.P. Consideraciones sobre la actividad de las empresas farmacéuticas en Mexico, *Comercio Exterior* Vol. 27, No. 8 (August, 1977), p. 934.
57. UNIDO, *Establishment of Pharmaceutical Industries in Developing Countries, op cit.*, pp. 12-13.
58. *Ibid.*, p. 13.
59. Bibile, S., *op cit.*, p. 27.
60. "More Non-Essential Drugs?" *Economic and Political Weekly* (September 24, 1977), pp. 1660-61.

## IV. PURCHASING

### 4.1 *The Formulary System of Drug Procurement*

A formulary is a list of approved or recommended pharmaceutical products designed to standardize selection and control costs. It differs from a simple listing of those drugs available in stock, commonly found in hospitals and pharmacies, in that it is written by a group of experts for the purpose of shifting utilization from one product to another on the basis of a set of preconceived and organized standards.

In some countries formularies have been used by large military and teaching hospitals since the early nineteenth century, and lengthy experience at this level has shown that a regulated drug list can serve a variety of useful purposes, e.g., minimize the procurement of duplicate brand name products, simplify inventory control, and serve as a teaching aid for medical students.<sup>1</sup> Formularies came into wider use after World War II as the increasing number of new drugs discovered by the TNCs was met by significantly higher drug utilization rates, particularly in the Western countries. The individual health benefits of these new, very effective drugs were soon perceived as being at least partially offset by certain social costs, particularly the drug information problem facing the medical profession and the cost of meeting rising national expenditures for subsidized drug products.

Governmental responses to these problems have varied in keeping with the type and extent of publicly supported national health services. The most common way in which the state sector has sought to control pharmaceutical costs has been through the establishment of a limited list of those drugs whose cost is to be covered by government.<sup>2</sup> The level and specific type of public involvement in health services affects the ways in which these formularies can be applied. In market economies in which social security systems cover the health service costs of specified proportions of the population, formularies list the drugs which may be prescribed for this population throughout both privately and publicly organized health services, e.g. in Mali, India, Mexico, New Zealand, Australia, France, Italy, and Switzerland.<sup>3</sup>

Some of the more recent advances in the formulary system of procurement have occurred in the Italian health system. Hospitals in Italy now follow purchasing guidelines limiting each institution to a formulary containing 500 approved drugs. This formulary was initiated in the region of Lombardy, where a Regional Committee prepared a list to be used by the 100 hospitals in the area. All regional authorities later approved the formulary. The role of each hospital's drug committee in the process of selection involves the choice of two drugs from each category listed. There

is some possibility for further flexibility in the listings (more than two types of related drugs or drugs outside the original list) if the selections are justified to the authorities. As in most market economies, the Italian Ministry of Health lists the drugs which are eligible for reimbursement by government. However, the listing has been revised with the specific intention of ensuring that available funds would be directed toward the most prevalent diseases.

Several developing countries have begun to procure drugs in bulk for their primary health care services. Formularies have a particularly important role to play in this regard. Basic drug lists can be designed to restrict purchases to only the most essential items, thus reducing costs and simplifying the prescribing tasks of auxiliary health workers. Standard drug lists have been prepared by, for example, Afghanistan, Nepal, Pakistan, Malaysia, Indonesia, and Ghana.

In countries where efforts are underway to make access to health services more equitable, as between urban and rural populations and varying socio-economic groups, rapidly increasing expenditures on drug supplies may become a serious bottleneck in the absence of careful controls over their purchase. This is likely to occur at the point when segments of the population with low income levels and associated low health service utilization rates realize access to subsidized medical services and drugs, and previously unmet health service needs are transformed into higher levels of effective demand. Data reported in a 1974 survey of pharmaceutical costs within various social security systems showed that countries in Southern Europe which have most recently substantially improved overall access to health services have also been faced with the highest relative rates of increase in drug consumption—upwards of 150 percent over a ten-year period.<sup>4</sup> An increase in health facilities and an improved distribution of services in Cuba have also been seen to result in higher utilization rates. In 1958 there was a severe imbalance between the number of pharmacies in Cuba's urban areas and those in the countryside. According to that country's Ministry of Health that situation has now been corrected, and prescribed drugs (approximately 50 percent of all drugs obtained) are readily available throughout the country.<sup>5</sup>

Cuba is one of a small group of countries which have national formularies that are compulsory for all of the public health sector. Prior to 1959 an estimated 40,000 different drugs, many of them duplicate, brand name products, were available in Cuba. Thereafter, a Commission of the National Formulary under the auspices of the Ministry of Health reviewed the therapeutic needs of the country and created a formulary containing about 1,000 listed drugs considered to be essential. Norway, Peru, Ecuador, Guyana, Jordan, Egypt, and Sri Lanka have national drug lists, with the ministries of health responsible in most cases for appointing the formulary committee.

The concept of a national formulary differs from that of a "basic drug list" in that it affects not only some part of the public health sector, but

the entire supply of publicly subsidized drugs. In Norway and Sri Lanka all drugs available for national utilization are subject to formulary limitation. Most types of formularies currently in use assist prescribers with rational drug selection and contribute to the control of costs. A national formulary offers the additional advantage of public control over total imports of pharmaceuticals and policy direction for potential drug production. Of course, its overall effectiveness in this regard increases when it is compulsory for both the public and private health services.

Sri Lanka's public health sector limited prescribing to a Hospital's Formulary as early as 1959, and thereafter public institutions used a list of drugs under their generic names that numbered about 500 (1,000 dosage forms).<sup>6</sup> In response to a balance of payments situation that required further import restrictions, the original Formulary Committee was asked in 1962 to recommend a formulary for the whole country, i.e. public and private health services. Their recommendations resulted in a somewhat broader listing of drugs (the national formulary now contains about 630 drugs) which were officially approved for import and local manufacture.<sup>7</sup>

From this brief overview it is evident that formularies can be used in a variety of ways, depending primarily on the extent to which any aspect of drug utilization is considered to be a problem, the form and coverage of publicly funded health services, and the amount of flexibility which is reserved for prescribers outside the public health sector. In the developed market economies, for example, the existence of national pharmaceutical industries which operate on a large scale and/or relatively high per capita incomes ensures that drug supply and utilization levels will be adequate among most population groupings. In such countries social security and other health insurance systems reinforce the financial accessibility of those groups which otherwise might not be able to afford drugs. Where formularies only involve drugs prescribed for social security or insurance recipients, total national purchases of drugs generally include a much wider array of products. Switzerland, for example, which included the unusually large number of 7,000 drugs in its formulary, has the much larger total of 36,000 medicaments available on the national market.<sup>8</sup> The number of physicians and pharmacists in the more developed market economies is relatively high, and much of the responsibility for maintaining the formulary guidelines of subsidized programs is decentralized to the level of the individual practitioner.

The least developed countries must import most of their pharmaceutical supplies from foreign firms, so balance of payments concerns become an additional issue of importance to purchasing patterns. Also, where access to professional health care services is inadequate for large population segments, the retail distribution of ethical drugs has resulted in the widespread practice of self-medication. This practice of "uninformed utilization" is difficult to regulate at the pharmacy, shop or market level for at least two reasons: among the rural poor, occasional purchases of a few pills or capsules may be the only form of curative

medicine that is readily available; on the supply side, the sale of modern drugs such as antibiotics can be very profitable for local merchants, especially those located in areas where drug industry financed advertisements are displayed prominently on billboards and posters.

This combination of factors appears to require a more comprehensive, centralized approach to national drug procurement in those countries in which high and rapidly rising overall costs and inefficient distribution practices are perceived as problems. In the forward to the Guyana National Formulary (1977) the Minister of Health outlined his case for national procurement guidelines as follows:

... it will underscore our determination to tackle the legacy in the area of drugs, prescriptions and medicines left us by our colonial past. A legacy in which we were the victims of the salesmen, advertisers, and some manufacturers whose primary concern was making money.

Secondly, it should help us to conserve Foreign Exchange by restricting the number of imported ethical drugs and the domestic market to the most essential, and available to the Guyanese people at fair prices.

Thirdly, it is a significant step toward demystifying the business of drugs and pharmaceuticals to our people.<sup>9</sup>

According to the WHO Expert Committee on the Selection of Essential Drugs, about 200 drugs will suffice to meet the basic health needs of the majority of the world's population. The Committee stressed the fact that in some countries drug expenditures account for more than 40 percent of available public sector health funds.<sup>10</sup> Rising costs in this area may be directly related to a limitation or reduction in other priority areas of health services development. The WHO Committee established a model list to be used as a starting point, or guide for comparison, by countries planning to develop and use a formulary. (see Annex B).

Criteria for the selection of drugs for any particular country's formulary include several elements. At the Fifth Conference of Heads of State of Non-aligned Countries, held in 1976, there was passed a "Resolution on Co-operation and Distribution of Pharmaceuticals." This resolution was based primarily on the "Proposal of a Group of Experts on Pharmaceuticals," who had met in the month prior to the conference.<sup>11</sup> That document utilized the following as special criteria for selecting priority pharmaceuticals:

1. the prevalence of specific diseases in the country;
2. the seriousness of the diseases;
3. the effectiveness of possible alternative drugs relative to their adverse effects;
4. the cost of the different alternatives (bearing in mind that generic equivalents may be obtained more cheaply than brand products);
5. the possibilities for local, national or regional production.<sup>12</sup>

Further criteria for selection were outlined by the WHO Committee, which noted in addition that the preparation of a drug list should be preceded by the creation of a standing committee with the specific responsibility of formulating the list and revising it when necessary. The creation of a formulary is a task requiring the constant attention of at least a small group of individuals, including clinical pharmacologists, pharmacists, statisticians, and clinical health workers drawn from all levels of health care service. This group should be prepared to monitor national trends in the areas of disease prevalence and drug utilization, and to point out such problems as continuous or rising curative expenditures on illnesses that are considered "preventable." A regular schedule of revisions ensures that changing factors in drug availability, such as the expiration of patents, receive consideration. In New Zealand, for example, the list of drugs formulated by the Department of Health that are provided free under social security legislation is amended three times a year on the basis of recommendations by the Pharmacology and Therapeutics Advisory Committee.<sup>13</sup>

#### *i. Therapeutic Need*

The first steps in identifying pharmaceutical needs include an examination of disease prevalence, preferably by age and sex, and the relative seriousness of the diseases, i.e., the development of a priority list of indications for medical treatment. The known therapeutic treatments for the various illnesses can then be listed next to the associated indications for use, and further data on quality and availability utilized to make the final choices. The actual process of determining therapeutic need will vary among countries, depending to a considerable extent on the priorities of the health sector in terms of population coverage and the desired balance between preventive and curative services.

In some countries the data on disease prevalence may be biased by exclusive dependence upon health service utilization rates, particularly if a large section of the population does not have adequate access to those health services. Furthermore, the accuracy of diagnosis upon which this kind of information is based is often limited by the broad range of etiological factors involved in the most prevalent communicable diseases and nutritional deficiencies.

For example, in many tropical countries gastroenteritis is reportedly the most common cause of mortality and morbidity among infants and children. However, gastroenteritis is often a routine diagnosis for an illness related to several underlying or associated conditions, particularly malnutrition.<sup>14</sup> The interaction of an inadequate diet and repeated episodes of diarrheal disease results in a "vicious circle" which worsens as the malnutrition linked to severe gastroenteritis creates a higher risk potential for further episodes of infectious disease.<sup>15</sup> The original source of the infection in areas where it is most common is often fecal

contamination of food and water and the unhygienic handling of food. These problems have been augmented in recent years by the increasingly widespread use of the feeding bottle, "even by mothers of poor families who have ample supplies of breast milk and cannot afford to buy adequate amounts of artificial milk powder."<sup>16</sup> Expensive milk powder is nutritionally inferior to mother's milk, and poor women have attempted to make it go further by diluting it and saving small quantities of it in the bottle. The difficulties of obtaining water that is not polluted and securing access to refrigeration facilities make bottled infant formula a potential breeding ground for bacteria, and the consequences of its use under these conditions may be deadly.<sup>17</sup>

This example serves to illustrate one very important aspect of the process of determining therapeutic need. Criteria for selection should include the alternative costs of non-pharmaceutical interventions for certain prevalent illnesses. Much of the illness in developing countries is associated more with an overall pattern of poverty than any specific disease entity, and these "diseases of poverty" can be eradicated only by an overall improvement in the productive capacities of the poor and the appropriation by the poor of the resultant economic surplus, coupled with the creation of social organizations at the community level that can take responsibility for the building of a system of preventive health services.<sup>18</sup> Otherwise, the vicious circle of infectious disease-malnutrition-infectious disease is likely to prove impossible to break, and the increasing physical debilitation of young children caught in this circular pattern of ill health will continue to be reflected in the mortality rates of infants and children as well as in the chronic weakness and depression of the adult working population.

Attempts to treat these kinds of health problems with medical services and modern drugs have resulted in a vicious circle of another kind, disease-treatment-recurrent disease.<sup>19</sup> One of the most notable examples in this regard is hookworm. While current treatment methods can eliminate hookworm in the individual, the illness will appear continually unless organized efforts are made toward prevention. In the case of gastroenteritis, the clinical replacement of fluids and electrolytes is especially vital in many cases, but requires trained health workers and is a time-consuming procedure. The lack of a community level primary health care system capable of providing treatment for dehydrated children will lead some parents to the purchase of antibiotic drugs in small amounts at the local pharmacy or market. However, these efforts will prove futile if the illness is initially caused by a virus, a digestive, or a nutritional problem, and a continuing loss of fluids may eventually result in death. Clearly, a quick diagnosis, though limited in preventive value, and correct treatment at a health center is preferable to this type of "self-care."<sup>20</sup>

Curative care for hookworm, gastroenteritis, or any of the major communicable diseases common to developing countries, cannot reasonably substitute for an alleviation of the life threatening conditions that

accompany extreme poverty, just as infant formula cannot substitute for mother's milk. Attempts at these kinds of substitutes are inappropriate health strategies and may have the effect only of draining away resources without offering any significant long-term benefits.<sup>21</sup> The use of expensive curative drugs outside of a system of social organization offering support to the income generating and preventive health activities of the poorest groups is likely to be both ineffective and wasteful of resources.

Pharmaceuticals, when used rationally in a decentralized basic health care system, are undoubtedly "powerful agents of health," and within a health care system that is based on community participation the evaluation of pharmaceutical needs can achieve a high degree of validity. Ideally, with public support and planning assistance accompanying this type of "grass-roots" organization, epidemiological conditions would become relatively easy to monitor. Furthermore, a decline in excessive demand for modern drugs and inappropriate self-treatment would be a likely result stemming from the establishment of a higher level of confidence in the adequacy and reliability of available health services.<sup>22</sup>

The emphasis on population coverage that is associated with a decentralized primary health care system requires national procurement guidelines which ensure that mass health problems receive the highest priority in the allocation of public health funds. The following principles have been suggested as general guidelines for a priority purchasing schedule emphasizing population coverage at the primary care level.<sup>23</sup>

*First-line pharmaceuticals* include the curative and preventive treatments that are used in large quantities at the primary care level. The WHO Expert Committee found that a list of only about 200 drugs could be considered sufficient to the essential health needs of a great majority of the world's population. It can be expected that the number of drugs required for primary care units alone will be considerably less. At this level it is especially important to guarantee a sufficient supply of medicines for common illnesses, otherwise a large proportion of the population may learn to bypass the nearest primary care unit in favor of larger health institutions, or may be forced to purchase drugs inappropriately (as discussed above) from private distributors of pharmaceuticals.

The range of first-line pharmaceuticals should include: widely needed curative drugs, symptomatic drugs—particularly for acute pain, preventive drugs such as serum vaccines and contraceptives, and possibly some sugar tablets or simple tonics. The latter products, or some other very inexpensive alternatives, have great potential value when inaccurate communication flows and extensive advertising have distorted the drug purchasing patterns of the local population and demands are being made for unnecessary treatments. However, only health workers with a good understanding of the existence of this problem in their communities are capable of judging the value of placebos. If used carelessly, they will only worsen the problem of inaccurate health care knowledge and practices.

Where they are widely utilized, traditional medicines may also be stocked. Due to differing local preferences and availability, a general lack of scientific data concerning their mode of action and effectiveness, and the specific skills sometimes required in their preparation, there is some question as to whether they should appear on a general procurement list. This is a decision that would clearly benefit from community level input and discussion.

Because treatments for serious infections or diseases require a relatively sophisticated diagnostic procedure, the average level of training given health workers staffing primary care units must also be taken into account. In formulating the list of first-line drugs, the type of treatment that can be accomplished safely and effectively by different primary care practitioners should be defined.<sup>24</sup> Needed changes in the list will probably become apparent over time and, as in the case of the national formulary, regular revisions should be expected on the basis of communications between health workers, regional and national authorities, and the formulary committee.

Accurate and complete drug information is an important aspect of any type of formulary and should include, at minimum, the indications for use, contraindications, and recommended dosages. The style in which this information is presented in the list of first-line drugs also depends on the training of different primary health care workers. This is particularly so if the list is to be useful as a guide for prescribing and proper storage. Some attempts have been made to create limited lists with simple instructions on how the various drugs are to be administered (e.g. injection, pill, skin ointment) and how dosages should be calculated for different age groups.<sup>26</sup>

*Second-line pharmaceuticals* include the remaining therapeutic categories that are deemed necessary for diagnostic and curative purposes at district and regional hospitals, and possibly an extension of the number of drug items in each category. Generally, treatments necessary for the more advanced stages of illnesses prevalent in the country, and perhaps for certain less prevalent conditions, would be added. As most of the drugs essential to primary care are no longer under patent protection and are likely to be purchased in large quantities, some of the second-line pharmaceuticals by contrast may be found to be more expensive. The length of this list (and the overall amount of each second-line drug that should be purchased) will depend to a considerable extent on the proportion of funds allocated to drug procurement after projected purchases of first-line drugs have been taken into account. It is to be expected that pressure to extend the number and volume of drugs procured for secondary care will exist in most countries in keeping with the concentration of the medical profession in and around the larger hospitals. The major problem which may result from this situation is that the primary care units will not receive a volume of drugs sufficient to meet basic needs, and efforts by health workers to organize community participation and build confidence in these units will suffer.

*Third-line pharmaceuticals* might include a large number of different drugs needed only for rare conditions or specialized tertiary care. If included in a national formulary, a special notation to the effect that only very small quantities of these drugs will be stocked may be in order. Alternatively, the list could comprise drugs that are available only on special order by authorized request.

Another category of pharmaceuticals might be created for the specific purposes of restricting importation and or production of certain drugs within the country, e.g., expensive, relatively ineffective drugs such as cough syrups and similar tonics that have in the past been sold in large amounts. Where government is cooperating with the private sector to stimulate the production of import substitutes, this category might simply include those drugs which will no longer be granted import licenses due to local manufacturing capability.

## ii. *Evaluation of Safety and Effectiveness*

After priority indications for drug use have been established within the framework of national health policy and a first list of essential drugs formulated, evaluation of additional pharmaceuticals presumably requires the appraisal of available pre-clinical and clinical pharmacological data. Drugs that are most effective in controlling a disease or symptom are also likely to harbor the greatest potential for harming the consumer. Ill effects may result from the toxic properties of a drug or they may result from an individual's physical reaction or misuse of a drug. The calculation of the therapeutic importance of a specific drug relative to its adverse effects is the drug's "benefit-risk ratio." Often several drugs are available for the same indication, but, generally speaking, the drug of choice would be the one having the highest benefit-risk ratio.<sup>26</sup>

Information needed by a formulary committee beyond that which has been gathered by health authorities depends mostly on the registration policies of the country. Although data on safety and effectiveness is required by most national health authorities prior to the registration of a drug, in practice approval of a drug is usually based upon its acceptance in neighboring or more developed countries. The documentation usually required for the registration of a drug for marketing or public sector distribution includes descriptive information from the manufacturer and approval from a division within the ministry of health or, in some cases, from an independent external group of experts. Detailed and clearly defined information from the manufacturer simplifies the task of monitoring pharmaceutical products. Minimum requirements for a drug manufacturer's certificate of quality include: the name of the manufacturer and the location of the production facilities; when applicable, the name and location of manufacturers involved in earlier stages of production; the generic name of the drug; the name and amount of each of the drug's active ingredients; specifications regarding strength, purity, and when applicable, the results of studies on stability or bioavailability; therapeutic

indications for use and the results of controlled clinical tests proving the effectiveness of the drug for the stated purpose(s); results of pre-clinical and clinical pharmacological and toxicological trials on test subjects; known contraindications or adverse effects; the unit price; and the recommended dosage form.<sup>27</sup>

Many of the drug producing countries participate in the WHO certification scheme on the quality of pharmaceutical products moving in international commerce. According to this scheme, exported drugs must be accompanied by information as to whether or not the indicated product is marketed in the country of origin and if not, why it has not been authorized to be placed on the market.<sup>28</sup> This certificate also ensures that authorities in the country of origin have determined that the manufacturer conforms to the requirements for good practices in the manufacture and quality control of pharmaceutical substances, as outlined by WHO. In some cases additional certification of quality of individual batches of the drug may also be necessary.

As mentioned earlier, significant international differences in the provision of information concerning the indications and contraindications for use have been found in examinations of the marketing practices of the transnational pharmaceutical firms. Therefore, it is advisable for registration authorities to include the requirement that therapeutic indications for use provided by the manufacturer be identical to those reported in the firm's country of origin. In some cases a drug is authorized to be placed on the market, but the indications for use are extremely limited. The above requirement would prevent the "dumping" of drugs in countries where standards for quality and effectiveness and laboratory facilities for drug registration are in a developmental stage.

Information on the benefits and undesirable effects of a drug, as determined by pharmacological studies demonstrating its expected therapeutic effect, mechanism of action, and the ways in which it is handled by the body fluids and tissues of test subjects, have great international value, particularly the data gathered in the lengthy pre-clinical stage of testing.<sup>29</sup> WHO has collected the data used by various national authorities for clearing drugs to be registered; this information may be of particular importance to countries with limited resources and personnel for drug evaluation. Health authorities from individual countries are also available for consulting purposes, e.g., officials of the U.S. Food and Drug Administration have assisted foreign countries with their testing procedures and facilities.

National certification of quality ideally includes additional documentation that sample batches of drug products meet specifications for strength, purity and stability. The testing may be completed within the quality testing division of the ministry of health or local research institutions. Countries which as yet do not have sophisticated facilities for performing pharmacological and toxicological tests on experimental animals might begin by forming groups concerned with the relationships

between locally prevalent diseases and other conditions common to the area and the "biological availability" of selected drugs—i.e., absorption, distribution, transformation and excretion by the body. The registration legislation in some countries requires that an application must be accompanied by sufficient samples to carry out clinical studies on humans in local hospitals or universities. Whereas the seriousness of potential adverse effects resulting from the use of a drug in a controlled experiment is important and valid information on an international scale, the likelihood of adverse effects also relates to local population characteristics and conditions of use.<sup>30</sup> Conditions which might affect the safe utilization of drugs among population subgroups include, for example, genetic traits; a higher than average intake of pesticides due to agricultural spraying practices; endemic malnutrition; and in some areas, defective excretion of drugs as a result of the prevalence of diseases which harm the liver and kidneys (see Table 4.11).

TABLE 4.11  
Problems and Potential Toxicity of Drugs Used in  
African Medical Practice

Patient at Risk	Drugs	Use	Toxic Effects	Reason
Liver disease	Hypnotics Morphine Paraldehyde (Chlorpromazine)	Delation	Coma and encephalopathy	Detoxicated in the liver
	Nitrazole	Schistosomiasis	Encephalopathy Change of behavior	Metabolized in liver
	Hycauthone	Schistosomiasis	Hepatic cell damage	Direct toxic effect
Acute infections	Tetracycline	Particularly pyelonephritis	Hepatic cell damage (if given intra- venously in pregnancy) Loss of weight	Direct toxic effect on liver  Reduced protein anabolism
Renal disease (failure)	Streptomycin	Tuberculosis	8th nerve damage	Excretion in glomerular filtrate
	All tetracyclines	Acute infection	Those above are enhanced	Excretion in glomerular filtrate
	Suramin	Gonocherciasis	Proteinuria	Direct toxic effect on kidney
	Amphotericin B	Deep mycoses	Proteinuria	Direct toxic effect on kidney
	Dioxin	Cardiac failure	Vomiting Arrhythmias	Excretion in glomerular filtrate
	Phenobarbitone	Delation	Drowsiness Respiratory depression	Excretion in glomerular filtrate
	Nitrofurantoin	Acute pyelonephritis	peripheral neuropathy	
	Morphine	Relief of pain	Respiratory depression	Over 50% excreted in glomerular filtrate
Asthma and tracheitis	Diethylcarbamazine	Filariaes	Bronchospasm	Part of reaction to treatment
Diabetes mellitus	Pentamidine	Cutaneous leishmaniasis Trypanosomiasis	Aggravated glycosuria	Unknown
Malaria anaemia strangury jaundice	Corticosteroids	Various uses	RAPID OVERWHELMING INFECTION	Altered immunity

Sources: S.H.G. Parry (ed.), *Principles of Medicine in Africa* (Ibadan, Nigeria: Oxford University Press, 1976), p. 529.

In addition to such physiological factors, demographic characteristics of the population affected by the formulary might also be considered an important aspect of safety and effectiveness studies. For example, many developing countries have demographic structures which are very different from countries in which most modern drugs have been developed, i.e., much larger proportions of the populations are infants and children. The fact that drug manufacturers have historically tended to neglect the testing of medications on children due to added expense and heightened risks is often overlooked. Some dosages for children can be safely calculated by mathematical formulae, but the type and dosage form of drugs selected for a formulary affecting large numbers of children should be planned with recognition of the special problems involved. It follows that possible contraindications to the use of various drugs by pregnant or lactating women should also be thoroughly discussed.

Another aspect of local conditions to be considered is the available drug delivery system—storage, handling, and prescribing. Warehouses and vehicles capable of preventing the deterioration of certain drugs are limited in some areas and different types of presentations, e.g., pills, injections, or liquids, may be more or less suitable depending on climatic conditions. Finally, the type of health worker administering specific drugs is an important factor in planning drug supplies, particularly when the first priority of the health sector is the expansion of treatment at primary care level. In areas where basic drugs are being distributed by health workers with relatively limited training, the benefit-risk ratio discussed earlier assumes even greater importance.

An additional aspect of pharmaceutical safety and effectiveness concerns the manufacturer's capability to produce products that meet desirable standards for "bioavailability." Bioavailability or "biologic availability," as defined earlier, involves both the time period and the extent to which an active drug ingredient is absorbed by the body and becomes available for biologic effect. Requirements for standards and batch testing must be particularly stringent when a drug has to reach a critical therapeutic level in the body in order to be effective and/or when a drug has a narrow safety margin.<sup>31</sup> A large number of manufacturers may produce chemically equivalent pharmaceutical products containing identical ingredients in identical dosage forms, but there is some possibility that variations in production techniques will alter the bioavailability of one or more manufacturers' products, or that there will be slight variations between the batches manufactured by any of the firms. As a result these products will not be "bioequivalent," i.e., the rate and extent of body absorption will be slightly different.

The belief that deficiencies in bioavailability are not encountered in brand name drugs has been encouraged by the transnational drug firms, and disclosures that many manufacturers sell bulk or finished drug products to each other for distribution under differing names has not

significantly altered that belief as yet. Informed pharmacopoeial standardization of drugs, particularly at an international level, is an important factor in each country's quality control system. The great majority of drugs do not require rigid tolerance standards in order to achieve their desired effect without harming the patient.<sup>32</sup> However, selected drugs likely to pose therapeutic problems if they do not conform to such standards (one to two dozen at most, e.g. digoxin and digitoxin tablets) should undoubtedly be accompanied by data from the manufacturer on dissolution rates based on blood level and urinary excretion samples obtained from human subjects. Repeated local testing of batches of such drugs, where possible, is highly desirable.

The suitability of including fixed ratio combination drugs in formularies is an important issue, largely because these drugs are likely to be effective treatments only for a smaller proportion of patients than individual active ingredients. Also, many combination drugs rely upon one key ingredient for their effectiveness, with others having been added only to create a "me-too drug," for commercial reasons. The WHO Expert Committee suggested that a fixed ratio combination drug be considered for formulary inclusion only when its therapeutic effect is significantly greater than the effect of the individual ingredients and when its cost is less than the total cost of the individual ingredients.<sup>33</sup>

A full discussion of the technical issues involved in the analysis of the safety and effectiveness of drugs is beyond the purposes of this monograph. It appears, however, that the most important contribution a limited formulary can make in this regard is the reduction of difficulties associated with analyzing and monitoring drugs, simply due to the lower overall number of drugs in circulation.

### iii. *Nomenclature*

Before the massive expansion of the pharmaceutical industry in the second quarter of the twentieth century, pharmaceutical preparations were marketed under their generic names. Since then the number of firms throughout the world has multiplied and the names used by firms to identify drugs have also multiplied. Brand name promotion has been one of the most effective marketing practices employed by pharmaceutical firms. Habit creation resulting from the heavy promotion of brand name drugs confers upon the manufacturer a type of monopoly power which in many cases extends well beyond the period of patent protection and in effect denies consumers the price advantage that may result from competition between firms.

The perpetuation of brand names results in confusion among both prescribers and consumers. For example, a prescribing practitioner may not be fully aware that several products are identical and as a result may prescribe products that are difficult for consumers to purchase at a local

pharmacy or at a reasonable price. The drug products could be easily available to consumers, both in terms of location and price, yet remain hidden by a lack of information about the identical nature of substitutes sold under generic names. In some countries private pharmacies have taken the lead in providing information to consumers about generic equivalents. Public sector regulations that require prescribers to refer to drugs by their generic names are relatively new developments in market economy countries.

The complexity of generic names has probably been an impediment to widespread acceptance in the past. New names generally have been created by modifying the chemical definition of a drug; as the number of new compounds has increased, the names have become longer and more difficult to recognize. A change in this procedure has been employed by WHO in its task of assigning non-proprietary names for pharmaceutical substances. This procedure basically involves the choice of a few letters (a stem) indicative of all the members of the therapeutic group for which it is selected. Letters are added before or after the stem to make each name unique. The list of "International Non-proprietary Names" published by WHO is widely used and in some countries legislation requires that these INN names be used within the health sector.

This method of assigning drugs generic names assists physicians in classifying drugs within a broader therapeutic group. The generic name of a new substance with the same basic properties of an older, established drug is apt to be similar, so it will be easier to seek out the actual improvements (if any) in the new drug. For example, the generic names ampicillin, cloxacillin and carbenicillin indicate that all are penicillins, whereas no such connection could be understood from their respective brand names, Penbritin, Orbenin, and Pyopen.<sup>35</sup>

Quality is the major issue in the name brand vs. generic debate, but several countries have already found that quality must be assured by means other than brand names or manufacturer identification. No differences in quality have been found to be associated with pharmaceutical brand names in the United States throughout the years of testing every batch of every antibiotic before marketing.<sup>36</sup> The likelihood that each product will be bioequivalent is reinforced by the fact that many manufacturers, regardless of size, buy the same bulk ingredients from the few companies engaged in the integrated production of drugs.

The Hathi Committee in India stressed the importance of strict quality control in their report, but also noted that they had found more instances of substandard quality in branded products than generic label products. It may be assumed from these findings that the real danger of poor quality drugs, particularly in countries with developing pharmaceutical industries, arises when enormous profits can be earned by small-scale imitators of brand name drugs patented by TNCs. In other words, the attraction of

high profit margins leads to the entrance of less reputable firms into the drug market.<sup>37</sup>

#### iv. *Criteria for Selecting Cost-effective Drugs*

... the doctor prescribes, the patient receives and the Ministry pays. If a new drug offers slight advantages over an old drug of similar type, but at many times the cost, the doctor will be persuaded to prescribe it because neither he/she nor the patient has to consider the price. In this situation the phrase "cost-effectiveness" is often used to justify the extra spending, but there is a limit on the total available for drugs; the patient who is thereby deprived of *any* drug must be included in the calculation of effectiveness.<sup>38</sup>

Aside from direct patient fees there are two basic ways that cost-effective utilization of drugs may be emphasized by the public health authorities—formulary restrictions on procurement and education of prescribing practitioners in the alternative costs of similar treatments. In this section the methods of restricted procurement are discussed.

A recent report from an African country with limited funds for drug supplies found that 79 percent of total expenditures for drug purchases were allocated to hospitals, 7 percent to health centers, and 14 percent to dispensaries. Furthermore, significant proportions of the hospitals' drug budget were spent on drugs that could not be considered lifesaving, e.g., 11 percent of one hospital's drug budget was spent on sedatives, tranquilizers and antidepressants. The report pointed out that the money spent on products such as these could protect half a million children against malaria.<sup>39</sup>

In the context of this broader view of cost-effectiveness, a formulary based on nationwide estimates of therapeutic need which complements preventive health measures and the treatment provided at primary health care units can be used as a method of improving on the value of current levels of drug expenditures. In recent years it has been widely acknowledged that in order to "optimize" available health resources, budget expenditures should be shifted away from expensive hospital services. However, many recurrent budget items are difficult to shift for technical as well as political reasons.<sup>40</sup> In comparative terms only, drug expenditures may have certain advantages in this respect. A reduction in the purchase of a number of duplicative and irrational fixed ratio combination drugs, as well as drugs with a high potential for toxic reaction and those with very rare indications for use is a basic principle involved in the formulation of a limited drug list which can make significant improvements in the value of publicly subsidized drug supplies.

Beyond these essential principles, the standing committee responsible for the creation and periodic updating of a formulary may also consider the evaluation of individual drug products in terms of the costs of possible alternatives. Some countries have programs relying on formularies which

specify approved drugs by their generic name and limit payment to the lowest price at which each drug is widely and consistently available.<sup>41</sup> In other countries the maximum prices that may be paid by the public health sector are determined by criteria such as the export price of the drug, the public price in the country of origin, the price of similar products available on the market, and the price of the same products in neighboring countries.<sup>42</sup> It is unlikely that the lowest price discovered by this method will be set as a ceiling in the majority of cases, because often specific quality considerations must be taken into account as well as the continuing availability of the drug in quantities required by the health services. Calculations of the total cost of a given treatment should also be considered in these comparative price studies because some drugs may be relatively inexpensive in unit dosage form, but require a significantly longer treatment schedule than similar drugs.

These specifications for establishing maximum price levels are based on "free-market" principles, in that the public sector is obligated to procure drugs from the most competitive sources. Even when only one firm manufactures a drug listed in the formulary, no alternate process of negotiation between that firm and the public sector is required in many of the countries using this method of procurement. Therefore, cost-effective selection within this process necessitates that all of the drugs chosen have as large a number of suppliers as possible. The role of the procurement officials (or agency) involves the international tender and bid system and/or the encouragement of a competitive industry within the country. A policy which might be associated with a selection process based on competition between firms is the nationalization of one or more pharmaceutical manufacturing plants, which would be granted licenses to produce needed drugs otherwise available from only a single patent holding firm.

Another widely implemented policy regarding the cost of drugs is the establishment of publicly fixed prices. By fixing drug prices the public sector does not actively seek out the least expensive drug product with the desired curative properties; rather, the state negotiates with drug manufacturers, distributors, and/or pharmacists in order to arrive at a suitable price. Roughly speaking, this type of policy does not involve the cost-effective selection of drugs so much as it requires the entire process of the delivery of drugs to patients to be as inexpensive as possible, acknowledging the costs of materials, transportation, wages and so on. Prices are fixed by the state in the planned economies of Eastern Europe, as well as in Italy, Portugal, Norway and several other countries.

Price fixing is particularly common in Europe and other countries in which the state supplies health services and drugs to the majority of the population at very low or no cost to the individual. There are, however, great variations in the actual implementation of a price fixing policy. In the United Kingdom the prices are controlled by a regulation system under which drug companies provide annual financial returns (supported

by audited accounts), and the health department assesses drug prices in terms of the return on capital attributable to National Health Service business. As was pointed out in the case of Hoffman-La Roche products, cost price controls are more difficult to operate when foreign based companies are involved. However, compared to other Western European countries the United Kingdom has been relatively successful in holding down pharmaceutical prices. Norway's National Center for Medicinal Product Control negotiates prices with manufacturers before their products may be registered, and pharmacists' profits are fixed by regulation. On the basis of these regulations, new price lists are published four times a year.<sup>43</sup> In China, unified drug prices have been set and current prices of drugs are reportedly a fraction of their cost in the early 1950s.

It should be stressed here that price fixing has not been a particularly successful method of controlling costs in non-socialist countries with the exception of Norway and the United Kingdom, both of which exhibit a fairly high degree of public control. Unless manufacturers' costs and profit margins are closely monitored and controlled, usually through a process of negotiation, it appears that regulation of wholesale or retail profit levels alone will not contribute to lower prices.\*

When a drug list has been written with clearly defined therapeutic indications for use, maximum allowable prices or fixed prices can be used to estimate the recommended cost of drugs per case of illness. A comparison of the recommended figure and a sample of actual prescriptions written for a particular illness could point to a number of problem areas, e.g., incorrect substitutions of expensive short-stocked drugs for first-line drugs which, in turn, may reflect the need for further shifts in the priority schedule being used for purchasing. With a recommended treatment cost list, budgetary allocations for drugs could be based on the projected disease incidence or the projected caseload of public health services at regional or district level.

#### *4.2 Centralized Procurement*

Most countries have centralized purchasing systems which obtain the drugs and medical supplies used by the public health services. Drugs procured in this way usually are limited to either an official formulary drafted by a committee of the ministry of health or to a central medical stores list. The central stores list may have the same function as a formulary, i.e., to standardize selection according to a set of preconceived guidelines and standards, but in some cases it may have been developed simply as a response to the demands of public hospitals and regional health authorities.

\*Drug prices are discussed further in Section 5.1.

The economic benefits of a formulary that emphasizes population coverage, particularly at the primary care level, are associated with bulk purchasing. Savings from larger purchases of widely used, basic drugs are often directly related to the lower costs borne by manufacturers when they are assured of longer production runs and larger shipments.<sup>44</sup> The amounts of each pharmaceutical product requested on public sector purchasing orders depend on the percentage of national drug utilization which is accounted for by 'central medical stores' and the estimated projections of therapeutic need for each drug that have been calculated by procurement officials at the institutional, district/regional, and/or national level.

The percentage of national drug supplies procured by the public sector varies among countries in much the same way as does the extent of formulary coverage (as described earlier). In many developing countries the health authorities have concentrated on the development of an "essential drug list" for the priority coverage of preventive health campaigns and primary health care services. In these countries private sector imports are under the more general controls of the drug registration system. Restrictions of imports at the point of registration may include the encouragement of bulk imports by a heavy tariff charge on finished drug products, limitation of imported drugs to those with generic labels, and numerous requirements with regard to effectiveness, safety, and quality.<sup>45</sup>

In other countries, notably Sri Lanka, formulary procurement by the central medical stores has been augmented by further direct controls over the content of private sector imports. The State Purchasing Corporation in Sri Lanka has reduced private sector imports to 600 different drugs (1,000 dosage forms) and imposed a purchasing system based on competitive international bidding. The savings that have resulted from this system are depicted in Table 4.21. In a similar move, a "Generic Drugs Law" was passed in Afghanistan specifying that:

- a. With immediate effort, government health institutions shall only use generic drugs, and "patent drugs" can be used only if generic equivalents are not available;
- b. From 1979, *private sector wholesalers can import and distribute only generic drugs listed in the Afghan National Formulary at prices determined by the Ministry of Health*. When generic forms are not available such drugs will be imported by the Avicenna Pharmaceutical Institute (state organization). Local producing institutions shall produce and distribute their products only under generic names [emphasis added];
- c. Commercial promotion of "patent drugs" is prohibited;

- d. Schools of medicine, pharmacy and veterinary sciences shall teach drugs under their generic names.<sup>46</sup>

TABLE 4.21

Price Comparison of the State Pharmaceuticals Corporation  
and Previous Suppliers, 1972-1976 (U.S. \$)

Year	Number of Drugs	Previous Supplier's Price	SFC Price	Foreign Exchange Savings	Previous Price as % of SFC Price
1972	50	487,000	190,000	195,000	60
1973	50	1,014,500	141,000	873,500	38
1974	50	1,114,000	257,000	857,000	38
1975	60	1,953,500	319,000	1,634,500	30

Source: UNCTAD: Case Studies in the Transfer of Technology: Pharmaceutical Policies in Sri Lanka, Study prepared by S. Fible (TD/B/C.6/21), p. 77.

Most of the centrally planned Eastern European countries also employ restricted lists of drugs which may be imported and special authorization is required for drugs not included on these lists.

Among the developed market economies, Norway has implemented one of the most highly centralized procurement systems. According to Norwegian law, all pharmaceutical items must be approved and registered by the Committee of Pharmaceutical Specialities appointed by the Ministry of Social Affairs. The duration of approval is usually five years and products must be imported solely by the Norwegian Medicinal Depot. Less than 2,000 drugs have been approved and are currently being marketed.<sup>47</sup>

A system of accurate recording of the inventory turnover of the health services supplied by the central stores is a necessary component of effective control over the total volume of purchases. In countries where a broadening of the publicly supported health services is envisioned, a strict budgetary cutoff on the amount of drugs ordered by the ministry of health could be planned. The budgeted amount could be allocated according to a priority purchasing schedule (as described earlier). However, without a continual accounting of the distribution of drug shipments (i.e., an itemized cost accounting of all purchase orders) to hospital and regional stores, the budgetary allowance might not be acknowledged and purchases allowed to continue unchecked, or it might mask a very unequal distribution of publicly subsidized drugs to the various regions and institutions.<sup>48</sup>

One method of estimating the therapeutic need for various drugs involves the decentralization of this accounting procedure to the regional or provincial level. As was pointed out in the earlier discussion of cost-effective selection, when standardized costs for different drug treatment schedules have been calculated the planned budgetary allocation can be based on regional targets for the number of curative treatments and preventive services to be accomplished by each health unit. Central procurement officials in this case would be responsible for ensuring that the priorities of the public health sector are adhered to in the requests of the regional stores, and that regional authorities establish separate allocations for each health unit in their area. With a continual system of recording inventory turnovers, the determination of the amount of drug supplies needed by the various health units should improve in accuracy over time. In order to assure that allocations are well distributed throughout the regions (i.e., that regional hospitals do not retain a disproportionate amount of supplies) policy guidelines devised by the ministry of health could be augmented by an improved system of communications between pharmacy workers, who are the ones most likely to be aware of shortages or continually incorrect estimations of need. The problems of illegal sales of public stocks and other forms of profiteering by health workers involved in the distribution of drugs are additional areas that might be addressed by regional meetings of pharmacy and other health workers.

The greatest potential disadvantage of bulk procurement of pharmaceuticals by central stores is that certain products have a limited shelf-life and if procured in excessive amounts may eventually have to be discarded.<sup>49</sup> The actual shelf life of many drugs is not always entirely clear, particularly in tropical climates. Also, in some cases countries participating in international trade may employ somewhat different methods of estimating shelf life and dating drug labels. The establishment of regional standards in this regard, based on knowledge of the effects of environmental and available storage conditions, is one way of reducing potential wastage, but the combined effect of a limited formulary and a procurement system based on carefully planned usage is undoubtedly the best way to control this particular problem.

#### *4.3 The Organization of the Drug Supply System*

Any major change in the drug procurement system, such as an extension of the system to include both public and private sector imports, or a shift from reliance on a limited number of supplying firms to the international circulation of tenders for competitive bids, should be preceded by a detailed study by the ministry of health or other agencies responsible for drug procurement. Existing supply sources, prices, the total quantities of drugs imported, and local manufacturing capability should be examined in a study of this kind. To some extent the study

could contribute to the estimation of therapeutic need, but more importantly it would allow for the calculation of potential savings expected to result from the proposed changes.

In many countries, the key motivation for major changes in the drug procurement system is likely to be the possibility of foreign exchange savings, and firm data on imports could be an important aspect of a reform proposal likely to face strong opposition from many different groups. The experience of Sri Lanka in rationalizing its drug supply through the creation of a state purchasing corporation can serve as a model for many less developed countries.<sup>50</sup> Countries with supply networks involving a larger number of nationally based manufacturers are capable of even broader reforms, including the nationalization of pharmaceutical production. However, experience in this regard has shown that the effectiveness of organized opposition to reforms such as those attempted by Sri Lanka increases with the size of the privately controlled drug sector.<sup>51</sup> Furthermore, where the pharmaceutical industry is dominated by subsidiaries or joint operations with foreign-based TNCs, centralized procurement of intermediate products might be the most important reform in terms of foreign exchange savings, but the most difficult to impose on firms which are likely to be enjoying substantial profits from the unrestricted practice of transfer-pricing.<sup>52</sup>

All such political factors aside, further planning for the distribution of pharmaceutical supplies to the health sector involves: (1) the degree of additional public control or investment required; (2) the establishment of reliable methods of processing and circulating international tender forms (assuming that all countries will continue to import some pharmaceutical products); and (3) the development of improved methods of forecasting need and controlling inventory.

Obviously, the strongest emphasis on local production would involve state ownership of manufacturing plants. In addition to the centrally planned economies, several countries directly control at least one major drug manufacturing facility, e.g., Australia, Austria, Sweden, Syria, Tunisia, and India. A significant number of developing countries have entered into joint production agreements with private sector firms, including the African states of Ghana, Zambia, Ethiopia, and Egypt.<sup>53</sup>

Alternatively, some countries have imposed further controls on drug production by a policy emphasis on the purchase of generic label drugs at the lowest cost available (see previous section). Such a policy tends to reinforce the position of small private firms supplying the domestic or regional market, and in theory the competition between these firms is expected to result in lower prices. Regardless of the level of public investment in drug production, compulsory limitations on the kinds of drugs marketed (such as Afghanistan's Generic Drug Law) are extremely important elements of plans to emphasize local procurement. Some developing countries actually would have an advantage over the highly industrialized market economies in this regard as they would not have to

act later to halt the production of a large number of ineffective or duplicative drug products.

Despite varying levels of industrial development most countries continue to import at least some pharmaceutical products. Many of the newer drugs representing therapeutic improvements are still under patent protection. These drugs are only available from the patent holding firms until production rights have been licensed to other firms. The exceptions to this rule are those relatively new drugs which are available from non-patent observing countries. The countries best known for inexpensive exports of pharmaceutical products are Italy and the Eastern European planned economies, largely because patents are not recognized in these countries and their well developed pharmaceutical industries are capable of copying new developments in drug technology in a period of a few years. Therefore, most standard drugs no longer under patent protection as well as many of the newer drugs are available on the international market at very competitive prices. Legally, however, a country that recognizes patent protection of new drug products or processes risks charges of patent infringement when purchasing products from non-recognizing sources. As noted previously, pharmaceutical firms have made the registration of their multifaceted product patents (even in countries where drugs are not being produced) one of their major marketing strategies.

Policies of various countries covering the purchase of patented drugs include: a total ban on such products, with the implicit assumption that older established drugs are generally safer and more useful for broad-based health care programs; the amendment of patent laws to allow for the suspension of protection when it is deemed critical to national health, i.e., when a significant new breakthrough in pharmaceutical technology has occurred; and, reduction of the period of patent protection or the elimination of patent rights within the country. Because the most essential drugs are no longer under patent protection this issue would be of less importance to those countries seeking to increase the volume of needed drugs by restricting international purchases to a limited formulary.

The economic benefits of bulk procurement are furthered by the issuance of tender forms calling for bids from drug manufacturers. Unless the public sector has direct control over an integrated pharmaceutical production industry and can thereby apply mandatory cost/price limitations, calling for bids on the international market is one of the best methods for assuring the lowest possible purchase price. The distribution of tenders is not a complex procedure, but it does require sufficient information to assure that potential suppliers are using good manufacturing practices.<sup>54</sup> Unfortunately, this information may be more difficult to obtain from the smaller, least expensive sellers. The more widespread use of the WHO certification program on drug products moving in international commerce should alleviate this problem to some extent. The process of informing a large number of potential suppliers about product

tenders has also been difficult with regard to smaller international suppliers. Not surprisingly, the distribution of tender forms to foreign embassies and newspapers appears to draw a disproportionate response from the larger transnational firms. Bulk procurement agencies such as ECHO (a charitable organization based in Britain) can be requested to assist in the process of tendering and, where possible, regional cooperation can serve to broaden the market for new and smaller manufacturers—particularly among the developing countries.<sup>55</sup>

The amounts of each formulary drug item needed should be estimated as soon as realistic information is available, preferably over a projected 1-3 year time span. Estimates may be made on the basis of therapeutic need (as described earlier), health service plans for annual vaccination/immunization campaigns, projected caseloads of the health units to be supplied by central stores, past retail sales levels of approved drugs, current stock levels, or any combination of these data. Long range projections are useful because they permit the planning of target delivery dates for drug shipments from various suppliers. Targeted delivery dates are important components of an inventory control system for several reasons--they contribute to the assurance of adequate storage space, to the prevention of shortages, and to production planning. In centrally planned economies such planning is often completed more than a year in advance of shipment. Producers failing to meet agreed upon arrival dates contribute significantly to supply problems, and their future bids should be viewed by procurement officials accordingly.

## FOOTNOTES

1. Recent research in the area of hospital formularies is summarized in Conley, B.E., *Social and Economic Aspects of Drug Utilization Research* (Hamilton, Ill: Drug Intelligence Publications, 1976). Chapter 10: Drug Formulary System Research, pp. 255-271.
2. Kastner, F. *Volume and Cost of the Supply of Medicaments* (Geneva: ISSA, 1974), pp. 37-53.
3. *Ibid.*, p. 39; Silverman, M. and Lydecker, M. Drug Coverage Under National Health Insurance: The Policy Options. NCHSR Research Report Series, U.S. Department of Health, Education, and Welfare (1977), pp. 37-43.
4. Kastner, F., *op cit.*, pp. 23-24.
5. *Organization of Health Services*, Ministry of Health, Cuba (1974), pp. 63-64.
6. UNCTAD, *Case Studies in the Transfer of Technology: Pharmaceutical Policies in Sri Lanka*, Report prepared by S. Bibile (TD B C.6 21) pp. 6-7.
7. *Ibid.*, the initial recommendation included 2,100 different drugs, which was later reduced to 630. Bibile points out that the list could be reduced to 400 with no detriment to therapeutics.
8. Kastner, F., *op cit.*, p. 41.
9. *Guyana National Formulary*. Produced by the National Formulary Committee, Georgetown, Guyana (1977).
10. The Selection of Essential Drugs, *WHO Technical Report Series* 615 (1977), p. 9.

11. Resolution NAC CONF. 5 S RES-25, August, 1976.
12. Action Programme for Cooperation Among Non-aligned and Other Developing Countries on Pharmaceuticals, Document HAC CONF. 5 11, August, 1976.
13. Silverman, M. and Lydecker, M. *op cit.*, p. 40.
14. Dyson, T. Levels, Trends, Differentials and Causes of Child Mortality --A Survey. *World Health Statistics Report* 30, No. 4 (1977, pp. 293-294; Puffer, R.R. and Serrano, C.V. Patterns of Mortality in Childhood, PAHO WHO *Scientific Publication No. 262* (1973); Ransome-Kuti, O. Gastroenteritis in Infants, in Parry, E.H O. (ed.), *Principles of Medicine in Africa* (Ibadan, Nigeria: Oxford University Press, 1976), pp. 168-178.
15. Dyson, T. *op cit.*, p. 294.
16. Ransome-Kuti, O., *op cit.*, p. 168. Since 1974 WHO has noted with alarm the general decline in breast-feeding, and criticisms of misleading promotion and sales tactics that have resulted in this decline have been expressed throughout the world. The decline of breast-feeding is thought to be a major cause of infant mortality and malnutrition.
17. Breast Milk vs. the Baby Bottle: Life and Death Struggle in the Third World, American Freedom from Hunger Foundation, *Bulletin IV*, No. 1 (Jan.-Feb., 1978).
18. Segall, M. Pharmaceuticals and Health Planning in Developing Countries, IDS Communication 119 (Brighton: Institute of Development Studies at The University of Sussex, 1976), p. 6. The most important initial result of improved economic status among the very poor is their access to better food. Poorly processed grains and donated milk powder are directly related to gastroenteritis in many parts of the world. In Africa, certain tribes have a predisposition to lactose malabsorption, and feeding with milk can lead to chronic illness. Illness can also be expected to follow the introduction of foods having a high degree of roughage to infants and small children, but often the only alternative is starvation.
19. For example, see Segall, M., *op cit.*, p. 5.
20. The relative risks and benefits of distribution of oral rehydration treatments to parents in communities having organized health care services are still unclear.
21. Referring to the writing of Chilean economist, de Ahumada, Navarro claims that, generally speaking, "each dollar spent in Latin America on highly specialized hospital services costs a hundred lives. Had each dollar been spent on providing safe drinking water and in supplying food to the population, a hundred lives could have been saved." Navarro, V., *Medicine Under Capitalism* (N.Y.: Prodist, 1976), p. 2.
22. It is interesting to note that an extensive array of ethical drugs and traditional medicines are apparently sold over-the-counter in small pharmacies throughout China. The absence of any mention of problems in this regard is perhaps due in part to the confirmed reliance of the Chinese on the less toxic traditional forms of medicine, but the absence of drug advertisements and the widespread availability of primary health care services undoubtedly remove much of the potential excess in demand. See, for example, American Herbal Pharmacology, *Herbal Pharmacology in the P.R.C.* (Washington, D.C.: National Academy of Science, 1975).
23. Action Programme for Cooperation Among Non-Aligned and Other Developing Countries, *op cit.* Further elaboration on priority purchasing can also be found in Segall, M., *op cit.*
24. The Selection of Essential Drugs, *op cit.*, p. 13.
25. For example, *The Primary Health Care Worker: Working Guide* (Geneva: W.H.O., 1977). Annex I. Medicines, pp. 236-239.
26. See the Guidelines for Evaluation of Drugs for Use in Man, *WHO Technical Report Series No. 563* (1975).

27. See various sections on the assessment of drugs by regulatory authorities, *Clinical Pharmacological Evaluation in Drug Control: Report on a Symposium*, WHO Regional Office for Europe, Copenhagen (1972, 1973, 1974, and 1975).
28. Certification Scheme on the Quality of Pharmaceutical Products Moving in International commerce, recommended by the W.H.O. in WHA 28.65.
29. Guidelines for the Evaluation of Drugs for Use in Man, *op cit.*, pp. 14-17.
30. The formation of expert groups is suggested here as an alternative to rigorous laboratory testing on local populations. A great many potential adverse effects relating to physical conditions common in Third World countries are already known, and the attendant problems in individual areas can be projected by using available demographic and health profiles.
31. Bioavailability of Drugs: Principles and Problems, *WHO Technical Report Series*, No. 536 (1974).
32. Drug Bioequivalence. A report of the Office of Technology Assessment Drug Bioequivalence Study Panel, U.S. Congress O.T.A. (Washington, D.C.: U.S. Government Printing Office, 1974), 78 pp. In Sri Lanka, bioequivalence was considered a problem for 25 drugs on the import list. The Parcost Programme in Ontario, Canada considers the bioavailability of only 13 drugs.
33. The Selection of Essential Drugs, *op cit.*, pp. 12-13.
34. (By a Special Correspondent) In Defense of a National Drug Industry, *Economic and Political Weekly* (March 27, 1976), p. 498.
35. Non-proprietary Names for Pharmaceutical Substances, *WHO Technical Report Series*, No. 581 (1975), pp. 506. Wickremasinghe, S.A. and Bibile, S. *The Management of Pharmaceuticals in Ceylon* (Colombo, March, 1971), p. 6. See also O'Brien, P. *Trademarks, the International Pharmaceutical Industry, and the Developing Countries*, ISS Occasional Papers No. 63 (The Hague, Netherlands, 1977).
36. Simmons, H.B. Brand vs. Generic Drugs: It's Only a Matter of Name, *FDA Consumer* (March, 1973).
37. Hathi Committee on the Indian drug industry, *Report of the Committee on Drugs and Pharmaceutical Industry* (New Delhi: Minister of Petroleum and Chemicals, 1975).
38. Yudkin, J. To Plan is to Choose, University of Dar es Salaam, Mimeo.
39. *Ibid.*, pp. 6-8.
40. WHO UNICEF, *Alternative Approaches to Meeting Basic Health Needs in Developing Countries*, Djukanovic, V. and Mach, E.P. (eds.) (Geneva: WHO, 1975).
41. The U.S. Maximum Allowable Cost (MAC) program administered by the Department of Health, Education, and Welfare specifies a price ceiling for each listed drug that is drawn from a comparative price analysis. The Parcost Program in Canada is similar, though more advanced in its implementation.
42. For example, in Jordan the price of drugs is set by using these criteria, and in the process of lifting an official price freeze on drug products Iran began to use similar decision-making criteria.
43. Wertheimer, A. (ed.) *Proceedings of the International Conference on Drug and Pharmaceutical Services Reimbursement*, NCHSR Research proceedings Series (Wash., D.C.: U.S. Department of Health, Education, and Welfare, National Center for Health Services Research, 1976), see T.D. Whittet, Report from the United Kingdom and Bjorn Joldal, Report from Norway, pp. 85-120.
44. Discounts from standard prices may also be offered in return for the payment of bills within a specified time period, and are more likely to be granted to public institutions than to small-scale private distributors.

45. Bloomfield, J.D. (ed.) *Survey of General Practice Pharmacy 1974 (Federation Internationale Pharmaceutique, Section for the General Practice of Pharmacy, 1974) Table VII E.*
46. *Generic Drug Law Resolution 418 of 1976. Republic of Afghanistan. Section reproduced in UNCTAD, Case Studies in Transfer of Technology: Pharmaceutical Policies in Sri Lanka, op cit., p. 14.*
47. Bloomfield, J.C., *op cit.*, Table VII E, p. 104. There are actually only about 750 drugs, but the 1975 total of 1850 includes a variety of presentation forms and potencies.
48. Yudkin, J., *op cit.*, pp. 16-18.
49. Interview with Chief Pharmaceutical Officer, UNICEF, New York.
50. Sri Lanka is not only a good model in terms of proposals for beneficial reforms, it is also an example to other countries of the likely responses from oppositionist elements, both national and international. See Lall, S. and Bibile, S., Political Economy of Controlling Transnationals: Pharmaceutical Industry in Sri Lanka, 1972-76, *Economic and Political Weekly* (August, 1977).
51. Both India and Mexico offer examples of the difficulties involved in implementing reforms. India in particular has had a long history of reformist policy proposals rendered ineffective or completely overcome by opposing groups, particularly the foreign-based drug houses. See In Defense of a National Drug Industry, *op cit.*, and Mouse that Roared, *Economic and Political Weekly* (April 1, 1978). Also see, Una industria con "lucropatia" recurrente: la farmaceutica, *Comercio Exterior* 27, No. 8 (August, 1977), pp. 913-918.
52. Lall, S. and Bibile, S., *op cit.*, pp. 1427-1427.
53. Bloomfield, J.D. 9ed.), *op cit.*, Table VII A.
54. As Lall and Bibile, *op cit.*, p. 1427, noted, neither Brazil nor Italy—two of the major Third World industrial countries that do not observe patents—have seen any massive withdrawal of capital or refusal to sell newer technological goods on the part of the transnational firms.
55. UNICEF has also responded to requests to assist with international procurement of drugs.

# V.

## UTILIZATION

### 5.1 Drug Prices

Methods for influencing the price of drugs are similar to the practices described as components of a cost-effective procurement system. In some of the market economies it is expected that basic competition between firms will result in appropriate prices. However, because of the market power of the leading firms and the reliance of patients on the physician's product choice, competitive pressures have been constrained and prices have not always fallen as would be expected in theory. Countries which continue to rely primarily on free trade theory appear to be moving toward a type of price fixing for their publicly subsidized health services based upon cost-effectiveness analyses of specific products and a continual process of pharmaceutical market surveys. These market surveys are intended to provide health planners with information about the minimum prices at which drugs are widely available. With this information in hand, drugs capable of similar curative effects can be analyzed in terms of their relative benefits. To date, very little evidence has been gathered about the success of this type of system in lowering prices to the patient, but the experience of Sri Lanka appears to prove its value in at least reducing the costs of drugs to the public health sector.

European countries exhibit some of the highest rates of drug consumption in the world. Because in most cases it is responsible for a large share of the total social expenditure on drugs, the public sector in countries throughout Europe plays a more direct role in the determination of prices. Various methods are used, but in general the manufacturing and dispensing costs are considered in price formulation. These costs may be established percentages of the final prices, e.g., in France drug price composition has involved the following formula:

Drug Price Composition*	
Manufacturers	48.33%
Value added tax	11.11%
Wholesalers	7.12%
Pharmacists	<u>33.44%</u>
	100.00%

In several countries only the commercial margins of the wholesaler and the pharmacist/retailer are fixed. As mentioned earlier, these methods have not been particularly successful in controlling the prices of drugs in market economy countries, primarily because manufacturers' costs are not closely monitored. The costs of producing pharmaceutical raw

materials and active ingredients are rarely public information in market economies, but they implicitly form the basis of all further calculations.

The costs that must be borne directly by patients are an important aspect of drug utilization policy. Lack of financial access to drugs is felt most keenly by the poorest population groups in countries where there are neither social security systems nor public health services capable of providing a substantial proportion of the population with subsidized prescription medicines. Capability on the part of the public sector may be limited in many cases by absolute economic restrictions on the amount of public resources available for social services, but various aspects of each country's social structure and political tradition also influence public control and spending on pharmaceutical products.

For example, a few of the most industrialized market economies as yet do not have established social security or public health systems that offer health services and medicines to lower income groups.<sup>1</sup> Average per capita income in these countries may be relatively high, but the lack of publicly subsidized services has resulted in a situation in which many of the poorest people must spend a disproportionate part of their income for drugs.<sup>2</sup> Less developed socialist countries also have relatively few resources to allocate to health services but, perhaps because of the lack of opposition from extensive private medical and insurance sectors, plans have emerged which are aimed at the public provision of health services and essential drugs to low income populations. In China, the emphasis on population coverage is reflected in the medicines which are provided free of charge, primarily widely used preventive drugs such as vaccines, contraceptives, and children's medicines.<sup>3</sup>

Most of the population throughout Europe is covered by either social security systems or publicly organized health services. Payment for drugs under the European systems commonly involves a co-payment by the patient with the bulk of the total price provided by the government. In the United Kingdom and Sweden only a nominal fee is required by the purchasing individual, and throughout Eastern and Western Europe all prescriptions are free to specified groups, e.g., the elderly. In principle, all prescription drugs are free to public health service patients in many African countries, but as compared to the industrial countries of Europe coverage of the population with even the essential drugs is far from complete.

Even in the least developed countries there may be some potential advantage in attaching nominal fees to publicly subsidized drugs. Patient fees may contribute to the discouragement of requests for more drugs than are medically required. The use of a limited formulary and the establishment of priority plans for population coverage would facilitate the creation of a system of charges for various drugs. Alternatively, a set fee for all or some drugs might accomplish the same ends. Each drug should be charged separately, in any event, in order to reduce the

common, but often unnecessary and hazardous practice of prescribing several different drugs at the same time.

If drug fees are to be charged in order to discourage unnecessary consumption it may be appropriate to exclude hospital patients from them as inpatients are rarely "self-referred," i.e., their illness has usually been diagnosed prior to admission. Also, those taking part in preventive or maternal and child health activities should not be required to pay pharmaceutical fees.

For operational purposes the collection of fees must be as simple as possible. It might be helpful to utilize the prescription itself as the receipt of payment. Prescription books could be made up of numbered, perforated pages so that the health unit can retain information on the patient and the prescribed drug, while the patient has the bottom half as a receipt. In some outpatient primary care units prescriptions may be written on occasion for second-line drugs, or drugs which are not listed in the health service formulary. There might be two colors utilized in printing the prescription/receipt books, one color for standard, subsidized drugs and another for other prescribed drugs and devices.<sup>4</sup>

Inter-country comparisons of the final price of drugs to individuals are very difficult to make, due to widely varying degrees of public coverage and to the different prices being charged by transnational drug companies in each country. Possibly the most notable aspect of private payments for drugs is, as one social security official stated, "... an astonishing degree of indifference to the cost factor in regard to requirements of medicaments."<sup>5</sup> In France and Finland, where insurance covers the cost of most drugs to patients, the purchase of drugs not covered by social insurance has increased at the same rate as the purchase of reimbursable drugs.<sup>6</sup> Health administrators in some African countries have noted that patients sometimes choose to procure medicines from private distributors, even though the same drugs are available at no charge through the public health service. The reasons for this seeming indifference to costs are not entirely clear, but the evidence points to a complex pattern of social and commercial influences that have combined to maintain demand for drugs despite low personal income and a typical lack of knowledge about the actual effectiveness of the product.<sup>7</sup>

## 5.2 *Drug Prescribing*

The problem of high social costs resulting from the utilization of modern drugs cannot be controlled entirely by public restrictions on the prices of drugs and the number of formulations on the market. Among six countries examined in a WHO study the highest drug consumption levels were found in the two countries with the most doctors to population, Austria and Hungary.<sup>8</sup> Prescribing physicians have directly contributed to rising drug consumption. If drug expenditures are to be prevented from taking an increasingly larger share of national health resources, physi-

cians will have to be held responsible for inappropriate, needlessly expensive prescribing practices. At issue here are the sources of drug information used by physicians, the link between the volume and type of drugs prescribed and the economic interests of the physician, and public monitoring of drug utilization.

Most studies of drug utilization point to the rapid changes that have occurred as a result of recent pharmaceutical discoveries. It has been estimated that 80 percent of today's major preparations were not known prior to the last 10 to 15 years.<sup>9</sup> An even greater percentage were not on the market a generation ago, indicating the vast amount of new information concerning drug therapy with which physicians are having to contend.<sup>10</sup> Most of what physicians do know about drugs is acquired after the completion of medical school, particularly because basic pharmacology is generally a relatively minor component of medical education. In the market economies postgraduate education in pharmaceuticals has been primarily the domain of the drug manufacturers.

The great influence of the industry on drug information has substantially limited the choices of physicians to brand name drugs that have been widely advertised. Furthermore, the commercial nature of the information has contributed to the practice of overprescribing. As noted previously, recent increases in per capita drug costs have been found to be related mostly to the increased prices of drugs (i.e., the continual entrance of higher priced new drugs to the market) and to the expansion of subsidized health services in such areas as Southern Europe and many of the former colonial territories.<sup>11</sup> Throughout this period of rising costs, the utilization of ineffective and inappropriate drugs has assumed increasing importance. Although the lack of nationwide sample data on drug utilization is such that it would be impossible to calculate the precise proportions of health resources now being wasted on inappropriate prescribing, substantial evidence has been gathered confirming that the problem is widespread. Stated another way, overprescribing is the basic problem, *augmented* by rising drug prices and extended public commitment to subsidized drugs.

For example, in the U.S. some 60 percent of all drugs being prescribed against the common cold are antibiotics and sulfonamides, which are expensive, ineffective as cold remedies, and potentially harmful to some patients.<sup>12</sup> Such misuse is common throughout the world. A British utilization study found that the appropriateness of a prescription for the stated diagnosis could be verified in only 45 percent of the sample of cases examined.<sup>13</sup> The problems of overprescribing have been strongly emphasized by WHO, especially because the further development of resistant bacteria strains at current rates conceivably could result in epidemics comparable to the pre-antibiotic era. Also, while such drugs have been used ineffectively for colds, viral infections, and diarrheal diseases, expenditures on such preventive health measures as environmental sanitation have been insufficient to stop the spread of the resistant strains of bacteria.<sup>14</sup>

Overprescribing is related to the "optimistic" view of drug therapy that is prompted by promotional literature, particularly in those countries in which ethical drug advertisements are subject to relatively few restrictions. The promotion of drugs in developing countries which are considered unsafe elsewhere has been well documented. Aminophenazone (aminopyrine) and its derivative noradopyrine (dipyron) are prime examples of such international discrepancies in the drug information provided to both physicians and consumers. Both drugs are analgesics (as is aspirin), and apparently are advertised in Africa and Latin America as remedies for minor indications such as headaches and toothaches. They are included in a wide variety of brand name combination drugs, some of which are sold directly to the public in pharmacies and other shops. In the African Monthly Index of Medical Specialities (M.I.M.S.) 34 such drugs were found to be commended as analgesics. Adverse reactions listed in this volume for products containing aminopyrine and dipyron included "very rare agranulocytosis," but in some cases such products were described as having a "wide margin of safety."<sup>15</sup>

In the 1930's, a causal relationship between aminophenazone and fatal agranulocytosis was found in a series of studies, one of which provided evidence that more than 90 percent of all cases of agranulocytosis reported in that country had been associated with aminophenazone.<sup>16</sup> The development of the derivative product, noramidopyrine, about thirty years later was followed by a rise in the incidence of drug-related agranulocytosis, and since then the drugs have been put under special regulatory control in several countries. They have been completely withdrawn from the market in the U.S., Australia, the U.K., and some other Northern European countries. Similar cases of the understatement of known adverse reactions in information provided by manufacturers to developing countries include, most notably, chlorophenical, anabolic steroids, and estrogen-progestogen combinations.

The apparent confidence of the leading pharmaceutical companies in the profitability of investments in advertising and promotion was discussed earlier in connection with the great cost of their sales campaigns. In the Federal Republic of Germany, for example, each medical practitioner may see between 15 and 20 industry salesmen, "detail men," every month.<sup>17</sup> Estimations of their impact on prescribing have stressed the influence of sheer numbers, e.g., one detail man for every three physicians in certain countries of Latin America. Regarding detail men and other forms of pharmaceutical advertising, the British Labour Party has argued that:

Until an alternative, effective way of disseminating important information to all doctors on really useful new drugs exists, we accept that there is a need for the advertising of drugs of choice, provided that the information is accurate, balanced, sufficient for its purpose and presented in an educative rather than a promotional format. If it had been left to professional channels of communication, there is no doubt that these advances would have been accepted much more slowly.<sup>18</sup>

It might be argued, however, that slower acceptance of new drugs need not necessarily inhibit good medical practice. The interrelationship between good medical practice and rapid technological development might result in greater reliance on industry representatives and literature, but there is considerable doubt that the information provided by physicians would lead them to classify 80 percent of all new discoveries in a given time period as offering "little or no therapeutic gain," as did the public drug bureau in the U.S. (Table 5.21). In fact, during that same period only 3.3 percent of all new registered drugs represented an "important therapeutic gain."

TABLE 5.21  
U.S. BUREAU OF DRUGS CLASSIFICATION OF DRUGS FOR WHICH  
NEW DRUG APPLICATIONS WERE AWARDED,  
OCTOBER 1976 - APRIL 1977

<u>Chemical Type</u>	<u>Therapeutic Potential Type</u>				<u>Total</u>
	<u>Important Therapeutic Gain</u>	<u>Modest Therapeutic Gain</u>	<u>Little or No thera- peutic Gain</u>	<u>Other</u>	
1. New molecular entity	50 2.58%	167 8.63%	538 28.80%	20 1.02%	775 40.05%
2. New salt, ester or derivative	2 0.10%	19 0.98%	137 7.08%	1 0.05%	159 7.21%
3. New formulation	1 0.05%	48 2.48%	186 9.61%	3 0.14%	238 11.20%
4. New combination	4 0.20%	21 1.08%	56 2.89%		81 4.18%
5. Already marketed drug product	2 0.10%	25 1.29%	445 22.99%	3 0.15%	475 24.54%
6. Already marketed drug product by the same firm	5 0.25%	19 0.98%	175 9.04%	8 0.41%	207 10.69%
7. Bureau of Drugs Totals	64 3.30%	299 15.45%	1,537 79.43%	35 1.80%	1,935 100.00%

Source: SCRIP, 24 September 1977.

Aside from the potential bias present in all commercial information activities there is the additional possibility that the drug information problem discussed above has been accentuated through the creation and utilization of increasingly broad and varied channels of commercial communication, i.e., the dependence of the medical profession has been fostered by the industry. The availability of detail men to provide physicians with background information apparently has been tacitly accepted as one aspect of therapeutic decision-making, especially as medical school and continuing education programs remain relatively weak in the teaching of basic pharmacology, clinical pharmacology and therapeutics. An example of dependence on industrial sales representatives in the area of medical products is illustrated by the following experience of the former president of the American Medical Association (U.S.):

... when Dr. Russell B. Roth ... did a prostate operation ... he used a new machine that was being demonstrated by a salesman. When the machine, called a continuous-flow resectoscope, was turned on, it did not function properly. Dr. Roth recalled the incident: "I didn't know what the problem was but the salesman suggested the machine was plugged by a blood clot. He suggested we take the machine apart (which we did) to remove the clot, and then we moved along smoothly in the operation. I don't know how long it would have taken me to figure out what was wrong if the salesman had not been present."<sup>19</sup>

Profitable high technology developments have been introduced to physicians and health administrators at a rate that would be likely to hinder the diagnostic tasks of medical professionals were it not for this type of assistance. Whether or not industrial sales representatives can contribute to *rational* therapy is a question which is assuming increasing importance. What appears to be massive overprescribing of new drugs is one important sign pointing toward a negative answer to that question.

Uncertainty about new products leads to dependent relationships, but the economic interest of the physicians may reinforce this relationship. Gifts, free lunches, samples and paid vacation/conventions may appear as minor advertising gambits, but they are part of a process of economic rewards intended to persuade practitioners to prescribe drugs that are (in most cases) expensive brand name preparations which, in developing countries at least, are beyond the reach of the majority of people. A U.S. \$4000 investment in advertising per doctor in one country can easily be seen as related to the 89 percent rate of brand name prescribing in that country.<sup>20</sup> Also, direct encouragement for the overprescribing of powerful drugs, e.g., certain antibiotics, can be seen in individual sales campaigns in which the quantities of drugs prescribed or purchased by physicians are directly related to the amounts of those drugs given as free samples by the company.<sup>21</sup> Organized lobbying by the medical profession to prevent the passage of such measures as compulsory generic prescribing can be

tributed, at least in part, to these direct economic benefits.<sup>22</sup> The less obvious reasons for supporting the pharmaceutical manufacturers include the ownership of stock in these companies, which is apparently not uncommon among medical associations and individual practitioners.<sup>23</sup> Finally, in some areas a doctor's image, therefore economic status, is associated with the prescribing of a large number of drugs. This situation has evolved to the point where a "good doctor" is expected to know many different drugs and at least one and usually more prescriptions per patient visit are considered signs of good care.<sup>24</sup>

The varied pressures of rapid technological development felt by practitioners are often compounded by an abundance of patients with trivial complaints, many of them in need of counseling or related types of treatment. Too often both the physician and the patient have been satisfied to end a consultation with a prescription—a harmless placebo such as a vitamin preparation, a tonic, an herbal remedy, or far worse, a tranquilizer or antidepressant. A survey in one highly industrialized country found that the two most prescribed drugs were tranquilizers (i.e., Valium and Librium); the rather ineffective painkiller Darvon was third on the list.<sup>25</sup> Attempts to seek out better treatment methods oriented toward the whole patient, taking into account his or her environment, have been made in an effort to reduce overprescribing.

One method attempted in a high morbidity area of northeast England involved:

1. A refusal to accept requests for repeat prescriptions for new episodes of previously treated minor illnesses.
2. After careful examination, patients with minor illnesses were taught the low value, and possible harmful effects, of unnecessary drug treatment and relevant aspects of health education were discussed.
3. Health visitors working in the community advised people in their homes about managing minor illnesses.
4. The follow-up consultation for patients with minor illnesses was handled by a nurse (could be another health worker) rather than the physician.<sup>26</sup>

The broader involvement of the community in preventive health activities and the choice of village health workers with high levels of understanding and concern for their community should also reduce pressures on clinical health workers for unnecessary drug treatment. Almost any policy instruments intended to reduce overprescribing are likely to enjoy greater success as a result of an integrated approach reaching both practitioners and patients that also involves a system of utilization review by the public sector.

Quantitative units that have been used by the public sector to monitor drug utilization (i.e., prescribing patterns and medicine consumption) include the numbers of prescriptions dispensed or acquired, the frequency

of consumption of specific medicines, and the value in terms of pharmacy sales, purchases or patient costs.<sup>27</sup> Comparable statistics of this sort are now available among a few countries, particularly those of Northern and Eastern Europe. Utilization review was initially used in most areas of the world to combat the problem of narcotic drug use. Czechoslovakia was one of the first to establish committees on national drug therapy so as to ensure the economic use of drugs and, in the long run, analyze the relationship between drug therapy and the state of health of the population.<sup>28</sup> Drug utilization data can also be used to measure new price or supply control policies and the impact of drug information activities.

The monitoring of prescribing patterns in Czechoslovakia involves special data processing techniques, which in countries with fewer health resources might be replaced by such basic written information as the following: identification of the prescriber, identification of the patient (by number if possible), a code number for the diagnosis for which the drug was prescribed, a code number for the drug, and the amount prescribed.<sup>29</sup> In Sweden, a random sample of all prescriptions is collected from the pharmacies. The information required on the prescription forms allows for the analysis of prescribing patterns, e.g., drug and amount prescribed, and age and sex of patient. An agreement with the national drug industry also allows the Swedish health authorities access to net sales figures for pharmaceutical products. Access to sales figures has resulted in information and health education campaigns intended to reduce consumption of substances which are judged as being sold in excess amounts.<sup>30</sup> Direct restrictions could also be imposed on the sales of drugs apparently being over-utilized by the population.

One of the most important aspects of this type of public review of drug use is that it offers a means of educating and/or applying pressures on practitioners who are in the habit of prescribing "extravagantly." The resources used for excessive ethical drug consumption cannot prevent illness, nor can they compensate for overcrowded clinics or sparsely distributed health workers. The question of cost-effective selection of drugs was discussed earlier in terms of limitations on the supply of drugs, but in order to assure acceptance by the medical profession of these kinds of limitations, practitioners will have to be made aware of their responsibility to prescribe drugs which are of relatively low cost. Medical education has been lacking in adequate training in pharmacology, and is virtually devoid of the study of the economic aspects of drug therapy. A study of prescribing in Tanzania pointed out that hookworm is not likely to be immediately eradicated and reinfection is common; therefore the difference between 100 doses of tetrachlorethylene (TCD) at 60 cents and 100 doses of Alcopar (bephenium) at 80 shillings (one shilling = 100 cents) is primarily economic, in the sense that doctors prescribing the far more expensive (but only moderately more effective) medication with government funds are actually prohibiting wider population coverage with any medication at all.<sup>31</sup> In the U.K., among other countries, one response to

this information problem has been the distribution of colored graphs to physicians depicting the large cost differences among similar therapies.

A national utilization study could be planned by the formulary committee within the ministry of health well in advance of implementation by the creation of code numbers for both approved drugs and the indications for use that have been associated with each drug on the list.<sup>32</sup> Various methods of utilization review can contribute to the forecasting of need for pharmaceutical products at both regional/district and hospital/health center levels. Because of the difficulties of collecting and managing the large amount of data involved, nationwide analysis of medicine consumption is likely to be beyond the immediate capability of the great majority of countries. However, national health authorities in all countries should be capable of collecting samples of prescriptions from the pharmacies and other outlets supplied by the public health sector. Efforts to win the support of health workers for a policy emphasizing the rational, cost-effective use of drugs are perhaps most important in the short run, although, as was pointed out in the example of Czechoslovakia, good statistical data on drug consumption can also be used for other than strictly economic reasons, the most important of which is the discovery of the relationship between drug therapy and the long term health status of the population.

### 5.3 *Pharmacy Workers*

Shortages of trained dispensers are common to most of the developing countries. Such shortages are usually particularly acute in predominantly rural market economies characterized by patterns of land ownership which restrict the ability of communities to generate enough income to support many highly trained professional workers (Table 5.31). In many such countries laws require all pharmacies to be owned and/or operated by a graduate pharmacist.

Data from some of the more industrialized countries show that the poorest segments of the population tend to rely heavily on retail drug sales for their pharmaceutical needs.<sup>33</sup> The situation is similar in many developing market economy countries, but because the cost of a physician visit and prescription is less likely to be subsidized and there are limited numbers of trained pharmacy workers, a much higher risk potential is added to the medication practices of the poor. The sale of ethical drugs from pharmacies, rural shops, and markets may be performed by workers whose knowledge of modern drugs is limited to the information printed on the labels or package inserts of the products.<sup>34</sup>

The solution to this problem does not appear to require heavy investments in graduate pharmacy programs (i.e., five-year university courses). The tasks of professional pharmacists throughout the world have been modified by the increasing number of drugs sold directly by manufacturers in finished dosage form. Whereas compounding medicines

TABLE 5.31  
POPULATION PER PHARMACIST 1973

---

<u>Country</u>	<u>Pop./Pharmacist</u>
Afghanistan	494,430
Haiti	444,000
India	8,700
Indonesia	76,670
Liberia	237,000
Malaysia	233,330
Paraguay	44,070

---

Source: World Health Statistics Annual 1973-1976, Table 2.3.

was once the principal duty of pharmacists, now they tend to have broader supervisory or managerial roles. Compounding work is more heavily concentrated in hospitals and regional stores, and in these settings only a limited number of pharmacists are needed to supervise such largely mechanical tasks as receiving, counting, pouring, and storing ingredients. Increasingly, most of the tasks are being performed by auxiliary workers. However, in many countries pharmaceutical auxiliaries cannot legally own a pharmacy or dispense drugs without the supervision of a graduate pharmacist.

The response to the need for more pharmacy workers to staff expanding public health services has varied considerably between countries, but the trend is generally toward the development of more training programs for auxiliaries. The basic differences in the content of these programs relates to the goals of national health planners. Often the training has been oriented to hospital pharmacy practice. For example, Mauritius and Singapore recognize a grade of pharmacy technician, but the training and the employability of these workers is limited to government hospitals. In Thailand, nurses have been given three to four months additional training so as to fulfill the dispensing requirements of rural hospitals.<sup>35</sup>

In the socialist developing countries pharmacy training programs, like medical training in general, have been organized in a pyramidal fashion in response to the immediate health needs of communities. For example, the program drawn up by the Vietnamese Ministry of Health called for the medical service of each province to train the number of pharmaceutical assistants necessary to staff all rural drug shops. By reducing the training period to 9 to 12 months the provinces are reported to have quickly reached this goal.<sup>36</sup>

Vietnam now recognizes three categories of pharmacists, the first of which allows for the expansion of the total number of pharmacy workers with minimal public investments in training. The next grade of pharmacy worker is required to have a combination of further technical training and in-service experience. To the extent they are needed for teaching and supervision, a limited number of workers complete the five-year graduate pharmacist program at universities.<sup>37</sup>

Considering that primary health care services may expand relatively slowly without training programs oriented toward community needs, the best short-term option for predominantly rural countries appears to be the creation of programs aimed at training workers with average levels of formal education to handle and dispense basic medicines. For many countries, especially those in which a large part of the population is chronically ill, it is only such decentralized priority planning directed toward immediate basic needs that can be expected to show any results at all.

In some countries, legislation regarding pharmacy management would have to be amended so that pharmacy workers with newly planned minimal levels of training and/or experience could be granted licenses to operate small pharmacies independently or act as the principal dispensers for primary health care units. However, there would be little purpose in expanding the number of pharmacy workers without some conception of the desired ratio of pharmacy workers to the total population of each region, district or community, as well as the projected personnel requirements of the central and regional stores, hospitals, and laboratories.

Finally, the expansion of the total number of workers involved in distributing drugs should be associated with plans for reducing the irrational use of drugs, particularly among populations exposed to the promotional practices of the large drug firms. In areas where pharmacy workers are usually expected to give advice on drugs and their use, efforts should be made by health authorities to provide them with brochures and posters depicting the dangers of incorrect drug consumption. A limited national formulary is of great value in this regard, particularly when it specifies the drugs that can legally circulate in both the public and private sectors.

Auxiliary training programs tailored to current realities of community drug distribution are a very significant aspect of planning for an

appropriate pharmacy work force, but a small group of highly trained workers are also needed to function at national, regional and district levels as members of formulary committees, and as teachers, research specialists and directors of quality control in pharmaceutical production operations. In 1970 a WHO Study Group pointed out the extreme shortage of workers skilled in clinical pharmacology (the study of drugs in man), but despite current interest in national formularies and expanded drug production a shortage of this particular group of specialists is still evident in most developing countries.<sup>38</sup> Although the addition of a university degree program in this field is beyond the educational resource capabilities of many countries, the value of sending students abroad to countries offering clinical pharmacology programs may be very great, especially as compared to other medical training programs in areas of highly specialized curative care.

## FOOTNOTES

1. In the United States, for example, a 1970 University of Chicago study showed that 80 percent of the payments for prescription drugs were made directly by the consumer, with no reimbursement from insurance or social security. Excepting the elderly and social welfare recipients (the very poor or unemployed) prescription drugs are not covered by any national program in Canada either, although some individual provinces do offer drug benefits to their populations. More than 60 percent of the population of Mexico is not covered by any system of social security. The situation is generally even worse in other Latin American countries that are largely rural.
2. In other words, lower income working people, who in any event show a greater prevalence of chronic illness, cannot always purchase a lower priced substitute drug, as is possible in the case of other basic necessities.
3. Sidel, R. and Sidel, V., *Serve the People*, (Boston: Beacon Press, 1973) p. 189.
4. These comments are drawn from Gish, O., *Planning the Health Sector*, (London: Croom Helm, 1975 and 1978), pp. 64-65.
5. Kastner, F., *Volume and Cost of the Supply of Medicaments*, (Geneva: ISSA, 1974), p. 81.
6. Rabin, D. and Bush, P., The Use of Medicines: Historic Trends and International Comparisons, *International Journal of Health Services*, Vol. 4, No. 1, (1974), p. 81.
7. Extensive discussion of the determinants of drug consumption is not within the limits of this paper, but, as pointed out in the introduction, commercial influences felt directly by individuals (i.e., advertising) have apparently coincided with an historical fascination with curative and mind-altering drugs on the part of peoples throughout the world.
8. Rabin, D. and Bush, P., The Use of Medicines: Historic Trends and International Comparisons, *International Journal of Health Services*, Vol. 4, No. 1, (1974), p. 81.
9. Kewitz, H., Drug Utilization: The Role of Medical Schools, *Clinical Pharmacological Evaluation in Drug Control*, Report on Symposium. (Copenhagen: Regional Office for Europe, WHO, 1976), p. 56.

10. J. R. Crout, former Director of the Bureau of Drugs in the U.S. estimated that 90 percent of prescriptions written today were not available a generation ago. Statement by J. Richard Crout, M.D. before the Subcommittee on Monopoly, Select Committee on Small Business, *Competitive Problems in the Drug Industry*, (Washington, D.C.: U.S. Government Printing Office, 1976), Part 30, p. 14068.
11. Kastner, F., *op. cit.*; Schieke, R. K., The Pharmaceutical Market and Prescription Drugs in the Federal Republic of Germany: Cross-National Comparisons, *International Journal of Health Services*, Vol. 3, No. 2, (1973). Data reported by Schieke correspond to Kastner's assumption that extended health service coverage in Southern Europe accounted for most of the increased expenditures; during 1966-70, of total drug consumption costs in Italy 75 percent were attributable to increased utilization (p. 231).
12. Containing the rising cost of medical care under social security, *WHO Chronicle* 31: 408-412 (1977).
13. Schieke, R. K., *op. cit.*, p. 230.
14. Uncontrolled use of antibiotics in animals presents similar problems.
15. Yudkin, J., To Plan is to Choose, University of Dar es Salaam, mimeo, p. 13.
16. Kracke, R. and Parker, F., Relationship of Drug Therapy to Agranulocytosis, *JAMA*, 105 (1935) pp. 960-966.
17. Kewitz, H., *op. cit.*, p. 56.
18. *The Pharmaceutical Industry* (London: The Labour Party, 1976) p. 27.
19. Altman, I., Physicians, technicians, even salesmen, some distinctions blur, *New York York Times*, 19 November 1977.
20. Buraek, R., *New Handbook of Prescription Drugs*, New York: Random House, 1975) p. xxiii.
21. A set of Pfizer sales materials for Terramycin (Oxytetracycline) were intended to increase sales of the product, and the "inducement to buy the Pfizer product was that the more they bought the more they got free." Mintz, Drug Industry Payola Told, *Washington Post*, (9 March 1974).
22. Lall, S. and Bible, S., Political Economy of Controlling Transnationals: Pharmaceutical Industry in Sri Lanka, 1972-76, *Economic and Political Weekly*, (August, 1977) p. 1423.
23. In 1973, the American Medical Association retirement fund owned stock in 16 companies in the drug or medical supplies fields. Hines, What's Behind AMA Drug Suit, *Chicago Sun Times* (4 August 1975). In a typical drug company in Bangladesh, "Seventy-six percent of the shares are owned by Americans and 6 percent of the shares distributed to local doctors for the explicit purpose of encouraging the sale of the products of the company." Briscoe, Politics of an International Health Programme, *Economic and Political Weekly* (18 March 1978).
24. Kewitz, H., *op. cit.*, p. 56.
25. Moertel, C.G., et al., A comparative evaluation of marketed analgesic drugs, *New England Journal of Medicine*, 286: 813-815 (1972).
26. Marsh, G.N., "Curing" minor illness in general practice, *British Medical Journal* (12 November 1977) pp. 1267-1269.
27. Rabin and Bush, *op. cit.*, pp. 82-83. This article is one of the very few which analyzes the possibilities and difficulties of international comparisons of medicine consumption involving variations in the number of drugs available directly to consumers, variations in illness behavior, and national policies with regard to health insurance, cost control, advertising and prevention of illness.
28. Stuka, L., Differences in National Drug-Prescribing Patterns, *Clinical Pharmacological Evaluation in Drug Control*, (Copenhagen, WHO Regional Office for Europe, 1976) pp. 48-53.

29. *Ibid.* p. 48.
30. Liljestand, A., Drug Utilization: The Role of Drug Control Agencies, *Clinical Pharmacological Evaluation in Drug Control*, op. cit., p. 59.
31. Speight, A.N.P., Cost-effectiveness and drug therapy, *Tropical Doctor*, (April, 1975) pp. 89-92.
32. The inclusion of a great many traditional medicines in a utilization review of this sort might make for particular difficulties. The importance of monitoring their use would have to be determined on the basis of local conditions.
33. Recent data from developed countries reflect higher utilization of prescription drugs among the poorest groups, who usually have access to subsidized health services at this point. However, these groups continue to have higher rates of morbidity due, apparently, to their general living conditions. For U.S. statistics in this regard, see Silverman and Lydecker, *op. cit.*, pp. 7-8. This is not to say that this type of drug use is particularly beneficial, as was pointed out earlier in relation to the "vicious circle" of illness-treatment-recurrent illness, but the risks are obviously lower than if these drugs had not been prescribed by a health worker at all.
34. A survey of sources of health care in Afghanistan showed that people who lived far from a pharmacy turned to village merchants for ethical drugs, some of which had been smuggled. Most of the practitioners surveyed seemed to realize the potential danger of uninformed utilization of modern drugs, and the traditional Afghan practitioners (Hakims) understood they were not legally allowed to distribute ethical drugs, although they acknowledged their importance in cases of serious illness. Appendix 4, A Field Survey of Health Needs, Practices, and Resources in Rural Afghanistan (Cambridge: Management Sciences for Health, 1975).
35. Fendall, N., *Auxiliaries in Health Care* (Baltimore: Johns Hopkins, 1972) "Pharmacy and the Auxiliary", pp. 142-155. Bloomfield, J.C., *Survey of General Practice Pharmacy 1974* (Federation Internationale Pharmaceutique, 1974) Table VIII A.
36. McMichael, J. (ed.) *Health in the Third World: Studies from Vietnam* (Nottingham: Spokesman Books, 1976), pp. 176-179.
37. Table VII A in Bloomfield, J.C., *op. cit.*, describes a similar educational structure in Sri Lanka.
38. Clinical Pharmacology--Scope, Organization, Training: Report of a WHO Study Group. *WHO Technical Report Series No. 446* (1970).

# VI.

## DISTRIBUTION

### 6.1 *National Patterns of Drug Distribution*

Transnational drug companies have contributed to the elimination of intermediary wholesale firms in their home markets by producing an increasing number and volume of finished drugs in retail package form and integrating warehousing and storage activities into their own operations. In developing countries, much of the attention given to pharmaceuticals planning has thus far been placed on the initial procurement or wholesale level. Particularly in countries with limited production capacities, the wholesale/import sector will remain a very important determinant of overall social expenditures on drugs and national patterns of drug distribution.

In some countries government acts as the national wholesaler of finished drugs. Public control at this level may be extended throughout the distribution system by channeling purchases of all medical supplies through a network of state-controlled dispensaries which, in conjunction with plans for national primary care services, are organized for the supply of needed medicines to as many people as possible. In remote areas rural medical depots linked to the dispensaries and run by local health workers are an important element of the public distribution system in that they facilitate the provision of health care and medicines to the poorest consumers at minimal prices.<sup>1</sup>

Central procurement agencies may also act as suppliers for both the national health service and the private sector. In general, this type of arrangement is most suitable in countries with privately owned indigenous pharmaceutical industries to which potential savings on imports of raw materials and intermediate chemicals may be important for cost-efficient production. To the extent that international purchases are centralized, government can maintain better control over imports and thus the balance of payments situation. However, total social expenditures on drugs will vary depending upon agreements made by governments with the private sector regarding wholesale and retail markups and the amount of the dispensing fee that is included in prices charged by private pharmacists and other dispensing practitioners.

Regardless of the degree of centralization at the wholesale/import level of distribution, the geographic patterns of drug supply likely to result from particular combinations of public and private distribution practices will be strongly related to the relative proportions of nationally produced drugs flowing into public health service channels and private sector outlets. Particularly in the developing market economies, retail pharmacies tend to be clustered in urban areas because of the proximity of

suppliers and the generally higher levels of purchasing power. For this reason, the distribution of medicines to rural areas is reliant on plans for the public provision of primary health care services to outlying populations. However, it should be noted that in several developing countries significant inroads into the rural market for pharmaceuticals have been made by multinational firms by means of extensive promotional practices. As a result, in some countries a haphazard system of drug distribution has developed which is particularly difficult to regulate as it is not integrated into the public health care system. Whether or not public control over international purchasing will be augmented by measures to further rationalize the distribution of modern drugs, e.g., regulatory restrictions on promotion and retail sales, is an important issue for national health authorities.

Often in the developing countries the public sector supplies the health services through "central medical stores" and a private wholesale/import sector supplies private markets by purchasing finished drugs and chemicals from the international market. Each private "store" usually represents a number of pharmaceutical firms. Again, patterns of distribution resulting from private sector supply and demand flows tend to result in an urban supplied bias, with some drugs reaching the rural areas through poorly regulated retail sales by village merchants. One of the greatest problems that predominantly rural developing countries must contend with in regard to private sector distribution is that, in seeking areas of highest return on investment, firms have little interest in contributing either capital or technical expertise to the wide areal gaps in infrastructure that characterize poor countries. A lack of well-paved roads, communication facilities, and educational programs for the training of dispensing personnel contribute to overall distribution problems, yet are not likely to be addressed by the private sector. The efforts of pharmaceutical firms to increase demand levels for their products without contributing to basic improvements in the distribution network may, in fact, be an impediment to the health of people consuming drugs which have been subject to inadequate storage and delivery conditions.

## 6.2 *Delivery Systems*

The operational aspects of drug distribution involve the transfer of drugs from the producer or importer to their final end point. Problems facing poor countries in this regard are of particular importance, as all efforts at cost-efficiency in central procurement are lost if storage facilities are not organized and equipped to handle delicate preparations, and the transportation and communications systems are not sufficient for the supply of the right medicinal products to those places where they are needed most. Prepackaging and labelling are briefly discussed in this section, as these activities are often carried out by health service workers

and their correct handling can result in considerable improvements in inventory control and safety.

In a recent technical report about delivery of medical commodities in developing countries, it was pointed out that much of the early health delivery work in rural areas was done by Christian medical missions. As these were usually relatively isolated units, rarely integrated into national health care services, they handled their needs for medical commodities independently, accomplishing all supplies ordering and transportation tasks with their own vehicles and staff.<sup>2</sup> Although it is difficult to say whether or not the model of the mission facility has in any way inhibited present delivery systems in rural areas, it is certainly true that in many countries these systems have not progressed much beyond this stage in terms of centralized control and or reliability.

Meeting rural needs for vaccinations has often been accomplished by mobile units equipped with refrigerated storage containers. In the short run this has been a practical measure. However, storage and delivery systems fully integrated into community health care structures can offer much greater benefits in terms of improved communications flows between the rural areas and central supplies stores, as well as in assuring a more systematic coverage of the population.

The technical report on medical commodities delivery mentioned above proposed that the implementation of a drug delivery system be the responsibility of a Central Level Delivery Unit, which would develop policy guidelines for the distribution of medicines to the various stores or directly to rural areas in countries where storage facilities do not exist much beyond the central level. The initial element in the physical distribution chain would be the central warehouse facility, which receives bulk supplies from the manufacturer for the provision of hospitals and other health service units.<sup>3</sup> Storage facilities linked to the main warehouse offering support to local health service units exist in many countries. The development of a such a chain of storage facilities is a critical factor in reducing supplies shortages at the regional, district and community health service level. This is particularly true in areas where difficult terrain presents a problem. Countries with developing pharmaceutical industries should also consider the possibilities for small-scale production facilities at decentralized locations.

Some aspects of warehouse operations are directly related to the efforts of the pharmaceutical technicians and other staff, e.g., the orderly arrangements of stocks, cleanliness and the prevention of mice and insect infestation, and the responsible ordering of stocks. Other aspects concern the makeup of the facilities and are more closely related to the sophistication of the equipment and the underlying infrastructure, e.g., power supplies for refrigeration. A WHO report from Ghana stressed the problems of unreliable power supplies and insulated equipment involved in the storage of vaccines, which have occasionally led to substantial losses of vaccines.<sup>4</sup> Health service administrators in tropical countries

should regularly carry out special examinations of the cold chain elements in their delivery system, e.g., refrigerators and cold chests, to ensure their equipment is appropriate for national conditions. In order to achieve better care in the handling of vaccines, the following requirements were proposed for a national store in Accra: allocation of space by temperature separated by insulated partitions, an alarm for compressor failure, and an auxiliary compressor valved into the circuit for uninterrupted maintenance.<sup>5</sup> In many developing countries, however, the costs of building such a store might preclude its construction.

Experience has shown there are significant economies to be gained through purchase of bulk packaged units of drugs at the central level and relegation of further prepackaging to local pharmacy and dispensary workers. In the case of vaccines perhaps 80 percent of the cost of finished dosages is involved in final packaging. Clearly, lower cost packaging of vaccines would be of immense benefit to health sector immunization programs. In the case of less widely utilized second-line drugs, decisions on the size of the units ordered should be taken together with consideration of utilization levels, so that inventories will not be overloaded at any point. Quality control considerations in packaging involve checking the containers and closures for their ability to withstand rough handling and further storage and ensuring that contamination will not occur. In instances of long-distance transportation over land, careful packaging is a critical factor in preventing the deterioration of some drugs and may warrant special training for warehouse workers.

In areas where long distances and difficult terrain present particular problems and air freight deliveries cannot be made on regular schedules, the establishment of regional supplies depots is especially important. Many of the problems of commodity distribution in poor countries are directly related to difficult transportation conditions, or simply to a lack of vehicles. An adequate supply of vehicles is necessary, as is a repair and maintenance staff to keep them in working order. Not only are vehicles needed for the delivery of medicines, they can also be used to transport personnel and collect information. To a considerable extent, underutilization of rural primary health care units in many countries is directly related to unreliable deliveries of medicine, frequently because of transport difficulties.

The collection of data on regional and/or district level drug consumption is required for central planning, and a drug consumption report form should be included with drug deliveries. The monitoring of these forms by responsible personnel would not only be an aid to planning, but would also assist in the prevention of the diversion of supplies from their appointed destination. Particularly in areas where a regular delivery schedule has not previously existed, the establishment of a standard schedule of drugs sufficient for a specified time period is a logical starting point for a more systematic approach to distribution. The creation of this

drug list (formulary) by district or region and/or specific health unit might be based on some combination of data concerning current consumption patterns, the size and age structure of the (actual and potential) patient population, and reported cases of diseases such as malaria, tuberculosis, and so on. Overall it is much easier to distribute a limited number of different types of drugs, especially to the smaller rural units. However, in order to assure that the quality of primary health care is not adversely affected by a shortage of needed medicines, drug lists at these units should be subject to district or community level revision.

Certain options in prepackaging and labelling are available in the final stage of distribution to the consumer. In busy hospital environments prepackaging in unit dosage form by pharmacy staff may be useful. Several studies have shown a decrease in the number of medication errors resulting from this system, as well as the more efficient use of time by nursing staff. Especially where staff-patient ratios are poor, the centralization of dose preparation is valuable in transferring these duties from medical staff to pharmaceutical auxiliaries. Alternatively, as an aid to inventory control, the prepackaging of drugs by the hospital pharmacy in single unit dosage form may be limited to rarely used, and/or relatively expensive drugs which are stocked only in small quantities.<sup>6</sup>

The presentation of drugs to patients outside the hospital also merits some attention. Labelling cannot be a substitute for correct verbal instructions to the consumer, but the inclusion of applicable warnings and other information deemed useful by health authorities is of obvious benefit. If bulk procurement of all drugs is an aspect of national or health services purchasing policy, labelling will be carried out by pharmacy or other health care workers in hospitals and supplies stores. In areas where illiteracy is common, a special study of relevant symbols on drug labels might be warranted. Clearly, where distribution of the more potent drugs through village shops and pharmacies is allowed, printed consumer information increases in importance.

## FOOTNOTES

1. Summary report of the Secretary-General of WHO, *WHO Chronicle* 29 (1975), pp. 342-343.
2. Lane, N. Medical Commodities Delivery in Support of Primary Care Programs, Addis Ababa, Ethiopia (October 1976), p. 10.
3. *Ibid.*, p. 6.
4. Lloyd, J.S. Improving the Cold Chain for Vaccines, *WHO Chronicle* 31 (1977), pp. 13-18.
5. *Ibid.*, p. 15.
6. Conley, B.F. (ed.), *Social and Economic Aspects of Drug Utilization Research* (Hamilton, Ill.: Drug Intelligence Publications, 1976). Drug Distribution Research; pp. 160-188.

## VII.

# SUMMARY CONCLUSION

### 7.1 *Summary, Recommendations, and Research Needs*

The issues discussed in the preceding sections are briefly summarized here as follows:

- i. Supply Conditions (2.1-3.3)
- ii. Procurement Planning (4.1-4.3)
- iii. Planning the Drug Utilization System (5.1-6.2)

Recommendations and some questions for further research are also outlined and, in conclusion, there is discussion of some ongoing regional and international efforts to improve pharmaceutical supply and utilization systems.

#### i. *Supply Conditions*

The pharmaceutical production process, particularly the extraction of raw materials and the manufacture of active ingredients, has evolved within an increasingly oligopolistic international market structure. While control of most of the world market for pharmaceutical products has allowed the one or two dozen leading firms to carry the primary responsibility for developing new drugs, the value of their function as innovators has been offset by their power to determine the product mix and cost of drug supplies in diverse countries with widely varying disease patterns and resource availability. The market power of the transnational firms is derived from their ownership of the patent rights to manufacture and sell many of the important drugs and the effectiveness of their marketing practices in displacing drugs no longer under patent protection.

The costs of dependence on an oligopolistic international pharmaceutical industry include: the difficulty of asserting public control over the prices of drugs due to the international fragmentation of the production process and the consequent opportunity for "transfer-pricing," the difficulty of regulating the multifaceted promotional campaigns financed by the industry which influence pharmaceutical supplies purchasing by health sector planners and administrators; and the prescriptions written by physicians.

#### *Recommendations:*

a) The public health sector should already have available to it information on the quantities and prices of different drugs procured by government and the name and location of the suppliers. When possible, this information should be supplemented by data from private sector agents of foreign suppliers—orders placed by the agents, name and location of supplying firms, and prices charged. Pharmaceutical products

manufactured locally, the equity of local firms (i.e., direct and indirect foreign investments in the national drug industry), prices, and the total value of domestic sales by these firms should also be determined. These types of data provide *background information* indicating the extent of market concentration in the national pharmaceutical market. If the value of each supplying firm's sales to the private and public sectors is calculated, the percentage of the market held by the leading firms can be estimated.

b) A list of the total number of pharmaceutical products registered in the country that are currently subject to *patent restrictions* should also be readily available. This list can be used in conjunction with the information indicated above to estimate the percentage of national drug sales accounted for by products which are only available by monopoly price quotation.

c) Legislation aimed at controlling the *advertising practices* of pharmaceutical firms should be reviewed so as to assure that all the promotional activities of the drug firms are regulated and all such practices come under the continuing surveillance of the public health sector. The product information used by those with responsibility for pharmaceutical purchasing should be made available by the drugs division of the public health sector, and "detail men" prohibited from making direct contact with health service personnel. Information on the number of "detail men" might be gathered and their impact on prescribing physicians examined (e.g., number per physician, number of visits received by physicians each week). A code for marketing practices would be useful where the influence of private firms is extensive. In any event, all advertising and promotion connected with specific drug products should conform to the data sheet on the product that has been approved by the registration authorities.

d) To the extent possible, countries should attempt to achieve some level of *self-sufficiency in drug production*. The relatively small number of firms and governmental organizations selling pharmaceutical production technology and active ingredients in bulk should be investigated thoroughly, and *comparative cost information collected*. In order to protect independent firms entering into licensing agreements, *legislation controlling abusive practices* such as "tie-in" clauses and export prohibitions should be enacted.

e) Self-sufficiency in all aspects of modern drug production requires, in most instances, raw materials consisting of by-products from the basic chemicals industry (fine chemicals). If a chemicals industry already exists, it should be developed with a view toward future integration of as many aspects of chemical drug production as possible. In many countries an *alternative to chemical drug production* based upon the extraction of various substances from locally grown plant and animal material may be a viable option. The use of industrial fermentation techniques should be examined in this regard, as should the improved organization of

production of locally popular traditional medicines. Regional cooperation appears to be potentially valuable to the development of national drug industries, as each country can then concentrate investments on developing its own particular productive advantages.

f) *Quality control* in pharmaceutical production is a critical aspect of the supply situation. All countries should begin to implement the WHO guidelines for "Good practices in the manufacture and quality control of drugs," either with regard to domestic production or as a requirement of importing firms.

g) The *packaging of bulk drugs* should begin immediately in those countries lacking any form of drug industry. Local packaging saves health resources and allows for distribution of different products in forms appropriate to local conditions.

h) The most important overall aspect of the development of pharmaceutical production is *close cooperation between industrial and health planners*. The products manufactured should serve the health needs of the majority and, to the degree possible, industrial plants should be located at different points in the country in order to facilitate transport to health service units.

#### *Some Research Questions:*

1. What is happening to the prices of particular drugs over time? How might these price movements be explained?
2. Have the public health services uneconomically limited drug purchases to particular firms or exporting countries? If so, why?
3. Which of the products purchased by the public health services are subject to patent restrictions and only available from a single supplier? Do satisfactory alternatives exist?
4. Is there appropriate national legislation and sufficient regulatory personnel to monitor and control as necessary all forms of drug advertising? If not, how can the gaps be closed?
5. Which drugs are most needed nationally, and of these which can be produced from locally available raw materials? What are the financial implications of public investment in selected aspects of drug production and or formulation and packaging?
6. How can quality control procedures be adapted to probable local manufacturing conditions?
7. Are personnel available for interpreting and monitoring quality control standards? If not, what is the most efficient way of providing training for them?
8. Is a private sector pharmaceutical industry a viable alternative? What would be the benefits and costs of such an industry?

#### ii. *Procurement Planning*

Rapidly rising drug expenditures by the (public) urban hospital sector

may be directly related to a limitation of basic health services. In many poor countries the balance of payments situation and the irrational self-medication patterns that have arisen where organized health services are not available to offset virtually uncontrolled drug promotion and sales appear to require a strong policy commitment to more stringent control over the procurement and content of national drug supplies.

*Recommendations:*

a) The first step in planning the pharmaceutical supply is the creation of a *formulary* that reflects national therapeutic needs. A priority emphasis on the choice of drugs likely to be used by a majority of the population will ensure the possibility of at least minimum coverage of the essential drug needs of that population.

b) The most complex aspect of drug procurement involves *quality and safety considerations*—the surveillance of producers and their manufacturing practices, quality assurance through registration information on drugs in the country of origin, and national (or regional) batch certification of product strength, purity, stability and bioavailability. Characteristics of the local population and the types of health workers administering the drugs should be included as aspects of safety considerations. Restrictions on the number of active ingredients and formulations to those listed in a national formulary can significantly reduce pressures on limited technical personnel to analyze and monitor these substances.

c) *Brand names* are a key component of drug advertising, but they confuse prescribers, mystifying the relationship between new and established drugs, and usually carry higher prices than drugs sold by generic name. Use of WHO's International Nonproprietary Names should be encouraged at all levels, and formulary procurement should always be accomplished by nonproprietary names.

d) *Cost-effectiveness* is an absolutely necessary element in the criteria used for the choice of formulary drugs. In overall terms, the value of any particular drug increases relative to the importance of its contribution to the control of the most common important diseases. Many of the drugs listed in a formulary are likely to be interchangeable or therapeutically equivalent to other drugs. Often each of a group of similar drugs is available in a variety of different dosage forms and presentations. The least expensive of these products may not always be the safest and most appropriate for local use, and an evaluation of relative efficacy should first be accomplished by pharmacists and clinical pharmacologists. Prices offered by various suppliers should then be compared with a view toward the capability of the producer to produce the drug in adequate amounts within the context of certified good manufacturing practices. Prices are likely to change frequently, particularly as patent privileges expire, and a comparative selection process requires continual monitoring of market prices. The alternative to comparative selection is public price fixing. A good knowledge of probable minimum cost levels at all stages of drug

production is necessary to ensuring that nationalized companies or other companies subject to price regulations are operating in an efficient manner.

e) One of the chief economic benefits of a limited formulary oriented toward majority needs is the possibility of *centralized, bulk procurement*. It appears that savings from relatively large shipments can almost always be achieved, but centralized procurement requires a highly reliable inventory system based on well coordinated methods of forecasting need by region, district, and/or separate health unit. The publication of international tenders for competitive bids can further reduce procurement costs, particularly in countries without national drug industries.

#### *Some Research Questions:*

1. Is current epidemiological data on disease incidence and prevalence adequate for determining national therapeutic need? What type of additional surveys might be planned? What biases are likely to be present in a study of national drug sales, and how can they be corrected?
2. Are sufficient personnel available to establish and carry out quality control procedures? If not, what is the most efficient way of providing training for the necessary technical personnel? What are the possibilities for regional certification of quality and bioavailability?
3. How do recorded prices of generic name drugs vary over time? Can prices of similar generic and brand name drugs be compared over several years? What does the comparison indicate for future procurement policies?
4. How best can comparative price information be gathered? How can the bids resulting from international tenders be used by regional groups of developing countries?
5. Which prevalent health conditions are likely to influence the action of drug products in the body?

#### iii. *Planning the Drug Utilization System*

Efforts to establish a cost-effective procurement system will be significantly reduced in the absence of adequate information and education systems ensuring that physicians, pharmacy workers, and other health workers handling drugs are fully aware of the correct uses of formulary drugs, their costs, and the hazards of uninformed or incorrect utilization by patients. Patient demand for drugs as well as the advertising campaigns directed at physicians have contributed to the common practice of overprescribing. In many parts of the world, systems for reporting on the population's drug utilization patterns are either nonexistent or very limited in scope. The lack of such systems makes it difficult

for public health planners to observe the prevalence of overprescribing, adverse reactions, and the actual effectiveness of drug therapy in reducing or eliminating human disease.

The value of cost-effective procurement based on national therapeutic need is also reduced in the absence of a distribution system capable of assuring the timely delivery of drug supplies to all parts of the country, particularly those rural areas which are likely to be lacking in independent pharmacies. In developing countries, difficult terrain, a lack of transport vehicles, and the absence of storage facilities beyond the major urban areas are only some of the factors contributing to critical shortages of life-saving drugs in rural regions. When drug distribution is left entirely to private channels it appears that improper utilization often becomes a widespread problem associated with drug-induced illnesses as well as the development of drug resistant disease organisms.

*Recommendations:*

a) *Fees* charged for publicly procured drugs vary with national health services and sociopolitical conditions. The use of nominal fees for outpatient curative drugs may deter patients from requesting more drugs than are needed. This type of request may also be reduced by establishing a standard educational response regarding the dangers of excessive drug consumption, to be offered by the physician or other health worker during the patient's visit. In an established community health system, a drug education campaign could become the responsibility of the public health services.

b) Physicians must be made aware of the need to reduce needlessly expensive drug utilization. Information and *special training* in cost-effective prescribing techniques should be included in the curricula of medical schools and be stressed in planning for continuing medical education.

c) The *dissemination of information* on drugs as well as the establishment of utilization review procedures is the responsibility of the public health authorities. The indications, contraindications, safety hazards, and recommended dosage forms accepted by drug registration authorities (and or the formulary committee) as the basis for establishing a drug product's therapeutic value should be published in the form of an approved drug information sheet, and this information collected and published for prescribing practitioners and pharmacy workers in the form of a national drug compendium.

d) If *limited formularies* are specially designed for use in the procurement of drugs for basic health centers operated by auxiliary personnel, the formularies should be distributed with similar information on indications, contraindications, and safety precautions. Additional attention should be given to evaluating these lists so as to assure that the information is presented in a way that will be easily understood by health workers.

e) The use of a limited formulary throughout the health services that clearly shows the relationship between drugs and associated indications for use can be the basis of a system of *standardized prescribing*. Standardized prescribing would greatly facilitate the forecasting of need, the monitoring of drug utilization, and the reduction of unnecessary drug prescribing.

f) All drugs listed in the national compendium, and especially the drugs listed in the health services formulary, should be coded according to methods established in a *national drug classification system*. Coding facilitates drug utilization surveys, which can be of significant value in pointing out incorrect or over-utilization and, if used in conjunction with surveys of disease prevalence, contribute to estimations of the overall cost-effectiveness of drug utilization.

g) A *central delivery unit* should be established wherever centralized procurement methods are used for purchasing national drug supplies. This unit should develop guidelines for the distribution of drugs to regional or district units or in some cases directly to populations (e.g., preventive vaccinations). These guidelines should include specific packaging and labelling procedures, any special storage conditions required for certain drugs, particularly vaccines, methods of stocking drugs to facilitate orderly shipments and inventory control, clearly defined procedures involved in inventory control, and a method of guaranteeing planned delivery dates.

h) A well distributed number of *pharmacy workers* that are publicly certified to handle specified drugs in specified situations is clearly preferable to a much smaller number of highly trained graduate pharmacists. Technical training courses of limited duration (less than one year) should be arranged in order to increase the total number of workers capable of handling drugs in an informed fashion. To the extent that it is possible these training courses should be available on a regional basis.

#### *Some Research Questions:*

1. How can public information and education programs be developed to simultaneously reduce unnecessary demand and teach self-medication for minor illnesses?
2. Are drug labels and package inserts likely to be understood by most patients? If not, how should they be modified?
3. How might special formularies be created and used by various types of health workers?
4. How can physicians participate in a planned shift from the use of brand name drugs to generic name drugs? How can incorrect prescribing be avoided during this move?
5. Is information available about the ownership of pharmacies? What effects might ownership by either private pharmacists, doctors, the drug industry, or government have on sales practices, types of drugs in stock, personnel employed, etc.?

6. What effect might cost-sharing have on the utilization of drugs? How could the price of refills be set so as to reduce unnecessary consumption yet not discourage the continuation of therapy when it is indicated?

## *7.2 Regional and International Cooperation*

Regional agreements concerning one or more aspects of pharmaceutical production, trade, and/or quality control already exist in many areas of the world. The European Economic Community (EEC) has established a common basis for handling applications for the granting of licenses to market proprietary medicaments, as well as for their labelling. Further EEC directives involve standard protocols for the type of technical information (descriptive information and the results of testing) which should accompany license applications. Many European countries have also participated in the Pharmaceutical Inspection Convention, during which members exchange information on specific manufacturers and/or various aspects of the manufacturing of particular pharmaceutical products.

EEC directives are primarily concerned with removing obstacles to free trade between member countries. Regional efforts based upon scientific and technical cooperation were enhanced by the members of the Council of the Arab Economic Union in 1974 with the establishment of the Arab Organization for Medicaments Research and Control. Article 3 describes its tasks as:\*

- (1) examining, analysing, and controlling [pharmaceutical] raw materials and preparations imported into or manufactured in Arab countries, establishing the necessary technical requirements and/or their conformity [with such requirements], and selecting sources from which the above may be imported;
- (2) issuing certificates legalizing Arab products upon request and holding such certificates to be valid in each member state, without prejudice to the pharmaceutical legislation in force in each Arab country;
- (3) examining methods for ongoing assessment and analysis by local laboratories in Arab states and making proposals regarding the development of such methods;
- (4) training specialists and technicians in control and research laboratories in this type of work;
- (5) advising Member States on the inspection of local factories and ensuring the efficacy of imported medicaments;
- (6) examining foreign medical preparations from a legal point of view, establishing methods for their analysis, and advising Member States concerning such medicaments and whether they are suitable for registration or use;
- (7) carrying out research on medicaments with a view to utilizing national resources;
- (8) undertaking research into the development and improvement of Arab medicinal products and

\*International Digest of Health Legislation, Vol. 28, No. 1, (1977), pp. 137-138.

endeavoring to resolve manufacturing and analysis problems encountered by Arab factories.

A Resolution on Cooperation Among Developing Countries in the Production, Procurement and Distribution of Pharmaceuticals that was adopted in 1976 by the Conference of Non-Aligned Countries has yet another focus, concentrating as it does on the rationalization of procurement methods and the revision of the industrial property system with regard to pharmaceutical products. The recommendations endorsed by the Resolution include: the preparation of priority lists of pharmaceutical needs by developing countries; the curtailment of the duration of pharmaceutical patents and the elimination of brand names; the cooperative development of pharmaceutical production; and, the provision of information only from official sources. The Non-Aligned countries have also supported the development of regional centers for the transfer of technology in order to further collective self-sufficiency in pharmaceutical production. Other potential areas for regional cooperation include the collection of alternative tenders for pharmaceutical products and the evaluation of specifications for quality, safety, and manufacturing practices. The comparison of bids received might in some cases contribute to improved regional understanding of lowest probable procurement costs. The development of regional research and development resources and the construction of pilot plants are also reasonable goals for national groupings.

On a wider international scale, several branches of the United Nations have made special efforts in recent years to contribute to a better understanding of the technical and administrative aspects of pharmaceutical quality, safety, and information (WHO), to the exchange of experience and the creation of pilot plants designed to increase the productive capability of developing countries (UNIDO), and to the establishment of international codes and guidelines for pharmaceutical trade and the transfer of technology (UNCTAD).

The special tasks of WHO have included the maintenance of an international register for the reporting of adverse reactions, the creation of International Nonproprietary Names and an International Pharmacopoeia, the development of a model list of essential drugs, and expert consultation on matters of pharmaceutical safety, quality, and effectiveness.

Technical assistance offered by UNIDO has included all forms of expert consultation on production and quality control, feasibility studies on the establishment of pharmaceutical plants, and the arrangement of special meetings and seminars on the utilization of locally available medicinal plants and animal by-products for pharmaceutical production. A Pharmaceutical Center in Africa has received expert guidance from UNIDO, and the specific area of contraceptive production has been studied at the request of the U.N. Fund for Population Activities

(UNFPA). Several publications on the pharmaceutical industry are available from UNIDO.

UNICEF also participates in a number of activities relating to the supply and distribution of pharmaceuticals. UNICEF has primary responsibility for distributing emergency supplies such as drugs, chemicals for water purification, and vehicles to member states. The U.N. central supply store in Copenhagen (UNIPAC) procures supplies in bulk and repackages them in response to UNICEF program orders. Contributions of pharmaceutical production facilities and equipment have been channeled through UNICEF to several developing countries, and assistance with plans to procure and distribute pharmaceutical products is also available.

UNCTAD has sponsored several valuable studies on the transfer of pharmaceutical technology, and joined with UNIDO, WHO, and other U.N. bodies in setting up a task force to assist with the implementation of the Resolution (described earlier) adopted in 1976 by the Non-Aligned Countries. The significant contributions of the United Nations network of agencies and regional groupings in the area of pharmaceutical supply are available to all member states seeking to improve the pharmaceutical component of their health services.

Although numerous and varied problems in the areas of pharmaceutical supply and utilization remain to be solved, much is already known that could be put to good use in many parts of the world. It is within the less industrialized countries of the world, however, that the need to close the gap between already existing knowledge and its application is most urgent. The current international concern over the lack of appropriate and efficient primary health care services in many countries offers an important opportunity to deal with the issues under discussion here in more creative, forceful and, it is hoped, successful ways than has been the case in the past.

## ANNEX A

### TYPES OF ABUSE IN THE PATENT LICENSING AGREEMENTS AND REGULATORY PRACTICES IN SELECTED COUNTRIES\*

186. In view of the significant extent to which abuses or restrictive practices are to be found in licensing agreements, and in view of the instrumentalities which have been developed to safeguard public interest, considerable importance attaches to having a fairly comprehensive list of these practices, so that the main lines of action for dealing with them can be determined. The degree of prevalence, as well as the relevance of each of these practices will, of course, vary from case to case. An attempt has been made here, based on published materials and replies from 43 countries to UNCTAD questionnaires on transfer of technology (sent on 29 April 1971 and 15 June 1973), to present such a list in table 3 and to show the countries where the given practice is controlled. Since systematic work of this type has just begun,<sup>90</sup> it must be stressed that the listing of the countries and items is to be treated as provisional only.

#### 1. TERRITORIAL RESTRICTIONS ON EXPORTS

187. The following territorial restrictions on exports are frequently included in agreements involving licensees of developing countries: (a) total ban on exports; (b) prior approval by the licensor required before exports can take place; (c) prohibition of exports to certain countries; (d) exports allowed only to certain countries; and (e) requirements to channel exports through the licensor's agents.<sup>91</sup> As already indicated, export restrictions are the most common limitations imposed on licensees (see table 1).

188. Agreements involving restriction of exports affect directly and indirectly the export potential of technology-receiving countries. They are particularly relevant in view of the importance of raising the exports of manufactures from developing countries. Moreover, restrictive clauses in contractual arrangements limit the benefits that may be derived by developing countries from the generalized system of preferences and their own efforts at regional integration and economic co-operation.<sup>92</sup>

189. The new laws of transfer on technology in Argentina, Mexico, Spain and the Andean Group countries, as well as the patent law of Brazil, forbid the inclusion in licensing agreements of export restrictions. Decision 24 of the Commission of the Cartagena Agreement permits some flexibility in this area of the law but states that in no case shall clauses of this kind be accepted in respect of subregional trade or the export of similar products to third countries.

\*UNCTAD, *The role of the patent system in the transfer of technology to developing countries*, TD/B/AC.11/19/Rev. 1 (1975).

190. In the United States of America it has been held that the purchaser of a patented article in one part of the United States may resell it anywhere in the country, despite any territorial restrictions in a license agreement. Moreover, patent rights, because they are co-extensive with the geographical limits of the country, do not themselves justify agreements by licensees not to export the patented product from the country, according to decisions in Japan and the United States of America.

191. National attempts to prohibit contractual restrictions on exports would not automatically make it possible for the licensee to export the patented goods. Patent validity extends solely within the boundaries of the granting country. If the licensor has obtained a patent for the same invention in the country where the licensee intends to export, the licensor may resort to the local courts for legal remedies against the licensee for infringement. This point is taken up in BIRPI's Model Law on Inventions: section 33 of the Model Law provides that clauses which impose on the licensee restrictions that are outside the scope of the patent are null and void. The official commentary on this section states that an example of such restrictions may consist in "stipulating that the licensee will not export to certain foreign countries when exportation is not already limited because of patents existing in such countries."<sup>93</sup>

## 2. RESTRICTIONS ON OUTPUT, SALES OR PURCHASES

192. The following restrictions have been included under this subheading: limitations (i) on sources of supply of raw materials, spare parts, intermediate products, capital goods and/or competing technologies (generally called "tie-in" clauses); (ii) on the pattern of production and on sales and/or distribution.

193. The question of the adverse effects of "tie-in" clauses has been widely discussed in the literature on transfer of technology. Some of the points in this discussion may be briefly summarized here. There are at least three reasons why technology suppliers insist on tied-purchase provisions. First, where the plant in the developing country carries out main assembly operations, the foreign enterprise may wish to preserve an exclusive right to supply the necessary processed and semiprocessed inputs. Secondly, the tied-purchase clauses may be connected with the need for guaranteeing the quality of the product through the utilization of specific inputs, particularly in cases where foreign brand names and trade marks are involved. Thirdly, the foreign enterprise may also use such provisions as a means of enlarging its profit margin. While there may, in some cases, be a justification on technical grounds for the first two kinds of tying, no such justification exists for the third kind. As discussed in the following paragraph, the adverse effects of the third kind are so important that the "tie-in" provisions of the first two types should be examined very carefully to ensure their legitimate justification. And even then the necessary justification and the quantities and amounts involved should be

specifically stated in the contracts.

194. Most of the goods that are currently produced or planned for production in the developing countries are available on the world market from several sources, and potential purchasers of these products in the developing countries can buy them at world market prices. But when contractual agreements tie part or all of the inputs to a single source of supply, developing countries are deprived of the possibility of exploiting market opportunities and are faced with a price structure determined by the unique supplier. Tied-purchase provisions thus result in a monopoly control of the supply of equipment and other inputs by foreign enterprises, leading to what has come to be known as "transfer pricing," "transfer account" or "uneconomic output."

195. By reason of his exclusive position, the supplier is able to charge higher prices<sup>94</sup> than for comparable equipment and other inputs that could otherwise be obtained elsewhere. Overpricing of inputs in this way constitutes a "hidden cost" of the transfer of technology which is much the same as that of aid-tying.

196. Tied-purchase clauses connected with the transfer of technology not only affect production costs through the overpricing of inputs but may have important indirect effects on the import substitution, export diversification and growth efforts of developing countries. When the source of supply is determined by the supplier, rather than by the receiver, of technology, a bias in favor of imports is only to be expected. Furthermore, since the imported technology itself originates in a developed country it is usually ill adapted to factor endowments and the availability of domestic resources in developing countries. Both these factors contribute to raising costs of production in developing countries and rendering the resulting product less competitive in world markets. The high cost of imported technology and inputs imposes a heavy burden on the balance of payments of developing countries. Together with reduced export possibilities, this affects adversely the rate of growth of the economy by preventing backward and forward linkages.<sup>95</sup>

### 3. ABUSES RELATED TO FINANCIAL PROVISIONS

#### (a) Payments for unused patents

197. Article 20 of decision 24 of the Commission of the Cartagena Agreement considers that clauses requiring the payment of royalties to patentees in respect of unexploited patents are of an abusive nature. In order to receive governmental approval for patent license agreements, it is necessary, in Brazil, to prove that the licensee is, in fact, exploiting the patented invention, and that the patent is not a mere fiction in the contract, designed to justify the payment of royalties.<sup>96</sup>

198. In Japan, the Federal Republic of Germany and the United States of America, the requirements of the payment of royalties by a licensee

covering patents which he is not using is not in itself objectionable. However, where a patentee coerces a licensee to accept a license under one patent on condition that the licensee accept licenses under another patent or a whole package of patents, the scheme may be attacked as beyond the grant of the patent monopoly and as a violation of the anti-trust law.<sup>97</sup>

#### (b) Package licenses

199. Package licensing, that is, the licensing of several of the licensor's patents or subjects of know-how imposed upon the licensee as a condition for obtaining the license, is a common practice in international licensing. Recent legislation in Spain regards package licenses as an abuse not to be permitted in licensing agreements. In the United States of America package licenses may constitute an anti-trust violation where the package is coercively imposed by the licensor on the licensee, rather than freely embraced by both parties for purposes of convenience.<sup>98</sup>

#### (c) Long terms of enforcement

200. The practice through which royalty payments have to be paid during the entire duration of the manufacture of a patented product or the application of a patented process involved in a patent license without any specification of time is unlawful per se, being against the nature of the patent grant. Patent grants are basically temporal, and the corresponding license agreement cannot extend beyond the temporal constraints of the patent. However, it is necessary to bear in mind that where a patent is linked to know-how the patent constraints do not apply automatically to the know-how. Under the Mexican law, an agreement containing an excessively long term of enforcement is not accepted. The law states that in no case may these terms exceed a ten-year obligation on the importer company.<sup>99</sup> The recent Spanish legislation adopts a similar position against long-term undertakings.<sup>100</sup> In India, according to the "Guidelines: policies and procedures concerning foreign collaboration agreements" (January, 1969), royalty payments should normally be restricted to a period of five years from the date of commencement of production, provided production is not delayed beyond two years from the signing of the agreements (i.e. a maximum period of seven years from signing of agreement).

#### (d) Price fixing and excessive prices

201. Price fixing, as shown in table 3, has been considered by all recent laws as an unlawful practice. Some of these laws also control practices by which excessive prices are charged for the technology transferred. The Mexican law provides that a contract shall not be registered "when the

price or counter-service is out of proportion to the technology acquired or constitutes an unwarranted or excessive burden on the country's economy."<sup>101</sup>

202. The United States of America's position on the subject is that the fixing of prices within the United States by agreement generally constitutes a per se violation of the anti-trust laws.<sup>102</sup> Under the Japanese law, clauses restricting resale prices of patented goods in Japan may be treated as unfair business practices.<sup>103</sup>

(e) Improper or discriminatory royalties

203. Improper or discriminatory royalties or prices may constitute an abuse of patent right. Under the United States law, the improper formulation or imposition of royalties in a license agreement is a ground for application of the patent misuse doctrine and a possible violation of anti-trust legislation. The reasoning is that a patent cannot be used to exercise leverage on a licensee so as to extract compensation from him in areas outside the licensed subject matters.<sup>104</sup>

#### 4. LIMITATIONS AFFECTING THE ECONOMY IN GENERAL (THE DYNAMIC EFFECTS OF THE TRANSFER)

(a) Limitations on the field of use of the technology

204. Limitations on the field of use take place when a licensor grants a license for a limited or restricted use of the patented subject matter, declining to license all the other uses of the invention and reserving some uses of the invention for self-exploitation, or exploitation by other licensees. These restrictions may be considered as within the rights conferred by the law on the patent holder. Section 33(2) of the BIRPI Model Law considers limitations concerning the degree of exploitation of the subject of the patent as within such rights. The Japanese Guidelines also adopt a similar position.<sup>105</sup> Under the United States law, restrictions of this kind placed on a purchasing licensee are illegal per se; however, restrictions placed on manufacturing licensees are sometimes considered legal.<sup>106</sup>

(b) Grant-back provisions

205. Grant-back provisions are inadmissible when they in practice establish a unilateral flow of knowledge and innovations for the sole benefit of the licensor. Section 29 of the Brazilian law provides that "all rights to improvements made by the licensee to the product or process shall belong to him."<sup>107</sup> Under the EEC rules, a grant-back clause is not considered a restrictive practice, provided the undertakings are not

exclusive and the licensor has entered into similar undertakings.<sup>108</sup>

206. Under the antimonopoly laws of the United States of America, grant-back arrangements are not necessarily invalid but depend on the mode of operation, the importance of the improvements and the effect on competition. Since improvements come later, it is difficult to know at the inception of the agreement whether these problems will arise later or not. The rule is that grant-back provisions are not invalid if they operate to encourage invention and ensure that any improvements are made available without discrimination and on reasonable terms. Schemes intended to result in putting the patentee in a dominant position and which are used to lessen competition are, however, considered invalid.<sup>109</sup>

207. Collaboration agreements on the exchange of information and new improvements related to the subject of the agreement make sense between equal parties. Where these agreements are entered into by enterprises from developing countries, grant-back provisions should be evaluated from the standpoint of improving the technological capabilities of these countries and avoiding the perpetuation of technological dependence.

#### (c) Other limitations

208. Other limitations on the dynamic effects of the transfer of technology may include, as shown in table 3: designation by the licensor of staff to be used by the licensee; limitations on research by the licensee; and limitations on management by the licensee. These three limitations are considered invalid in the recent laws of Mexico, the Andean Group countries, and Spain.

### 5. POST-EXPIRATION EFFECTS

209. A patent license cannot survive the life of the patent<sup>110</sup> covered by the agreement. The expiration of the patent on an invention means that the invention falls into the public domain and no legal basis remains for the patent licensing agreement. However, clauses are often included in license agreements by which the contract continues to be effective after its expiration or after the patent has expired. Clauses of this type that are abusive include:

(a) Limitations on or payment for the use of a patented invention even after the patent has expired;

(b) Achieving the same result by means of limitations on or payment for the use of related know-how included in the license agreement even after the agreement has ended.<sup>111</sup>

210. In the United States of America, the Supreme Court has held the imposition of a royalty obligation for post-expiration use of a machine covered by a patent was an unlawful effort by the patentee to extend the terms of his monopoly beyond that granted by the law.<sup>112</sup> The patent

statutes of New Zealand and South Africa also provide that any contract for the payment of royalties after the term of the patent expires can be rendered void at the option of either party. "The justification advanced for this legislative provision is that such a contractual arrangement is not within the boundaries of the monopoly granted by the patent."<sup>113</sup> In the United Kingdom, section 58(1) of the Patent Act provides that when all original patents have ceased to be in force, the licensee may terminate the license notwithstanding anything in the license to the contrary.

## 6. OTHER PRACTICES

211. Table 3 lists under this heading the following practices: (a) provisions not to contest the validity of patents; (b) imposing as the authentic text of the agreement one in a different language from that of the licensee's country—a practice deemed to be unlawful under the Spanish law; (c) provisions that a law or a jurisdiction chosen by the licensor should govern the agreement and decide disputes arising from its interpretation or implementation.

212. In a recent decision of the Supreme Court of the United States of America it was held that the licensee is not prevented from contesting the validity of the patent and that while challenging such validity he is not required to continue to pay royalties.<sup>114</sup>

## D. CONCLUSIONS

213. The preceding description of abuses of patent monopoly in licensing agreements has drawn attention to the variety of practices that are followed and to the wide extent to which they are included in contractual arrangements, particularly ones with enterprises in the developing countries. A number of studies at the national, regional and international levels have underlined the need for instituting safeguards against such abuses.

214. The legal and regulatory instrumentalities employed to counteract or prohibit such abuses are different from country to country; and interpretation of antimonopoly laws has a complex and not always clear history, particularly in the United States of America. But the underlying intent of these instrumentalities, be they earlier laws in the developed countries or more recent integrated approaches in some of the developing countries, is similar in that these instrumentalities all aim at safeguarding public interest against monopolistic practices through control or elimination of these abuses.

215. The Paris Convention for the Protection of Industrial Property from its very inception was concerned with "the repression of unfair competition" (article 1(2)).

216. It is against this background that the need for urgent action expressed in paragraph 37 of the International Development Strategy for the Second United Nations Development Decade<sup>115</sup>—coming 87 years

after the adoption of the Paris Convention—has to be appreciated. The paragraph states:

Restrictive business practices particularly affecting the trade and development of the developing countries will be identified with a view to the consideration of appropriate remedial measures, the aim being to reach concrete and significant results early in the Decade. Efforts will be made with a view to achieving these results before 31 December 1972.

217. Since the adoption of the Strategy on 24 October 1970—commemorating the twenty-fifth anniversary of the United Nations—it has not yet proved possible for the international community to achieve “concrete and significant results.”

218. Two subsequent developments have served to underline the importance of initiating the necessary action. In March 1973, a Group of Experts convened by UNCTAD<sup>116</sup> considered and identified some restrictive business practices which adversely affect the trade and development of developing countries. The Group adopted a twofold classification of practices: category A, where the restrictions, on the basis of knowledge and past experience, are likely to have significantly adverse effects, whether in developed or developing countries; and category B, where the adverse effects are less clear and may be offset by corresponding advantages and where, therefore, more complete analysis is required.

219. The second development concerns a recommendation of the Council of OECD, adopted on 22 January 1974. This recommendation concerns action against restrictive business practices relating to the use of patents and is very relevant to the present stage of discussion of the subject; its operative paragraphs may be quoted in full:

Recommends to the Governments of member countries:

1. That they should be particularly alert to harmful effects on national and international trade which may result from abusive practices in which patentees and their licensees may engage, and in particular, from the following:

(a) when negotiating or operating patent pools or cross-licensing agreements, unjustifiably imposing territorial, quantity or price restrictions or attempting to dominate an industry, market or new industrial process;

(b) by means of territorial restrictions in patent licenses affecting international trade, unjustifiably prohibiting exports of patented products or unjustifiably restricting trade in or exports of the patented products to specified areas;

(c) by means of clauses concerning tied sales, obliging the licensee to obtain goods from the licensor or his designated sources, when the tied sales are not justified, for instance, by technical reasons concerning the quality of the goods manufactured under the license;

(d) by means of grant-back clauses, unjustifiably requiring the licensee

to assign or grant back to the licensor exclusively all improvements discovered in working the patents when the effect of this practice is to reinforce the dominant position of the licensor or to stifle the licensee's incentive to invent;

(e) by means of clauses unjustifiably limiting competition, preventing one or more parties to the patent licensing contract from competing with others parties to the contract, or with third persons, in other industrial fields not covered by the licensed patent;

(f) arbitrary grouping and licensing all patents in a particular field and refusing to grant licenses for only some of the patents or using other forms of package licensing when these practices are coercive in character and when the selection of the patents is not negotiated for the convenience of the parties;

(g) contrary to national law, fixing the prices of patented products by means of patent licenses.

2. That they should give consideration to the desirability and feasibility of compulsory licensing of patents and, where possible, related know-how as a remedy to restore competition where such patents have been misused contrary to their restrictive business practice laws, when such a remedy is not already provided for in their legislation.

3. That they should give consideration to the desirability and feasibility of making available to the competent authorities procedures for the registration of international licensing agreements, when such procedures are not already provided for in their legislation.

220. With the developments summarized above, the stage is now plainly set for moving rapidly towards evolving an internationally acceptable set of standards for safeguarding the public interest against the abusive practices discussed in this chapter.

TABLE 3

Countries where certain practices in patent licence agreements  
are considered as abuses or otherwise controlled

<i>Types of abusive practice</i>	<i>Countries exercising control</i>
<i>Territorial restrictions on exports</i>	
1. Territorial restrictions on exports	Andean Group countries, Argentina, Brazil, Japan, Mexico, Spain
<i>Restrictions on purchases, output or sales</i>	
2. On sources of supply of raw materials, spare parts, intermediate products, capital goods, and/or competing technologies	Andean Group countries, Argentina, Australia, Brazil, EEC, India, Ireland, Japan, Malawi, Mexico, New Zealand, Spain, United Kingdom, United States of America, Zambia
3. On pattern of production	Andean Group countries, Japan, Mexico, Spain
4. On sales and/or distribution	Andean Group countries, Brazil, Japan, Mexico, Spain, United States of America
<i>Financial provisions</i>	
5. Payments for unused patents	Andean Group countries
6. Package licensing	Spain, United States of America
7. Payment of royalties during the entire duration of manufacture of a product, or the application of the process involved without any specification of time, or excessively long terms of enforcement	Mexico, Spain
8. Price fixing	Andean Group countries, Argentina, Japan, Mexico, Spain, United States of America
9. Excessive prices	Argentina, Mexico, Spain
10. Improper or discriminatory royalties	United States of America
11. To transform royalties or fees into capital stock	Andean Group countries
<i>Post-expiration effects</i>	
12. Limitations on use of patented inventions or related know-how once patent has expired or after termination of agreement and/or charging royalties	India, Malawi, New Zealand, Spain, United Kingdom, United States of America, Zambia
<i>Limitations affecting the economy in general (dynamic effects of the transfer)</i>	
13. Limitations on field of use	United States of America
14. To use staff designated by licensor	Andean Group countries, Mexico
15. Absence of provisions regarding training of national personnel	
16. Grant-back provisions	Andean Group countries, Argentina, Brazil, Japan, Mexico, Spain, United States of America
17. Limitations on the research or technological development of licensee	Mexico, Spain
18. Limitations imposed on the management of the licensee	Mexico, Spain
<i>Other practices</i>	
19. Not to contest validity of patents	United States of America
20. Authentic text of contract in foreign language	Argentina, Spain
21. Foreign law governing agreement	Mexico
22. Foreign jurisdiction in settlement of disputes arising from agreement	Andean Group countries, Argentina, Mexico

Source: National legislation as indicated in replies to the UNCTAD secretariat's questionnaire (cf. para. 124 above).

## FOOTNOTES

90. For details, see *Major issues arising from the transfer of technology to developing countries* (op. cit.); "Major issues arising from the transfer of technology: a case study of Chile" (TD/B/AC.11/21); *Idem*: a case study of Spain (TD/B/AC.11/17); *Restrictive Business Practices* (op. cit.); *Restrictions on exports in foreign collaboration agreements in the Republic of the Philippines* (op. cit.); *Restrictions on exports in foreign collaboration agreements in India* (op. cit.); *Restrictive Business Practices: Studies on the United Kingdom of Great Britain and Northern Ireland, the United States of America and Japan* (United Nations publication, Sales No. E.73.11.D.8); *Restrictive Business Practices in Relation to the Trade and Development of Developing Countries; Report by the Ad Hoc Group of Experts* (United Nations publication, Sales No. E.74.11.D.11); OECD, *Restrictive Business Practices Relating to Patents and Licenses...* (op. cit.).
91. Not all export restrictions take the form of territorial constraints. Their purpose can also be achieved through other practices, or through a combination of some of the practices listed in table 3. For other practices directed to the same objective, see *Restrictive Business Practices: Interim Report by the UNCTAD Secretariat* (United Nations publication, Sales No. E.72.11.D.10), para. 92.
92. See *Major issues arising from the transfer of technology to developing countries* (op. cit.), para. 67.
93. *Model Law for Developing Countries on Inventions* (BIRPI publication No. 801 (E)), Geneva, 1965, p. 56.
94. For an analysis on costs and overpricing, see paragraphs 370-378. Tying of aid has a similar effect on raising the cost of items and services imported for the project.
95. For further analysis of these effects, see *Major issues arising from the transfer of technology to developing countries* (op. cit.), paras. 44-52.
96. See *The role of patents in the transfer of technology to developing countries* (op. cit.), paras. 163 and 224.
97. *Ibid.*, para. 152.
98. See M.R. Joelson, "International technology transfer and the United States antitrust laws", *The Journal of International Law and Economics*, vol. VIII, No. 2 (June 1973), pp. 102-103.
99. See the Mexican law on the transfer of technology (cf. footnote 73 above).
100. See TD/B/AC.11/17, annex I.
101. Cf. article 7 of the Mexican law (cf. footnote 73 above).
102. See M.R. Joelson, *loc. cit.*, p. 96.
103. See "Antimonopoly Act Guidelines for International Licensing Agreement of Government of Japan," Staff Office of the Fair Trade Commission of the Government of Japan, reproduced in *Restrictive Business Practices* (op. cit.), p. 49, annex II.
104. See M.R. Joelson, *loc. cit.*, p. 105.
105. See footnote 103.
106. See M.R. Joelson, *loc. cit.*
107. *Brazil, Industrial Property Code (Decree Law No. 1005 of 21 October 1969)*. See *WIPO, Industrial Property*, 9th year, No. 7 (July 1970), p. 221.
108. EEC, "Notice on patent licensing agreements," *Official Journal of the European Communities* No. 139 (27 December 1962), p. 2922, reproduced in *Competition Law in the European Economic Community and in the European Coal and Steel Community*, published by the European Communities, Brussels-Luxembourg, 1972.

109. See L.W. Melville, *Precedents on Intellectual Property and International Licensing* (London, Sweet and Maxwell, 1972), p. 21.
110. See paras. 358-359, on extension of the patent duration.
111. However, restrictions in know-how agreements on the use of the know-how after the agreement has ended are normally regarded as valid, particularly in the case of the early termination of the agreement by reason of the default of one party.
112. See M.R. Joelson, *loc. cit.*, p. 105.
113. See *The role of patents in the transfer of technology to the developing countries (op. cit.)*; para. 130.
114. See *Lear, Incorporated v. Adkins*, No. 56, Decided by the Supreme Court on 16 June 1969, 162 USPQ 1.
115. The text of the International Development Strategy is contained in General Assembly, resolution 2626 (XXV).
116. See *Restrictive Business Practices in Relation to the Trade and Development of Developing Countries: Report by the Ad Hoc Group of Experts* (United Nations publication, Sales No. E.74.II.D.11).

## ANNEX B

### MODEL LIST OF ESSENTIAL DRUGS <sup>a</sup> 1]

Complementary <sup>b</sup>

#### Anaesthetics

##### *General anaesthetics*

ether, anaesthetic (2)  
halothane (2)  
nitrous oxide (2)  
thiopental sodium (2)

##### *Local anaesthetics*

bupivacaine (2, 9)  
lidocaine

#### Analgesics, antipyretics, nonsteroidal anti-inflammatory drugs and antigout drugs

acetylsalicylic acid  
allopurinol (6)  
ibuprofen (1)  
indometacin  
paracetamol  
colchicine (7)

---

<sup>a</sup> Numbers in parentheses following the drug names indicate :

- (1) Listed as an example of this therapeutic category : choose cheapest effective drug product acceptable ;
- (2) Specific expertise, diagnostic precision or special equipment required for proper use ;
- (3) Greater potency ;
- (4) Dosage adjustment necessary for renal insufficiency ;
- (5) To improve compliance ;
- (6) Best pharmacokinetic parameters for purpose ;
- (7) Adverse effects diminish benefit/risk ratio ;
- (8) Limited indications or narrow spectrum of activity ;
- (9) For epidural anaesthesia ;
- (10) For disease or organisms resistant to the proposed drug(s).

<sup>b</sup> Drugs under this heading are not essential. They are added as examples of drugs that provide (a) alternatives when infectious organisms develop resistance to essential drugs, (b) treatment in rare disorders, and (c) special pharmacokinetic properties, etc. : they should be available as funds permit.

1] The Selection of Essential Drugs, WHO Technical Report Series, No. 615, 1977.

**Analgesics, narcotics and narcotic antagonists** *Complementary*

morphine  
naloxone

pethidine (1)

**Antiallergics**

*Antihistamines*

chlorphenamine (1)

**Antidotes, chelating agents, etc.**

atropine  
calcium disodium edetate (2)  
charcoal, activated  
dimercaprol (2)  
pralidoxime

**Antiepileptics**

diazepam injection  
ethosuximide  
phenobarbital  
phenytoin

carbamazepine (10)

**Antiinfective drugs <sup>a</sup>**

*Anthelmintic drugs*

mebendazole  
niclosamide  
piperazine  
tiabendazole

bephenium (8)  
tetrachloroethylene

---

<sup>a</sup> In its decisions about drugs listed in certain therapeutic classes—anthelmintics, antifilarials, antileptotics, antimalarials, antitrypanosomals, and antischistosomals—the Expert Committee referred to the corresponding WHO publications (see section 12: Bibliography). No evaluation has been made of the newer drugs at present being used in research programmes coordinated by WHO.

*Antibacterial drugs*

ampicillin (1)  
benzathine benzylpenicillin (5)  
benzylpenicillin  
  
chloramphenicol (7)  
cloxacillin (penicillinase-resistant, 1)  
erythromycin  
gentamicin (4)  
phenoxymethylpenicillin  
salazosulfapyridine  
sulfadimidine (1)  
sulfamethoxazole + trimethoprim  
tetracycline (1, 4)

*Antifilarial drugs*

diethylcarbamazine  
suramin

*Antileprotic drugs*

dapsone

*Antiprotozoal drugs*

*Amoebicides*

metronidazole

*Antimalarials*

chloroquine  
primaquine  
pyrimethamine  
quinine

*Antischistosomes*

metrifonate  
niridazole  
oxamniquine

*Complementary*

amikacin (1, 4, 10)  
doxycycline (6, 5)  
procaine benzyl-  
penicillin (7)  
sulfadiazine (7, 8)

clofazimine (10)  
rifampicin (10)

diloxanide  
emetine (7)  
paromomycin

amodiaquine (10)  
sulfadoxine (10)

stibocaptate (10)

*Complementary*

*Antitrypanosomals*

melarsoprol (5)  
nifurtimox  
pentamidine (5)  
suramin

*Leishmaniacides*

pentamidine  
sodium stibogluconate

*Antituberculosis drugs*

ethambutol  
isoniazid  
rifampicin  
streptomycin

thioacetazone

*Systemic antifungal drugs*

amphotericin B  
griseofulvin (8)

flucytosine (1, 8)

**Antimigraine drugs**

ergotamine

**Antineoplastic drugs**

busulfan (2)  
chlormethine (1, 2)  
cyclophosphamide (2)  
doxorubicin (2)  
fluorouracil (2)  
methotrexate (2)  
vincristine (2)

**Antiparkinsonism drugs**

levodopa

levodopa + peripheral  
decarboxylase  
inhibitor (6, 5)

trihexyphenidyl (1)

**Blood and haematopoietic system drugs**

*Antianaemia drugs*

cyanocobalamin (2)

ferrous salt (1)

folic acid (2)

*Anticoagulants and antagonists*

heparin (2)

phytomenadione

protamine sulfate (2)

warfarin (1, 2, 6)

*Plasma substitute*

dextran 40

iron dextran  
injection (5)

**Cardiovascular drugs**

*Antianginal drugs*

glyceryl trinitrate

isosorbide dinitrate (1)

propranolol (1)

*Antiarrhythmic drugs*

lidocaine

procainamide

propranolol (1)

quinidine

*Antihypertensive drugs*

diazoxide injection (1)

guanethidine

hydralazine

hydrochlorothiazide (1)

propranolol (1)

methyldopa (7)  
phenolamine (1, 2, 8)  
reserpine (7)

*Cardiac glycosides*

digoxin (4)

digitoxin

*Drugs used in shock*

dopamine (2)

isoprenaline injection

*Complementary*

**Dermatological preparations**

*Topical*

*Antiinfective*

iodine (1)

neomycin + bacitracin

*Antiinflammatory drugs*

betamethasone (1, 3)

hydrocortisone

*Astringents*

aluminium acetate

*Fungicides*

miconazole (1)

nystatin

*Keratoplastic agents*

benzoic acid + salicylic acid

coal tar

podophyllin (7, 8)

*Scabicides and pediculicides*

gamma benzene hexachloride

benzyl benzoate

**Diagnostic agents**

edrophonium (2, 8)

tuberculin, purified protein  
derivative (PPD)

*Radiocontrast media*

adipiodone meglumine (1)

barium sulfate (1)

iopanoic acid (1)

meglumine amidotrizoate (1)

sodium amidotrizoate (1)

*Complementary*

**Diuretics**

furosemide  
hydrochlorothiazide (1)  
mannitol  
spironolactone

chlortalidone (6)  
triamterenc (1)

**Gastrointestinal drugs**

*Antacids*

aluminium hydroxide and/or magnesium hydroxide

*Antiemetics*

promethazine (1)

*Antihaemorrhoidals*

local anaesthetic, astringent, and antiinflammatory drug (1)

*Antispasmodics*

atropine (1)

*Cathartics*

senna (1)

*Diarrhoea*

*Antidiarrhoeal*

codeine

*Replacement solution*

oral rehydration salts (for glucose-salt solution for oral use)

For 1 litre of water :

sodium chloride (table salt)	3.5 g	Na <sup>+</sup>	90
sodium bicarbonate (baking soda)	2.5 g	HCO <sub>3</sub> <sup>-</sup>	30
potassium chloride	1.5 g	K <sup>+</sup>	20
glucose (dextrose)	20.0 g	glucose	111

## Hormones

## Complementary

### *Adrenal hormones and synthetic substitutes*

dexamethasone (long-acting) (1)  
hydrocortisone  
prednisolone

fludrocortisone

### *Androgens*

testosterone ester injection (2)

### *Estrogens*

ethinylestradiol (1)

### *Insulins*

compound insulin zinc suspension  
(lente) (1)  
insulin injection

### *Oral contraceptives*

norethisterone + ethinylestradiol (1)

### *Progestogens*

norethisterone (1)

### *Thyroid hormones and antagonists*

levothyroxine  
potassium iodide  
propylthiouracil (1)

## Immunologicals

### *Sera and immunoglobulins*

anti-D immunoglobulin  
antirabies hyperimmune serum  
diphtheria antitoxin  
immunoglobulin, normal human (2)  
snake antivenom  
tetanus antitoxin

*Vaccines*

BCG vaccine  
diphtheria–tetanus vaccine  
diphtheria–pertussis–tetanus vaccine  
measles vaccine  
poliovirus vaccine  
rabies vaccine  
smallpox vaccine  
tetanus vaccine  
typhoid vaccine

**Muscle relaxants (peripherally acting)  
and antagonists**

neostigmine  
suxamethonium (2)  
tubocurarine (1,2)

pyridostigmine (2, 8)

**Ophthalmological preparations**

*Topical*

*Antiinfective*

silver nitrate  
sulfacetamide  
tetracycline (1)

*Antiinflammatory*

hydrocortisone (2, 7)

*Local anaesthetics*

tetracaine (1)

*Miotics*

pilocarpine

*Mydriatics*

homatropine (1)

*Systemic*

acetazolamide

**Oxytocics**

ergometrine (1)  
oxytocin

**Peritoneal dialysis solution**

intraperitoneal dialysis solution  
(1.5% glucose)

**Psychotherapeutic drugs**

amitriptyline (1)  
chlorpromazine (1)  
diazepam (1)  
fluphenazine decanoate (1, 5)  
haloperidol (1)  
lithium carbonate (2, 4, 7)

**Respiratory tract, drugs acting on the**

*Antiasthmatic drugs*

aminophylline (1)  
epinephrine  
salbutamol (1)

ephedrine

*Antitussives*

codeine

**Solutions correcting water, electrolyte,  
and acid-base disturbances**

glucose (5% and 50%)  
oral rehydration salts (for glucose-salt  
solution for oral use) (see composition  
under **Gastrointestinal drugs**)  
potassium chloride injection (15%)  
and oral solution  
sodium bicarbonate (7.5%)  
sodium chloride injection (0.9%)  
sodium lactate compound injection  
water for injection

**Vitamins and minerals**

ascorbic acid

calcium gluconate (2)

ergocalciferol

hexavitamin : retinol, ergocalciferol,  
ascorbic acid, thiamine, riboflavin  
and nicotinamide

pyridoxine

retinol

## ALPHABETICAL LIST OF ESSENTIAL AND COMPLEMENTARY DRUGS \*

- |  |   |
|--|---|
| <p>acetazolamide<br/>acetylsalicylic acid<br/>adipiodone meglumine<br/>allopurinol<br/>aluminium acetate<br/>aluminium hydroxide and/or<br/>magnesium hydroxide<br/>amikacin *<br/>aminophylline<br/>amitriptyline<br/>amodiaquine *<br/>amphotericin B<br/>ampicillin<br/>anti-D immunoglobulin<br/>antihaemorrhoidal preparation : local<br/>anaesthetic, astringent and<br/>antiinflammatory drug<br/>antirabies hyperimmune serum<br/>ascorbic acid<br/>atropine</p> <p>bacitracin -I- neomycin<br/>barium sulfate<br/>BCG vaccine<br/>benzathine benzylpenicillin<br/>benzoic + salicylic acid<br/>benzyl benzoate *<br/>benzylpenicillin<br/>bephenium *<br/>betamethasone<br/>bupivacaine<br/>busulfan</p> <p>calcium disodium edetate<br/>calcium gluconate<br/>carbamazepine *<br/>charcoal, activated<br/>chloramphenicol<br/>chlormethine<br/>chloroquine<br/>chlorphenamine<br/>chlorpromazine<br/>chlortalidone *<br/>clofazimine *</p> | <p>cloxacillin (penicillinase-resistant)<br/>coal tar<br/>codeine<br/>colchicine *<br/>compound insulin zinc suspension<br/>(lente)<br/>cyanocobalamin<br/>cyclophosphamide</p> <p>dapsone<br/>dexamethasone (long-acting)<br/>dextran 40<br/>diazepam<br/>diazepam injection<br/>diazoxide injection<br/>diethylcarbamazine<br/>digitoxin *<br/>digoxin<br/>diloxanide *<br/>dimercaprol<br/>diphtheria antitoxin<br/>diphtheria-tetanus vaccine<br/>diphtheria-pertussis-tetanus vaccine<br/>dopamine<br/>doxorubicin<br/>doxycycline *</p> <p>edrophonium<br/>emetine *<br/>ephedrine *<br/>epinephrine<br/>ergocalciferol<br/>ergotamine<br/>ergometrine<br/>erythromycin<br/>ethambutol<br/>ether, anaesthetic<br/>ethinylestradiol<br/>ethinylestradiol + norethisterone<br/>ethosuximide</p> <p>ferrous salt<br/>flucytosine *<br/>fludrocortisone *</p> |
|--|---|

---

\* = complementary drug.

fluorouracil  
fluphenazine decanoate  
folic acid  
furosemide

gamma benzene hexachloride  
gentamicin  
glucose (5% and 50%)  
glyceryl trinitrate  
griseofulvin  
guanethidine

haloperidol  
halothane  
heparin  
hexavitamin : retinol, ergocalciferol,  
ascorbic acid, thiamine, riboflavin  
and nicotinamide  
homatropine  
hydralazine  
hydrochlorothiazide  
hydrocortisone

ibuprofen  
immunoglobulin, human normal  
indometacin  
insulin injection  
intraperitoneal dialysis solution  
(1.5% glucose)  
iodine  
ioganoic acid  
iron dextran injection \*  
isoniazid  
isoprenaline injection \*  
isosorbide dinitrate

levodopa  
levodopa + peripheral decarboxylase  
inhibitor \*  
levothyroxine  
lidocaine  
lithium carbonate

mannitol  
measles vaccine  
mebendazole  
megiumine amidotrizoate

melarsoprol  
methotrexate  
methyldopa \*  
metrifonate  
metronidazole  
miconazole  
morphine

naloxone  
neomycin + bacitracin  
neostigmine  
niclosamide  
nifurtimox  
niridazole  
nitrous oxide  
norethisterone  
norethisterone + ethinylestradiol  
nystatin

oral rehydration salts (for glucose-salt  
solution for oral use)  
oxamniquine  
oxytocin

paracetamol  
paromomycin \*  
pentamidine  
pethidine \*  
phenobarbital  
phenoxymethylpenicillin  
phenolamine \*  
phenytoin  
phytomenadione  
pilocarpine  
piperazine  
podophyllin \*  
poliovirus vaccine  
potassium chloride injection (15%)  
and oral solution  
potassium iodide  
pralidoxime  
prednisolone  
primaquine  
procainamide  
procaine benzylpenicillin \*  
promethazine  
propranolol  
propylthiouracil

\* = complementary drug.

protamine sulfate  
pyridostigmine \*  
pyridoxine  
pyrimethamine

quinine  
quinidine

rabies vaccine  
reserpine \*  
retinol  
rifampicin

salazosulfapyridine  
salbutamol  
senna  
silver nitrate  
smallpox vaccine  
snake antivenom  
sodium amidotrizoate  
sodium bicarbonate  
sodium chloride injection  
sodium lactate compound injection  
sodium stibogluconate  
spironolactone  
streptomycin  
stibocaptate \*

sulfacetamide  
sulfadiazine \*  
sulfadimidine  
sulfadoxine \*  
sulfamethoxazole + trimethoprim  
suramin  
suxamethonium.

testosterone ester injection  
tetanus antitoxin  
tetanus vaccine  
tetracaine  
tetrachlorethylene \*  
tetracycline  
thioacetazone \*  
thiopental sodium  
tiabendazole  
triamterene \*  
trihexyphenidyl  
trimethoprim + sulfamethoxazole  
tuberculin, purified protein derivative  
tubocurarine  
typhoid vaccine

vincristine

warfarin  
water for injection

---

\* = complementary drug.

**ANNEX C**  
**GLOSSARY OF TERMS**

1. **Antisubstitution laws**                      Laws which require the pharmacist to dispense the pharmaceutical product specified in the prescription. If the product is written under a brand name, that product must be dispensed. If it is written under its generic name the pharmacist may dispense a less expensive, chemically equivalent pharmaceutical product.
2. **Benefit/risk ratio\***                      The ratio of benefit of risk in a drug; a means of expressing a judgment concerning the role of a drug in the practice of medicine, based on efficacy and safety data along with consideration of misuse potential, severity and prognosis of the disease, etc. The concept may be applied to a single drug or in comparisons between two or more drugs used for the same indications.
3. **Bioavailability\***                      The rate and extent of absorption of a drug from a dosage form as determined by its concentration/time curve in the systemic circulation or by its excretion in urine.
4. **Biological equivalents**                      Chemical equivalent drugs which, when administered in the same amounts, will provide essentially the same biological or physiological availability, as measured by blood levels, etc.
5. **Branded generics**                      Pharmaceutical products sold under their generic name which retain a clear identification of the manufacturer on the label.
6. **Brand name**                      The registered trademark name given to a specific drug product by its manufacturer.
7. **Chemical equivalents**                      Multiple source drug products which contain essentially identical amounts of the identical active ingredients, in identical dosage forms, and which meet existing physicochemical standards in the official compendia.

8. Combination drug      A pharmaceutical product containing more than one drug along with other substances included during the manufacturing process.
9. Detail men      Pharmaceutical company sales representatives who are responsible for visiting prescribing practitioners and health administrators responsible for drug procurements in order to promote their companies' products. Detail men are not required to have any specific technical education, although they are trained to inform prospective buyers about the potential benefits of their products.
10. Dosage form.\*      The form of the completed pharmaceutical product, e.g., tablet, capsule, elixir, suppository.
11. Drug\*      Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the patient.
12. Drug formulation\*      The composition of a dosage form, including the characteristics of its raw materials and the operations required to process it.
13. Drug utilization\*      The marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.
14. Efficacy\*      The ability of a drug to produce the purported effect as determined by scientific methods.
15. Formulary      A list of approved or recommended drugs compiled by an individual practitioner or a group of medical and scientific professionals for a specific medical unit, or for a health, social security, or insurance plan system in order to specify those products for which reimbursement will be allowed.
16. Generic name      The official name given to a drug or drug product. After a patent has expired any

manufacturer may market a drug under its generic name.

17. Me-too or duplicative drug A new drug, often made by means of molecular manipulation, which offers no significant therapeutic advantage over a related drug already on the market.
18. Molecular manipulation A minor modification in the molecular structure of a chemical, yielding a new and patentable product which may not offer a significant therapeutic advantage over a related drug already on the market.
19. Pharmaceutical product\* A dosage form containing one or more drugs along with other substances included during the manufacturing process.
20. Therapeutic equivalence\* Pharmaceutical products which, when administered to the same individual in the same regimen, will provide essentially the same efficacy and/or toxicity.

\*Terms as defined by WHO Expert Committee on the Selection of Essential Drugs.

**ANNEX D**  
**SELECTED BIBLIOGRAPHY**

- Chaulet, P. and O.Y. Sow, 1974. The price of recovery, *Tuberculosis*, No. 33.
- Cilingiroglu, A. 1975. *Transfer of Technology for Pharmaceutical Chemicals*. Paris: Organization for Economic Cooperation and Development.
- Dunnill, P. 1977. The Provision of drugs by appropriate technology, *Appropriate Technology* 4, No. 2.
- Kastner, F. 1974. *Volume and Cost of the Supply of Medicaments*. Geneva: General Secretariat of the International Social Security Association.
- O'Brien, P. 1977. *Trademarks, the International Pharmaceutical Industry, and the Developing Countries*. ISS Occasional Papers, No. 68.
- Segall, M. 1975. *Pharmaceuticals and Health Planning in Developing Countries*. IDS Communication 119. Brighton: Institute of Development Studies at Sussex.
- Silverman, M. 1976. *The Drugging of the Americas*. Berkeley and Los Angeles: University of California Press.
- Speight, A.N.P. 1975. Cost-effectiveness and drug therapy. *Tropical Doctor*.
- UNCTAD. 1977. Case Studies in Transfer of Technology: *Pharmaceutical Policies in Sri Lanka*. (TD/B/C.6/21) Study prepared by S. Bibile.
- UNCTAD. 1975. Major Issues in the Transfer of Technology to Developing Countries: *A Case Study of the Pharmaceutical Industry*. (TD/B/C.6/4) Study Prepared by S. Lall.
- WHO Technical Report Series, No. 446. 1970. (*Clinical Pharmacology. Scope, Organization, Training*: Report of a WHO Study Group).
- WHO Technical Report Series, No. 563. 1975. (*Guidelines for Evaluation of Drugs for Use in Man*: Report of a WHO Scientific Group).
- WHO Technical Report Series, No. 615. 1977. (*The Selection of Essential Drugs*: Report of a WHO Expert Committee).
- Yudkin, J. 1978. Provisions of medicines in a developing country, *The Lancet* (April 15).



Funded under contract with the  
United States Agency for International Development