PHARMACEUTICALS IN DEVELOPING COUNTRIES

by
Arnold Worlock
Director, The Wellcome Foundation Ltd

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OFFICE OF HEALTH ECONOMICS

The Office of Health Economics was founded in 1962 by the Association of the British Pharmaceutical Industry. Its terms of reference are:

To undertake research on the economic aspects of medical care.
To investigate other health and social problems.
To collect data from other countries.
To publish results, data and conclusions relevant to the above.

The Office of Health Economics welcomes financial support and discussions on research problems with any persons or bodies interested in its work.

FOREWORD

The Office of Health Economics has recently widened its scope to take a special interest in the health care problems of the Poor World, with particular reference to the role of medicines.

As a contribution to the discussion in this area, OHE is publishing this paper, which was delivered by Dr Arnold Worlock of The Wellcome Foundation Ltd at the 11th Assembly of the International Federation of Pharmaceutical Manufacturers' Associations in Washington in June 1982.

In its Tables, the paper contains important data on the extent of some of the European pharmaceutical companies' activities in the Developing Countries. It also gives a glimpse of other ways in which the pharmaceutical industry in Europe has contributed to the transfer of technology to the poor nations.

Hence this publication underlines two facts. The first is that the industry has made a significant contribution to employment and to the production of pharmaceuticals in the developing world. The second is that much more detailed analysis of the whole international pharmaceutical industry's activities in the poor countries is badly needed.

Two decades ago, when the Office of Health Economics was first set up by the Association of the British Pharmaceutical Industry, a similar situation existed in Britain. The activities of the pharmaceutical industry in this country were shrouded in mystery, and this provided great scope for largely ill-informed criticism. This situation has now been corrected by better information and by the elimination of justifiable causes of criticism. The contribution of the pharmaceutical industry to the economy and health of Britain is no longer seriously questioned. It is to be hoped that the publication of progressively more solid data on the activities of the industry in the Poor World, together with improvements in its standards of marketing practice, will soon reveal the nature of its benefits there too.

GEORGE TEELING-SMITH

PHARMACEUTICALS IN DEVELOPING COUNTRIES

At the Tenth Assembly of the International Federation of the Pharmaceutical Manufacturers Association held in Madrid in October 1980, the Rt Hon Patrick Jenkin, PC, MP, the then Secretary of State for Social Services, Department of Health and Social Security said in relation to the Third World:

'My experience of dealing with the pharmaceutical industry in the UK is that they act responsively when the issues are fairly put, and that our co-operation with them is achieved, not by ignoring our different interests, but by recognising them. What is more needed here is to identify the issues, to make them known and to work towards co-operation on a world basis.'

Considerable progress has been made with WHO and UNIDO during the past two years in identifying the issues and many exchanges of views have taken place both formally and informally, to try and work with the UN agencies and the developing countries on an international basis.

I have the privilege to chair a working group representing eighteen of the major research based pharmaceutical companies in Europe who have generated data on their work in developing countries.

The companies involved in this survey are:

Astra
Bayer AG
C H Boehringer & Sohn, Ingelheim
Boehringer Mannheim GmbH
The Boots Company PLC
Ciba-Geigy AG
Glaxo Holdings PLC
Hoechst AG including Behringwerke
F Hoffmann-La Roche & Co
Imperial Chemical Industries PLC
Knoll AG
E Merck
Organon International BV
Rhône Poulenc
Roussel Uclaf
Sandoz AG
Schering AG
The Wellcome Foundation Limited

The major effect has been with:

1. WHO Action Programme for Essential Drugs (DAP)
2. The Special Programme for research and training in Tropical Diseases (TDR)
3. UNIDO

WHO PROGRAMME FOR ESSENTIAL DRUGS (DAP)

The industry is pleased to note the statement by Dr Mahler in January 1982 welcoming a new era of close co-operation with the pharmaceutical industry for the supply of 200 essential drugs to developing countries under favourable conditions.

It now needs WHO rapidly to establish a modus operandi in order that developing countries take up these offers, which, after all, have been around for three years or so.

Several of the European research based companies have already taken part in helping WHO to try and accelerate the identification of the most needy countries and also to advise on storage, distribution and procurement.

May we offer other advice—there is still pressure from various groups demanding a WHO Drug Approval System based on a Scientific Evaluation Document (SED). We believe this to be an unnecessary expense and duplication of already existing work. Several inexpensive options appear to be a possibility.

1. Each developing country (or group of neighbouring countries) should set up an elementary drug testing facility to conduct simple stability studies under local conditions and carry out quality control procedures. The European companies have already offered assistance in training personnel for this purpose.
2. Adequate information on branded drugs already exists for example, in the ABPI Compendium, Physicians Desk Reference, etc. and access to a copy of Martindale would shed light on generic drugs.
3. The WHO newsletter could be increased in frequency and include a data sheet of every new product from the country of first registration and translated in every WHO language.

These are relatively simple and low cost procedures for increasing information and understanding.

Similarly, the 'Health for all by the Year 2000' campaign defined an urgent need for developing countries to become proficient in the problems of quality control and quality assurance. Over two years ago the pharmaceutical industry, through IFPMA, offered as an initiative, an introductory scheme, with necessary funding for 25 suitably qualified candidates. To the best of my knowledge only 17 places have been taken up to date and only 8 trainees have completed the course of training.

SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES (TDR)

In 1976 WHO adopted TDR identifying the major problem tropical diseases and up to December 1981 the Programme had supported 1300 projects in 81 Member States. Over 2000 scientists from 118 WHO Member countries have thus far participated and the Programme, since its inception, has been funded to the value of over US $90 million, with the 1981-82 budget set at a level of US $26,579,000. The Special Programme recognises that there is no substitute for the expertise and facilities of industry in the search for, and the production of, new therapeutic entities to control the six tropical diseases of concern to TDR.

However, over the past five years many agencies have criticised the international pharmaceutical industry for walking away from the problem—usually on the grounds that this area was highly unprofitable. The facts are that there is a considerable contribution both in manpower, funds and facilities emanating from the pharmaceutical industry.

Recently, Professor Gordon Smith, Chairman of the Independent Commission set up by WHO to review the Oncho cerciasis Programme has expressed the view that, without new and effective drugs, the many millions of dollars spent on environmental control could well be wasted. The disease will re-occur when economic and/or political problems arise causing a halt to the vector control programmes.

From this has come the proposition that large amounts of money could be better, and more efficiently, used if it were directed to specific targeted goals, in the hands of the international pharmaceutical companies who have the skills and proven record of managing research to produce new chemical entities and these resources simply do not exist in Third World countries.

Figure A shows at *constant values* (1980) the direct R&D expenditure by the European research based industry. Between 1977-1980 the companies involved spent over US $100 million in research into tropical diseases. Although the figures are not directly comparable it is interesting that the total WHO spending was US $90 million at actual rates over the same period.

The real spending of the companies as shown in Figure B is higher again as the fixed overheads must be added to the direct costs. At say 25 per cent, this gives a more realistic figure of US $126 million at *constant values* over the 1977-1980 period.

The research based industry is not only criticised for its lack of research into tropical diseases, but also for not developing any new products. Table 1 illustrates that over the past 15 years there has been regular development of products, which have materially affected therapy and newer products are under clinical evaluation.

TABLE 1 Modern Drugs Developed by the Research Based Pharmaceutical Industry for the Treatment of Tropical Diseases Products with Primary Indication for Tropical Diseases

*YOL**	*Trade Marks*	*Approved Names*	*Indications*
1979	PIG-BEL	Necrotising enterocolitis vaccine	Active immunisation against N.E.
1979	BILTRICIDE	Praziquantel	Schistosomiasis
1978	RADANIL	Benznidazole	Anti-Chagas disease
1978	FLAGYL	Metronidazole	Amoebiasis
1977	ENTAMIZOLE	Diloxanide Furoate Metronidazole	Amoebiasis
1976	FLAGENTYL	Secnidazole	Amoebicide, Trichomonacide
1974	ARILVAX (stabilised)	Leucosis-free yellow fever vaccine	Yellow Fever
1973	BILARCIL	Metrifonate	Schistosoma haematobium
1972	LAMPIT	Nifurtimox	Chagas disease
1972	FANSIDAR	Sulfadoxine & pyrimethamine	Anti-malarial
early 1970s	JONIT	Bitoscanate	Hookworms (Ankylostoma duodenale & Necator Americanus)
1970	MALOPRIM	Pyrimethamine & Dapsone	Anti-malarial
1969	LAMPRENE	Clofazimine	Leprosy
1967	DAMETIN	Dehydroemetin	Amoebiasis
1966	AMBILHAR	Niridazole	Bilharziasis, Amoebiasis Dracunculosis
	ANTHEMAL	Sulfamethopyrazine & pyrimethamine	Anti-malarial
	FANTORIN	Stibophen	Schistosomiasis
1966-1980	Various Diagnostics for detection of Schistosomiasis, Amoebiasis, Chagas disease, sleeping sickness, Kala Azar.		Diagnostics

* *Year of launch*

FIGURE A **Actual and Projected R&D Direct Expenditure by Some Research Based Pharmaceutical Companies** Established in developing countries: Members of the United Nations.
Direct expenditure.

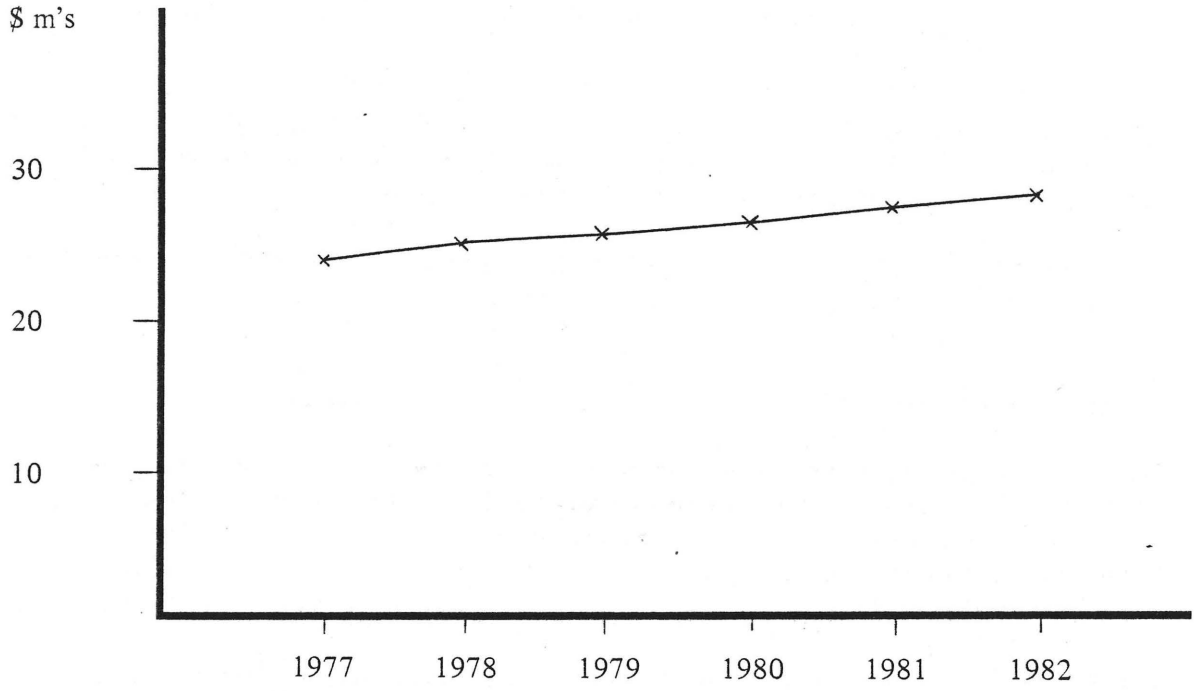
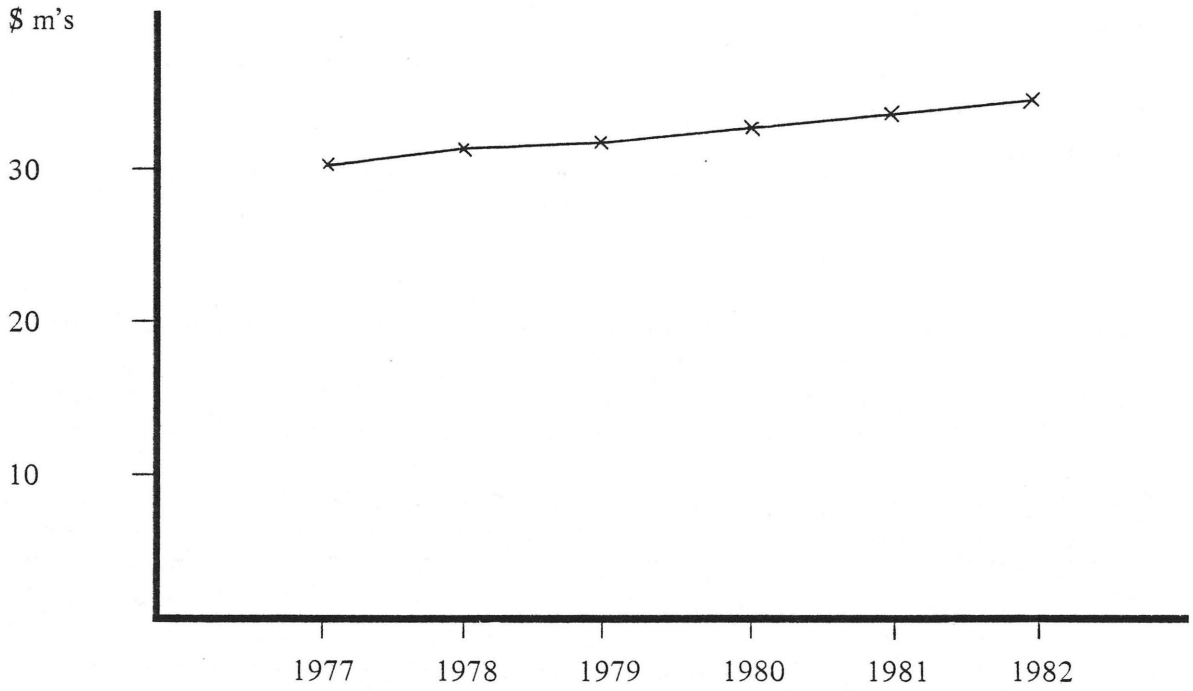


FIGURE B **Actual and Projected R&D Direct Expenditure by Some Research Based Pharmaceutical Companies** Established in developing countries: Members of the United Nations.
Direct expenditure plus overheads.



UNIDO

The first Consultation Meeting on the Pharmaceutical Industry was held in Lisbon in early December 1980 and, as I am sure everyone knows, one of the aims of UNIDO is to raise the share of the world's industrial output held by developing countries:

> 'to at least 25 per cent of the world's industrial production by the year 2000'.

The international pharmaceutical industry is convinced that it is already making a substantial contribution to this objective in developing countries through its subsidiary companies, third parties and in training programmes along with other indirect benefits.

One of the problems has been to put together reliable and contemporary data to show what, in fact, has been done and is being done to help the Third World.

Number of Staff Employed

Data has been generated to show the number of local personnel and of expatriate personnel in the Most Severely Affected Countries (MSAC's) and the other developing countries. In both groups the number of expatriates is extremely small—0.4% in the case of MSAC's, 0.7% in the other developing countries and, of the total 0.6%, Table 2 shows in more detail the breakdown of these data.

TABLE 2 Staff Employed by Some European Research Based Pharmaceutical Companies Established in Developing Countries, Members of the United Nations (1979-80 Survey)

Region	*Other Developing Countries*		*Most severely affected Countries*	
	Local Personnel	*Expatriates*	*Local Personnel*	*Expatriates*
Africa	11,184	38	2,211	48
Asia/Oceania	8,273	111	24,943	40
Europe	9,322	76	–	–
Latin America	25,932	154	708	18
	54,711	379	27,862	106
Total	55,090		27,968	
Total General	83,058			

The overall total of local nationals has increased from the 1977-78 figure of 73,482 by 9,091 to 82,573 in 1979-80. This is an increase of approximately 12.4 per cent in two years.

Table 3 shows the activities of the people employed illustrating that the majority of personnel are employed in production/quality control, storage, marketing/distribution, and administration.

The data show that the total number employed by the European research based pharmaceutical companies totals 83,058—it should be remembered that these activities also generate indirect employment. In several studies the pharmaceutical industry has been shown to be one of the highest in generating indirect employment.

TABLE 3 Staff Employed in Types of Activity–by Some European Research Based Pharmaceutical Companies Established in Developing Countries, Members of the United Nations (1979-80)

Region	*Total Numbers Employed*	*Type of Activity*				
		Production/ Quality Control	*Storage*	*Marketing/ Distribution*	*Administration/ Management*	*Others*
Europe	9,398	4,007	383	3,285	1,258	465
Africa	13,481	10,650	191	1,314	1,075	251
Latin America	26,812	11,582	1,050	10,129	3,493	558
Asia/Oceania	33,367	16,139	1,138	9,339	5,918	883
Total	83,058	42,378	2,762	24,067	11,744	2,107
%	100	51	3	29	14	3

At least one study† calculates that in developing countries this ratio is 3.5 : 1 and, if this is extrapolated to these data, then approximately another 300,000 people are involved and also contributing to the economy of developing countries. It is probable that, if the total pharmaceutical industry were included in the survey, then these figures would increase threefold.

Table 4 shows the various production facilities including Third Party production, in both developing countries and MSAC's including basic production and processing.

TABLE 4 Production Facilities of Some European Research Based Pharmaceutical Companies* In Developing Countries, Members of the United Nations (1979-80)

Region	*Number of Developing Countries Excl. MSACs*	*Number of most severely affected Countries*	*Total Number of Developing Countries*	*Number of Basic Production Facilities*	*Number of Processing/ Production Facilities*	*Number of Production Facilities with Third Parties*
Europe	5	–	5	21	43	45
Africa	6	10	16	1	24	42
Latin America	15	2	17	27	110	79
Asia/Oceania	16	5	21	32	69	76
	42	17	59	81	246	242

* *Including Third Party production facilities*

WHO correctly indicates that developing countries need training experience in production, storage and distribution, quality control and effective administration.

In Table 5 the data refer entirely to developing country nationals. It is of interest to examine the increase in the number of people undergoing training since the last survey in 1977-78 when approximately 3500 completed training, an average of 197 per company. For the latest period 1979-80 this increased to 7116, an average of 395 per company, and is expected to increase further in the next two years.

† *C. IFFLAND & A. STETTLER, Les Investissements Industriels Suisses au Brezil, Centre de Researches Européenes, Lausanne 1973.*

TABLE 5 Training Programmes by Some European Research Based Pharmaceutical Companies for Developing Countries, Members of the United Nations

Numbers Trained	
1979 & 1980	*Next 2 years**
7116	7554 (+6%)

Length of Training		
< 2 weeks	*< 3 months*	*> 3 months*
3050	3698	368

Cost of Training	
Total for 2 years $ '000s	*Average per person $*
12,360.3	1737

Numbers Employed	
By Company	*Not Company employees*
6285 (88%)	831 (12%)

By Activity (Numbers)

Production	*Storage & Distribution*	*Quality Control*	*Administration*	*Marketing/ Tech. Info.*	*Other/ Lab. training*
1177 (17%)	224 (3%)	274 (4%)	322 (4%)	3692 (52%)	1427 (20%)

Training Locations (Numbers)

Corporate HQ	*Africa*	*America*	*Asia/Oceania*	*Europe*
967 (14%)	633 (9%)	2168 (30%)	2197 (31%)	1151 (16%)

* *Estimate*

It is important to note that the majority of this training took between 2 and 13 weeks to complete compared to the last review when the majority of training was less than 2 weeks; this indicates longer and more substantial training programmes. In total this represents an estimated 27,000 man weeks of training.

It is relevant to review the costs of training—the costs in Table 5 refer to the direct expenses incurred during training and do not include any element for fixed costs. If these are taken into account, the figure of US $12 million could be increased by about 25 per cent to US $15 million which is a more realistic cost.

Of the 7116 trainees who have completed their training, 12 per cent or 831 were non company personnel and came mainly from government administration and state industries. This compares very favourably with the numbers achieved in the pilot scheme with WHO, for quality control, where only 8 out of 17 acceptances have so far completed their training.

Table 5 also shows the spread of activity and outlines the training locations of which the vast majority (86 per cent) took place in developing countries and has obvious benefits to them. The remainder took place in Western Europe corporate headquarters. This illustrates efforts by the European research based industry to work in the developing countries, with local nationals and transfer skills and technology on a wide scale.

The European research based industry has also helped developing countries in other fields, in particular with Educational Fellowships. During the period 1978/80 a total of 634 Educational Fellowships were awarded, usually progressing to a degree course and some postgraduate studies.

These were in the following areas:

Biological Research
Medical Research
Tropical Medicine
Drug Research and Testing
Production
Quality Control
Medical Services

In addition, emergency and other types of aid was received by large numbers of Third World countries during 1979/80. Particular examples of this type of aid included:

- the free supply of Pharmaceuticals: Analgesics, Antibiotics & Vitamins, Antiseptics, Wound Dressings

- establishing a school of laboratory assistants for public health services

- setting up a Research Centre for drugs for tropical diseases and pharmaceutical technology

- the financing of 190 student bursaries over 10 years in a variety of disciplines.

In an attempt to find out recent examples of transfer of technology (TOT) to developing countries, the following questionnaire was designed for each project reported by the companies:

Some specific examples of TOT follow:

PROJECT:
Foot & Mouth Disease Vaccine Plant to be built in Hyderabad by the Indian Dairy Corporation

1. Who is organising or financing the project?	1. Project is being financed by ODA (UK) and Government of India.
2. For whom is the project intended?	2. For the Indian Dairy Corporation.
3. Where is it being conducted?	3. Hyderabad, in the State of Andhra Pradesh.
4. What was the date of commencement?	4. Effective Date of Contract was 25th October 1979.
5. What was the date of completion?	5. Work is still underway–due to complete late 1982.
6. What is the advantage to the developing countries?	6. Eventually to eradicate Foot and Mouth Disease, which will increase very considerably the milk yield from cattle and buffalo, which are presently debilitated by the disease.
7. What is the advantage, or even profit, to your own company?	7. Transfer of know-how and technology in a very specialised and difficult vaccine production process. Technical credibility certainly could stem from this.

PROJECT:

Setting up formulation plant and bulk manufacture. Product licensing in India

1. Project organised and financed by company and by its Indian partners. Public shares will be issued.

2. Intended for joint venture company.

3. Bangalore.

4. Board decision—December 1977.

5. First phase of constructions started commercial production beginning 1982.

6. Input of latest development of GMP standards. Training of personnel. Organising of development work. Export potential.

7. Experience gained from work in developing countries. Possibility to develop and draw supplies of products especially designed for activities in tropical countries. Possibility of training technicians and administrators for employment with company in other developing countries at lower cost than from own company. Creation of alternative sources of raw materials which could result in reductions of costs for such raw materials.

PROJECT:
School for Medical Assistants, Ifakara, Tanzania

1. Swiss Tropical Institute, Government of Tanzania. Financial support by three pharmaceutical companies.

2. Paramedicals from Tanzania.

3. Ifakara, Tanzania.

4. Started 1960, enlarged 1972/73.

5. Handed over to Tanzanian Government 1978.

6. Schooling of local manpower. Research in the field of Trypansomiasis, Malaria, Yellow Fever, etc.

7. Helping to solve local health problems. Improvement of contacts to local health authorities.

PROJECT:
Goregaon-Bombay Research Center

1. Run by pharmaceutical company.

2. Students and scientists in the field of drug technology.

3. Goregaon-Bombay, India.

4. 1966.

5. Still underway.

6. To give access to the newest findings in the field of drug technology. Research in tropical medicine.

7. Company being recognised as offering top technology.

PROJECT:
School for laboratory assistants for Public Health Services, Jakarta

1. Joint pharmaceutical company and Indonesian Government.

2. Indonesian students of the Ministry of Health.

3. Jakarta.

4. April 1973.

5. First stage completed 1975—now owned and run by the Ministry of Health.

6. Filled a severe gap in the local education system and provided government agencies with qualified technical staff.

7. It is expected that the project will enhance the company's credibility and show its goodwill to government. No commercial advantage.

Other examples of TOT are:

1. Transfer of technology with government to establish production facilities, e.g. Afghanistan, Bangladesh.

2. Establishing research units in tropical diseases, e.g. Brazil and Egypt.

3. Offer to UNIDO of complete technology for drugs, e.g. isoniazide.

4. Delegation of senior staff to WHO scientific and field study groups, e.g. tropical diseases, Ruanda Burundi.

Currently the European research based industry has several areas of co-operation with UN Agencies. Among the more important are:

- co-operation with WHO on Primary Health Care resulted in the offer of supply of basic drugs at low cost.

- via UNICEF, medicines have been supplied direct under specially favourable terms.

- qualified personnel have been offered to assist in the mixed WHO-Industry Fact Finding Missions. These form part of the Action Programme on Drugs.

- through the IFPMA, various posts for trainees in Quality Control were offered by the Industry.

- help has been given by the companies for the transfer of technology and 'know-how' on certain products, and also on the supply of certain raw materials.

The research based pharmaceutical industry is well aware of the problems for health care facing the Third World and the data show that for several years this industry has had an on-going commitment. It would be fair to say that there are also some activities of UN Agencies which cause a great deal of concern to the industry. For example, the extreme slowness to get co-ordinated action to implement the Programme for Essential Drugs, in spite of the urgent needs and positive offers from the industry.

In addition there is concern over the whole question of transfer of technology, not about the subject itself but rather the various attitudes adopted. The pharmaceutical industry argues that it cannot be emphasised too strongly that any arrangement for a transfer of technology depends upon the willing seller and a willing buyer, particularly important because pharmaceutical technology is held by individual companies. Such technology which is created and held primarily by the private sector cannot be transferred anywhere compulsorily, but only under voluntary and mutually rewarding agreements, recognising that industrial enterprises respond most readily to pressures of competition and profit. The most important issue therefore is that *neither* side should put forward impossible conditions which would provide no incentive to either the supplier or receiver of TOT to conclude such agreements.

Industry disagrees completely with the notion that the weakening or abolishing of patent protection will encourage the flow of technology to developing countries and believes firmly that a strong and readily enforceable system encourages TOT by providing security to both supplier and recipient from unauthorised or accidental disclosures. The recent statement of WHO Policy on patents recommended that the WHO Assembly adopt a resolution to the effect that it should be the policy of WHO:

> 'to obtain patents or interests in patents on patentable health technology developed through projects supported by WHO'*

and that the Organisation would:

> 'use its patent rights and any financial or other benefits associated therewith to provide the development, production and wide accessibility of health technology in the public interest.'

This view on patents is quite encouraging, particularly when there are countries where the exercise of compulsory licences, licences of right and weakening of the patent system have already resulted in technology not being offered for registration of patents, for example in India. Hopefully this current view of the WHO Executive Board on patents and the protection of their industrial property will be adopted by other UN agencies, e.g. UNCTAD and UNIDO, to the mutual benefit of developing countries and the research based industry.

This paper has reviewed the ongoing commitment of some of the European research based pharmaceutical companies to the Third World and that this commitment is rising significantly as each year passes. I have no reason to believe this is not the case for the remainder of the industry.

The role of this industry can only be part of any solution to the 'Health for all' target in that, equally, nutrition, hygiene, clean water, sanitation, etc. also require major effort and aid programmes.

The industry cannot, and should not, solve the political issues, the allocations and management of national budgets, international aid programmes in the Third World, or the priority ranking for Health Care and Education. The pharmaceutical industry obviously cannot solve all the Health problems of the developing countries by itself, but it is on record that this industry wholly supports and is willing to further expand under mutually acceptable and fair terms, its contribution to the Health Care and industrial growth of the Third World.

* *WHO Executive Board 69th Session, January 1982.*