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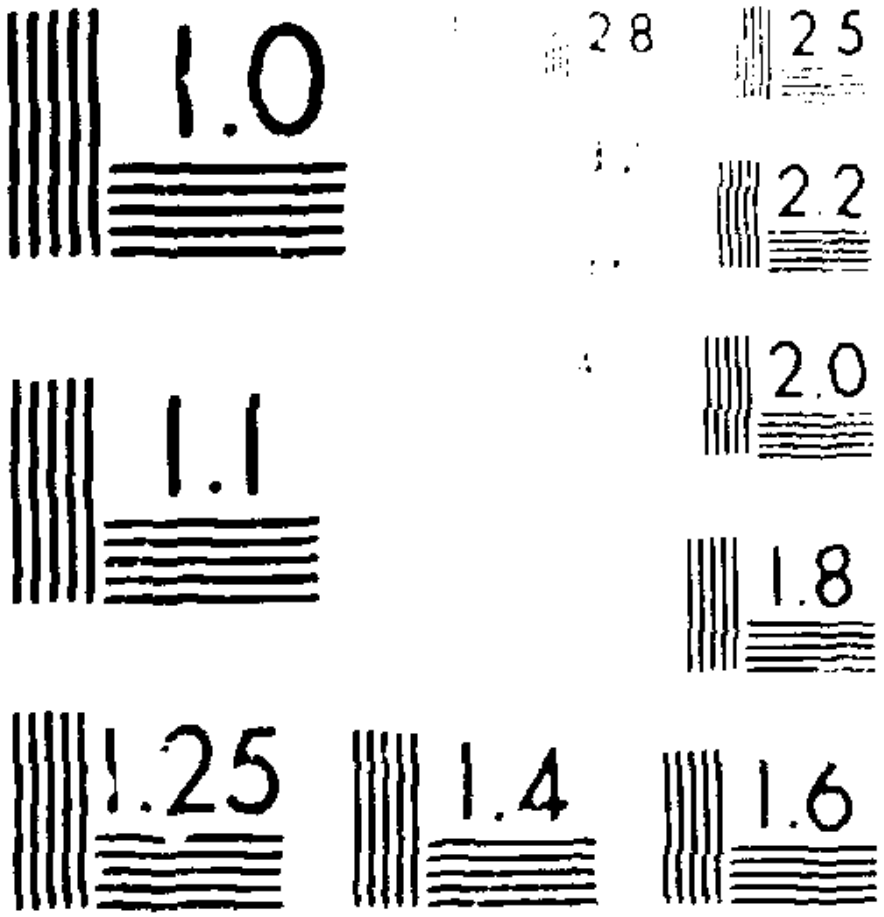
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THE PRICING AND AVAILABILITY OF INTERMEDIATES AND BULK DRUGS*

Prepared by

the UNIDO Secretariat

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PRICING AND AVAILABILITY OF INTERMEDIATES AND BULK DRUGS

Introduction

1. A review of the present status of the development of the pharmaceutical industry in developing countries reveals that there are some major constraints to the development of this industry. 1/ Amongst them the situation regarding the wide disparity in prices charged for bulk drugs used in the production of pharmaceutical formulations assumes considerable importance. 2/

Disparity in prices of bulk drugs

2(a) The disparity in the import prices of some essential bulk drugs is illustrated in table 1. It can be seen from table 1 that there is considerable disparity in import prices of bulk drugs offered by different suppliers to different countries ranging in some cases up to 11 times. In the course of the Global Preparatory Meeting, some participants from developed countries stated that there was nothing surprising in finding differences in bulk drug prices of the order 1 : 10 3/. While some attributed such a wide disparity to the absence of different suppliers and import tying, others felt that it was due to several factors such as volume of sales, the duration of the contract, the quality of the product and related services including research, the class of customer, specific tender requirements, the liability of the supplier, the patent situation and market conditions in general. Yet the fact remains that there is a big disparity in bulk drug prices.

2(b) Many developing countries have facilities to formulate a range of drugs. These countries import bulk drugs which are converted into ready-to-use dosage forms. With such a wide disparity in prices it would not be feasible to sustain viable manufacturing acitivites. The fluctuation in prices of bulk drugs will have direct impact on the prices of pharmaceutical formulations, which in turn will adversely effect the ability of the developing countries to make available these products at reasonable prices to the vast majority of the population who at present

1/ Global study of the Pharmaceutical Industry, UNIDO
2/ Issues that might be considered at the First Consultation UNIDO, ID/WG.317/1
3/ Global Preparatory Meeting for Consultation on the Pharmaceutical Industry UNIDO, ID/WG.317/3

Table I Disparity in import prices of bulk drugs (1979)

(in US Dollars per kg)

Bulk drug	Brazil	Egypt	India	Malaysia	Sources of Supply
Acetyl Salicylic Acid	1,63 (a)	3,63	1,86	2,35 to 3,05	Belgium, Germany, Hong Kong, Japan, USA, Graesser Salicylate, UK, Ciech, Poland, LPS, England, Siemsgluss and Sohn, W. Germany, China, Soviet Union, and other unidentified sources
Gentamicin		1650 to 4380 (b)	1884		Schering, USA; Medimpex Hungary, and other unidentified sources
Reserpine	1297,5 (a)	119,0	1537	302,5	Delta [illegible]ly; Boehringer, Germany; and other unidentified sources
Streptomycin	18,0 (a)	61,6 to 63,6	44,5	59,3	Glaxo, UK; Rhône Poulenc, France; Shin Kee, Hongkong

Source: Issues that might be considered at the First Consultation, UNIDO, ID/WG.317

(a) Average yearly price (1978)

(b) Licence

have no access to the same. It is,therefore,obvious that there is an urgent need to evolve a pricing scheme to ensure the availability of bulk drugs to the pharmaceutical formulation units at reasonable prices.

3. High cost of intermediates

Some of the developing countries are engaged in the manufacture of bulk drugs including synthetic drugs and antibiotics. The manufacture of synthetic drugs may be carried out from different stages, that is, from late intermediates, early intermediates or raw materials. The manufacture based on intermediates involves the last step or the last few steps of the process for the production of the synthetic drugs concerned. Most of these countries import the intermediates used in production of bulk drugs. The high price of intermediates in relation to the price of bulk drugs adversely effects the economics and feasibility of basic manufacture. 4/ The cost element contributed by imported intermediates alone renders the local manufacture of certain essential drugs uneconomic as can be seen from table 2. It is obvious from table 2 that due to increase in the price of imported intermediates in 1979, the estimated direct manufacturing cost (excluding overheads) of Acetyl Salicylic Acid amounted to more than FOB importation price of the drug. Similarly due to the steep increase in the price of imported intermediates in 1979, the direct manufacturing cost (excluding overheads) of Chloramphenicol was about 50 percent higher than the FOB importation price of the drug. This also highlights the need for evolving a pricing scheme for intermediates to ensure the availability of these materials at reasonable prices.

4. Indepth study of price structure of drugs

In view of above it is imperative that the disparities in the prices of bulk drugs should be narrowed down and intermediates should be available at reasonalbe prices in order to facilitate the growth and development of pharmaceutical industry in developing countries. With this objective in view UNIDO carried out an indepth study of the price structure of eight essential drugs with particular reference to the impact of the price of imported

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4/ op;cit. UNIDO/WG. 317/1

TABLE 2

Impact of high cost of intermediates on bulk drug cost

(in US$ per kg)

Name of drug	Intermediates required for manufacture	Price of imported intermediates		Cost of intermediates per kg of drug		Estimated Direct Mfg. cost of drug		F.O.B. Importation price of drug		Direct Mfg.cost compared to F.O.B. importation price of drug	
		1978	1979	1978	1979	1978	1979	1978	1979	1978	1979
1. Acetylsalicylic Acid	Acetic Anhydride	0.65	0.95	0.52	0.76						
	Salicylic Acid	1.20	1.785	1.104	1.642						
			TOTAL	1.624	2.402	2.436	3.603	2.50	3.20	- 2.6 %	+ 12.6 %
2. Chloramphenicol	L-Nitrobase	27.0	58.0	25.53	40.02						
	Dichloromethyl-ester	2.01	3.07	1.266	1.934						
			TOTAL	26.796	41.954	40.194	62.931	40.0	42.20	+ 0.5 %	+ 49.1 %

1. Data from a developing country

2. 0.8 kg of Acetic Anhydride and 0.92 kg of Salicylic Acid required per kg of Acetylsalicylic acid

3. 0.69 kg of L-Nitrobase and 0.63 kg of Dichloromethylester required per kg of Chloramphenicol

4. Estimated direct manufacturing cost does not include overheads

intermediates and raw materials on the cost of bulk drugs. The basis for the selection of these eight essential drugs for this study is explained below.

5. Essential drugs for integrated production

For the purpose of integrated production of bulk drugs from intermediates or raw materials, 26 essential drugs have been identified by UNIDO as shown in table 3 out of the model list of essential drugs drawn up by the World Health Organization Expert Committee and these have been approved by WHO 5/. The selection of these drugs is also in conformity with the criteria laid down by the UNIDO panel of Industrial Experts for the production of drugs in developing countries 6/. Further, these drugs cover therapeutic groups of utmost importance to the developing countries based on the most common diseases prevalent and are needed by these countries in large quantities. The technologies involved in the production of these drugs are relatively more sophisiticated and are available with transnational corporations, countries with centrally planned economies, smaller companies in developed countries as well as in some of the developing countries.

6. Out of the 26 essential drugs identified by UNIDO and approved by WHO, UNIDO again selected nine drugs as priority for establishing facilities for the local production of bulk drugs and these are indicated in table 4. These drugs are widely used in the developing countries for treating diseases most prevalent in these areas. Further the developing countries constitute large markets for these drugs. These drugs have also been in existance for several years and patents have expired in many cases. Besides, some developing countries are in the process of establishing or expanding their petro-chemical industry which will make available many of the basic chemical raw materials required for the manufacture of these drugs.

5/ The Selection of Essential Drugs, WHO Technical Report Series 641. 1979.

6/ Second Panel Meeting of Industrial Experts on the Pharmaceutical Industry, UNIDO, ID/WG. 267/4/Rev. 1978

TABLE NO. 3

ILLUSTRATIVE LIST OF 26 ESSENTIAL DRUGS FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES

ANALGESICS

1. Acetylsalicylic acid
2. Paracetamol

ANTI-INFECTIVE DRUGS

Anthelmintic drugs

3. Mebendazole
4. Piperazine

Antibacterial drugs

5. Ampicillin
6. Benzyl Penicillin
7. Erythromycin
8. Sulphadimidine
9. Tetracycline

Antifilarial drugs

10. Diethylcarbamazine

Antileprosy drugs

11. Dapsone

Antimalarial drugs

12. Chloroquine
13. Primaquine

Antituberculosis drugs

14. Ethambutol
15. Isoniazid
16. Streptomycin

CARDIOVASCULAR DRUGS

Antihypertensive drugs

17. Hydralazine
18. Propranolol
19. Reserpine

DIURETICS

20. Furosemide

ANTI-DIABETICS

21. Insulin

ORAL CONTRACEPTIVES

22. Ethinylestradiol + levo-norgestrel

IMMUNOLOGICALS

23. Blood and Blood fractions

VITAMINS

24. Asorbic acid
25. Hydroxocobalamin
26. Retinol

TABLE NO. 4

ILLUSTRATIVE LIST OF 9 ESSENTIAL DRUGS FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES AND WHICH SHOULD BE GIVEN TOP PRIORITY

ANALGESICS

1. Acetylsalicylic acid

ANTI-INFECTIVE DRUGS
Antibacterial drugs

2. Ampicillin
3. Sulphadimidine
4. Tetracycline

Antifilarial drugs

5. Diethylcarbamazine

Antileprosy drugs

6. Dapsone

Antimalarial drugs

7. Chloroquine

Antituberculosis drugs

8. Ethambutol
9. Isoniazid

7. The UNIDO indepth study of the price structure of bulk drugs referred to above covered the following aspects: 7/

A. General

(i) Producers - Major producers in the developed countries, producers in the developing countries.

(ii) Production - Total production in the world, production in developing countries.

(iii) Consumption - Consumption in the world
Consumption in developing countries

(iv) Patents

(v) International price

B. Industrial profile

(i) Outline of manufacturing process

(ii) Availability of intermediates

(iii) Plant capacity

(iv) Investment required

(v) Requirement of different intermediates and other raw materials per kg of the finished product

(vi) Cost breakdown of bulk drugs

(vii) Cost of intermediates and other raw materials as percentage of bulk drug cost

(viii) Cost breakdown of formulations

7/ Although Dapsone is an anti-leprotic drug of considerable importance, it has not been included in the present study due to non-availability of adequate data on the cost of production.

The data on the above aspects relating to the eight essential drugs are given in annexes I to VIII.

8. The cost data pertain to commercial scale production units in a developing country, as ascertained by an independent Governmental expert organization. The cost profile including investment requirement has been given under appropriate costing groups. While they are based on the actual experience in a developing country, the data should be assumed only as indicatory, given the wide variation between country to country in unit price of local raw materils, utilities, hourly compensation for manpower, etc.

The plant capacity and estimate of investment requirements are again indicatory and have to be understood in the context that synthetic drugs are often manufactured in multipurpose plants, a factor which has implication in regard to allocation of the investment to different products made in the plant.

9. Impact of bulk drug cost on cost of pharmaceutical formulations

In order to assess the contribution of the cost of bulk drugs to the cost of pharmaceutical formulations, the relative costs of various components of formulations pertaining to eight essential drugs have been worked out from the data presented in Annexes I to VIII and these are shown in table 5. It is evident from this table that the cost of bulk drugs in the formulation of eight essential drugs examined accounts for 52.04 to 84.9 percent of the cost of formulations. In view of this it is essential that bulk drugs are available to the pharmaceutical formulation units at reasonable prices and hence the necessity for evolving a pricing scheme for bulk drugs.

10. Impact of cost of intermediates and raw materials on bulk drug cost

With a view to finding out the impact of the cost of intermediates and raw materials on the cost of bulk drugs, the proportion of variable costs to total costs and of the share of the intermediates and raw material costs in the variable costs have been worked out from the ascertained cost data and these figures are indicated in table 6. It can be seen from table 6 that variable costs account for 77 to 93.5 percent of total production cost and cost of intermediates and raw materials account for 61.3 to 95.7 percent of the variable costs. Since the cost of intermediates and raw materials constitutes an significant component of bulk drug cost, it is necessary that intermediates are available to the drug manufacturers at reasonable prices

TABLE 5

MANUFACTURING AND PACKAGING COST OF FORMULATIONS

(Cost of Different Items as Percentage of Total Cost)

	Bulk Drug	Other Raw Materials	Packaging Material	Conversion Cost	Packaging Cost	Total
1) Acetyl Salicylic Acid Tablets 300 mg. per tablet	63.44	3.46	8.82	20.6	3.68	100
2) Ampicillin Capsules 250 mg. per capsule	57.19	10.9	21.40	3.86	6.65	100
3) Chloroquine Phosphate Tablets 250 mg. per tablet	82.78	4.69	5.07	3.6	3.86	100
4) Diethyl Carbamazine Tablets 50 mg. per tablet	62.86	8.1	5.47	18.81	4.76	100
5) Ethambutol Tablets 200 mg. per tablet	77.59	3.32	8.72	2.49	[illegible]	100
6) Isoniazid Tablets 50 mg. per tablet	65.66	4.38	6.82	18.26	4.88	100
7) Sulphadimidine Tablets 500 mg. per tablet	84.9	4.59	2.67	6.98	0.86	100
8) Tetracycline Capsules 250 mg. per capsule	52.04	31.87	8.19	7.32	0.58	100

TABLE NO.6

Proportion of variable cost as percent of total production cost of selected bulk drugs and proportion of raw material cost as percent of variable cost

NO.	Item	Variable costs in $/kg (a)			Fixed costs in $/kg (b)	Total costs $/kg	Variable cost as % of total production cost	Raw material cost as % of variable cost
		Raw Materials	Others	Total				
1	Acetylsalicyclic acid	2.59	0.295	2.88	0.453	3.33	86.48	89.93
2	Ampicillin	125	5.61	130.61	11.71	142.32	91.77	95.7
3	Chloroquine	28.7	6.36	35.06	9.94	45.0	77.90	81.86
4	Diethyl carbamazine	14.33	3.38	17.71	5.29	23	77.0	80.9
5	Ethambutol	71.43	5.01	76.43	5.31	81.74	93.5	93.45
6	Isoniazid	14.74	4.23	18.97	4.52	23.49	80.75	77.7
7	Sulphadimidine	15	1.32	17.32	2.38	19.7	87.9	92.38
8	Tetracycline	29.99	18.91	48.9	13.26	62.16	78.66	61.32

a) The element "others" in variable costs includes direct wages and salaries, consumable stores, repairs and maintenance.

b) The cost elements going into "fixed costs" are depreciation, factory and administrative overheads and return on capital.

c) Data relates to commercial scale production units in a developing country.

and the need, therefore, for evolving a pricing scheme for intermediates.

PRICING SCHEME FOR INTERMEDIATES

11. The high cost of intermediates leads us to the conclusion that it would be cheaper to import certain essential drugs than to manufacture the same from imported intermediates. In such an event the existing drug production units in the developing countries will have to close down or operate under government protection. Hence, the price of the intermediates should be such that the bulk drug production in a typical developing country becomes economically viable. It is in this context that a pricing scheme for intermediates has been evolved. For the purpose of illustrating the pricing scheme Ampicillin and Ethambutol have been chosen out of the eight essential drugs mentioned in table 4.

12. Pricing schem as applied to Ampicillin

Ampicillin is an antibacterial drug very widely used in the developing countries. The consumption of this antibiotic has gone up steeply during recent years in these countries. For example, the annual consumption of Ampicillin in the Andean Group of countries has increased fourfould from 25 tons to 100 tons during the period 1970 to 1978. Further, local production of Ampicillin has also been taken up by many developing countries. The manufacture of Ampicillin is carried out in two stages. In the furst stage, Penicillin is converted into 6-Amino Penicillanic Acid (6APA) by chemical or enzymatic process. 6 APA is then converted by chemical method to Ampicillin trihydrate/Ampicillin anhydrous/Ampicillin sodium. Until about 1978 the international market price of Penicillin was around US$ 13 /B.O.U. while the cost of 6 APA was about US$ 67/kg and that of Ampicillin US$ 82/kg. At that time, the operation of converting Penicillin to 6 APA and then on to Ampicillin was profitable. However in 1980, the price of Penicillin has gone up to US$ 22/B.O.U. (about 70 percent higher) while that of 6 APA went up to US$ 76/kg (about 13 percent higher) and that of Ampicillin increased to US$ 90/kg (about 11 percent higher). On account of the steep increase in the cost of Penicillin, the producers of Ampicillin (also producers of Penicillin) from developed countries could cover all their overhead expenses in Penicillin operations.

As far as the developing countries are concerned, the manufacture of Ampicillin from Penicillin became uneconomical due to high cost of Penicillin. In view of this, Penicillin to 6 APA route of manufacture of Ampicillin was closed to the developing countries and they were obliged to start production of Ampicillin based on the late intermediate 6 APA and this operation has, therefore, been taken as the basis for illustrating the pricing scheme.

13. Sources of information

Efforts were made to obtain authentic data for the preparation of industrial profiles from the actual manufactuers of Ampicillin and this requires close co-operation of the industry. However, such data could be obtained so far only from some developing countries and were not forthcoming from developed countries. In view of this, the prices of Ampicillin and intermediates prevalent in the international market have been taken into account and conversion data were taken from the developing countries where available.

14. Outline of pricing scheme

The main principle on which the pricing scheme is based is as follows: The elements going into the cost of production of Ampicillin include the cost of imported intermediates, cost of domestic raw materials, utilitites, direct wages, consumable stores, maintenance, depreciation, general overheads, return on capital, etc.

In view of this, two major components have been taken as the basis for the pricing scheme and these are: a) cost of imported intermediates 6APA and Dalpha Phenyl Glycine Chloride Hydrochloride and b) conversion cost which includes the following:

Utilities
Direct wages and salaries
Consumable stores
Repair and maintenance
Depreciation
Factory and general overheads

The residual value obtained by deducting the conversion cost from the imported CIF priceof Ampicillin is apportioned between the two imported intermediates in the ratio in which these are utilized in the process. The resulting figures show at what prices these intermediates should be available in the international market. The pricing scheme is explained in detail below:

15. Details of pricing scheme

(a) The cost structure of Ampicillin trihydrate produced from imported intermediates - 6 APA and D Alpha Phenylglycine in commercial scale production units in a developing country as ascertained by an independent governmental expert organization has been considered for illustrating the price scheme.

(b) The CIF price of the bulk drug imported through the National Central Purchasing Organization during the year in question by the developing country mentioned above has been taken as the bench mark prices for deriving the fair prices of the intermediates. This is an essential condition, inasmuch as the reasonable prices for the drug intermediates cannot be developed unless the transfer price adopted for the bulk drug is itself fair.

(c) Conversion cost incurred in a commercial scale production plant in the developing country mentioned above could be accepted as fair cost of conversion. The technology adopted by the developing country is stated to be competent. This cost could be verified either by a Government Cost Ascertainment Organization or a chartered firm of cost accountants. Fair cost of conversion so ascertained would be regarded as the first element of "value added" during manufacturing the bulk drug in the developing country. The conversion cost, however, does not include the contribution of domestic raw materials used and return on capital in the case of one of the developing countries.

(d) The CIF price of the bulk drug discounted to the extent of the computed value added in local manufacturing will constitute the residual value of the imported intermediates. Where only one intermediate is involved in the process, the fair CIF price of the intermediate can be calculated from the value and the consumption co-efficient. If multiple ingredients are

involved., fair CIF prices could be calculated on the assumption that the ingredients have the same weight in the residual value as they individually have in the aggregate foreign exchange outlay on the imported intermediates per kg of the bulk drug. Such a rough and ready formula is necessary in a context where the industry in the developed countries does not indicate the actual weights of these ingredients in their own costing.

16. Desirable prices of intermediates based on pricing scheme

Based on the above scheme, desirable prices of the intermediates - 6 APA and D Alphaphenylglycine used in the manufacture of Ampicillin trihydrate have been computed and these are shown in tables 7, 8 and 9. Table 7 is based on data obtained from a large developing country with central purchasing organization. Tables 8 and 9 are based on data obtained from private sector units in two other developing countries. In the case of tables 8 and 9, the cost of domestic raw materials used in the process is included in the conversion cost.

17. Developing country A

It can be seen from table 7 that while the desirable price of 6 APA works out to US$ 64.05 per kg, its actual price during 1979 - 1980 was US$ 75.90 per kg, that is, 18.5 percent higher. Similarly while the desirable price of D Alpha Phenyl Glycine works out to US$ 24.63 per kg, its actual price during 1979 - 1980 was US$ 29.74 per kg, that is, 20.5 percent higher.

18. The contribution of domestic raw materials used in the manufacture of above drug as well as return on capital in the case of developing country A have not been included in the conversion cost. Thereby a premium gets added to the residual value accruing to the imported intermediates. Conversely, if the cost of the domestic raw materials used in the process and return on capital are taken into consideration while computing conversion cost, the desirable prices of imported intermediates will be much lower compared to the actual prices prevailing in the international market.

TABLE 7

Ampicillin Trihydrate (ex 6APA and D Alpha Phenyl Glycine)

Computation of desirable prices of 6APA and DAlpha Phenyl Glycine (Developing country A)

Conversion cost excludes domestic raw materials

	Plant capacity 12 M/T per year; Employs competent technology.	Data pertains to 1979-80 $ / Kg
1.	CIF price of bulk drug	77.92
2.	Conversion cost incurred in domestic manufacture ex 6APA and D Alpha Phenyl Glycine (A)	17.32
3.	Residual value assignable to 6APA and Phenyl Glycine (1 minus 2)	60.60
4.	Value out of 3 which can be assigned to 6APA (74%) / (B)	44.84
5.	Consumption of 6APA	0.7 kg/kg of ampicillin
6.	Desirable price of 6APA (4 $\div$ 5)	64.05
7.	Actual price of 6APA	75.90
8.	Value which can be assigned to Phenyl Glycine - 26% of 3 above / (B)	15.76
9.	Consumption of Phenyl Glycine	0.64 kg/kg of Ampicillin
10.	Desirable price of Phenyl Glycine (8 $\div$ 9)	24.63
11.	Actual price of Phenyl Glycine	29.74

Note A: Conversion cost includes utilities, direct wages, consumable stores and maintanence depreciation and general overheads as in Note C below.

Note B: Please see next page

TABLE 7 (contd)

Ampicillin Trihydrate (ex 6APA and D Alpha Phenyl Glycine)

Computation of desirable price of 6APA and D Alpha Phenyl Glycine

conversion cost excludes domestic raw materials

(continuation sheet)

NOTE: (B)

Weights assigned to 6APA and D Alpha Phenyl Glycine have been computed as follows:

SNO	ITEM	Qty/Kg of Ampicillin	CIF in $ actually incurred per kg of Ampicillin	Proportion of each item in total
1	D Alpha Phenyl Glycine	0.64	18.82	26
2	6APA	0.76	52.50	74
			71.32	100

(C) - Itemized details of conversion cost

SNO	Item	$/Kg
1	Utilities	2.00
2	Direct wages and salaries	1.79
3	Consumable stores	0.66
4	Repair and maintanence	1.16
5	Depreciation	2.77
6	Factory and general overheads	8.94
	TOTAL	17.32

TABLE 6

Ampicillin Trihydrate (ex 6APA and D Alpha Phenyl Glycine)

Computation of desirable prices of 6APA and D Alpha Phenyl Glycine (Developing country B)

		$ Kg July 1980
1.	CIF price of bulk drug	88
2.	Conversion cost incurred in domestic manufacture ex 6APA and D Alpha Phenyl Glycine (A)	37.27
3.	Residual value assignable to 6APA and Phenyl Glycine (1 minus 2)	50.73
4.	Value out of 3 which can be assigned to 6 APA 73%	37.03
5.	Consumption of 6APA	0.6225 Kg/Kg of Ampicillin
6.	Desirable price of 6APA (4 ÷ 5)	59.49
7.	Actual CIF price of 6APA	77.50
8.	Value which can be assigned to Phenyl Glycine - 27% of 3 above	13.7
9.	Consumption of Phenyl Glycine	0.629Kg/Kg of Ampicillin
10.	Desirable price of Phenyl Glycine (8 ÷ 9)	21.78
11.	Actual CIF price of Phenyl Glycine	28.75

Note A: Conversion cost includes direct manufacturing expenses (direct labour), indirect labour, fuel, oil, lubricants, maintanence, electricity/water, depreciation, administrative expenses and 100 percent of cost of solvents. FOB

Data pertains to a private sector unit in a developing country.

TABLE 9

Ampicillin Trihydrate (ex 6APA and D Alpha Phenyl Glycine)

Computation of desirable prices of 6APA and D Alpha Phenyl Glycine (Developing country C)

Conversion cost excludes other raw materials

		Data pertains to 1980 $ / Kg
1.	CIF price of bulk drug Ampicillin	90
2.	Conversion cost incurred in domestic manufacture of ex 6APA and D Alpha Phenyl Glycine (A)	29.81
3.	Residual value assignable to 6APA and Phenyl Glycine (1 minus 2)	60.19
4.	Value out of 3 which can be assigned to 6APA 72% / B	43.33
5.	Consumption of 6APA	0.636 Kg of Ampicillin
6.	Desirable price of 6APA (4 ÷ 5)	68.13
7.	Actual price of 6APA	75.90
8.	Value which can be assigned to Phenyl Glycine - 28% of 3 above/(B)	16.85
9.	Consumption of Phenyl Glycine	0.636 Kg of Ampicillin
10.	Desirable price of Phenyl Glycine (8 ÷ 9)	26.50
11.	Actual price of Phenyl Glycine	29.74

Note A: Conversion cost includes utilities, direct wages, consumable stores, maintenance depreciation and general overheads.

Note B: Profit is not included.

Note C: Data pertains to a private sector unit in a developing country

19. Developing country B

It is oberserved from table 8 that the desirable price of 6 APA works out to US$ 59.49 while the actual price during 1980 was US$ 77.50 per kg, that is, 30 percent higher. Similarly, while the desirable price of D Alpha Phenyl Glycine works out to US$ 21.78 per kg, the actual price during 1980 was US$ 28,75,tnat is, 32 percent higher.

20. Developing country C

From table 9 it is evident that while the desirable price of 6 APA works out to US 68.13 per kg, its actual price during 1980 was US$ 75.90 per kg, that is, 11 percent higher. Similarly while the desirable price of D Alpha Phenyl Glycine works out to US$ 26.50 per kg, its actual price during 1980 was US$ 29.74 per kg, that is, 12 percent higher.

21. Pricing scheme as applied to Ethambutol

Ethambutol is an antituberculosis drug very widely used in developing countries. Ethambutol can be produced by heating ethylene dichloride with 2 Aminobutanol and this operation has been taken as the basis for illustrating the pricing scheme.

22. The main principles on which the pricing scheme is based are similar to those described in the case of Ampicillin above. The prices of ethambutol and intermediate prevalent in the international market have been taken into account and conversion data were taken from a developing country, as no such data were available from developed countries.

23. Desirable prices of intermediates based on pricing scheme

The desirable price of D2 Aminobutanol used in the manufacture of Ethambutol has been computed and this is indicated in table 10. It can be seen from this table that the desirable price of D2 Aminobutanol works out to US$ 26.45 per kg, while the actual price was US$ 42.0 per kg. In other words, the actual price was 58.8 percent higher.

TABLE 10

Ethambutol (ex d 2-Aminobutanol)

Computation of desirable price of d 2-Aminobutanol

Conversion cost excludes domestic raw materials

	Plant capacity 12 M/T per year Data pertains to 1979-80 Employs competent technology.	$ /KG
1.	CIF price of bulk drug	39.40
2.	Conversion cost incurred in domestic manufacture ex d 2-Aminobutanol (A)	10.31
3.	Residual value assignable to d 2-Aminobutanol (1 minus 2)	29.09
4.	Consumption of d 2-Aminobutanol	1.1 kg/kg of Ethambutol
5.	Desirable price of d 2-Aminobutanol (3 ÷ 4)	26.45
6.	Actual price of d 2-Aminobutanol	42

Note: (A) Conversion cost includes utilities, direct wages, consumable stores and maintenance, depreciation and factory and general overheads.

24. Pricing scheme as applied to Sulphamethoxazole

Sulphamethoxazole is widely used as an antibacterial drug and is one of the drugs included in WHO model list of essential drugs. The manufacture of this drug based on the intermediate Isoxamine has been considered for illustrating the pricing scheme which is summarized in table 11. The main principles governing the pricing scheme in this case are similar to those described in the case of Ampicillin and Ethambutol. Based on the pricing scheme, the desirable price of Isoxamine, as can be seen from table 10, works out to US$ 46.93 per kg while the actual price in the international market of Isoxamine during 1978 - 1979 was US$ 63.97. In other words the actual price is 36 percent higher than the desirable price.

25. Pricing scheme as applied to Trimethoprim

Trimethoprim is an antibaterial drug widely used and is included in the WHO model list of essentail drugs. The production of Trimethoprim based on the intermediate Trimethoxy Benzyl Morpholine Acrylonitrile (TMA) has been taken into account for illustrating the pricing scheme, which is summarized in table 12. The pricing scheme in this case is also similar to those applied in the case of Ampicillin and Ethambutol. According to this pricing scheme, the desirable price of TMA amounts to US$ 37.9 as against an actual price in the international market of TMA during 1978 - 1979 of US$ 131.21. From this it is evident that the market price was 246 percent higher than what it ought to be.

26. Impact of pricing scheme on the price of intermediates

The desirable prices of intermediates used in the production of Acetyl Salicylic Acid , Ampicillin, Sulphamethoxazole and Trimethoprim computed according to the pricing scheme described above are shown in table 13 in comparison with the corresponding prices of intermediates prevailing in the international market. It can be seen from table 13 that the market prices of imported intermediates are 11 to 246 percent higher than the desirable prices. The high cost of intermediates is therefore a major constraint to the successful functioning of bulk drug production units in developing countries.

ANALYSIS

27. As can be seen from above, the high cost of intermediates renders the manufacture of bulk drugs uneconomic and this is a major constraint to the growth and development of the pharmaceutical industry in the developing countries. As evidenced in the case of Ampicillin manufacture until 1978 the price of Penicillin was such that developing countries could take up the production of Ampicillin starting from Penicillin and going through 6 APA. However, in 1980 the price of Penicillin increased by more than 50 percent with the result that the production of Ampicillin starting from Penicillin became uneconomic and the developing countries engaged in Ampicillin production were obliged to start from the late intermediate 6 APA and this does not provide any cushion to them to ensure viable operations. On the other hand, the manufactuers in the developed countries who produce Penicillin and convert the same into Ampicillin were unaffected since they could recover all their expenses in Penicllin operations. It is, therefore, imperative, that there should be a mechanism whereby the intermediates are available at reasonable prices to enable the developing countries to sustain viable bulk drug manufacturing activities.

TABLE 11

SULPHAMETHAXAZOLE (ex-ISOXAMINE)

Computation of desirable price of Isoxamine

Conversion cost excludes domestic raw materials

Plant capacity 40.5 T per year; Employs competent technology

Data pertains to 1978-79

		$/Kg
1.	CIF price of bulk drug	28.87
2.	Conversion cost incurred in domestic manufacture ex-isoxamine (A)	7.94
3.	Residual value assignable to Isoxamine (1 minus 2)	20.93
4.	Value out of which can be assigned to Isoxamine	20.93
5.	Consumption of Isoxamine	0.4460 kg per kg of the drug
6.	Desirable price of Isoxamine	46.93
7.	Actual price of Isoxamine	63.97

Note (A) Data pertains to a developing country

Note (B) Conversion cost includes utilities, direct wages, consumable stores and maintanence, depreciation and overheads as in the note (c) below.

Note (C) Weight assigned to Isoxamine is 100%

Note (D) Itemwise details of conversion cost

S. No.	Item	$/kg
1.	Utilities	1.53
2.	Wages and Salaries	0.94
3.	Repairs maintenance and stores	0.39
4.	Factory overheads	2.50
5.	Administrative overheads	1.29
6.	Depreciation	1.10
7.	R + D	0.11
	TOTAL	7.94

TABLE 12

TRIMETHOPRIM (EX-TMA i.e. TRIMETHOXY BENZYL MORPHOLINE ACRYLONITRILE)

Computation of desirable price of TMA

Conversion cost excludes domestic raw materials

Plant capacity 10.23 T per year; Data pertains to 1978-79
Employs competent technology

		$/Kg
1.	CIF price of the bulk drug	81.88
2.	Conversion cost incurred in domestic manufacture ex-TMA (A)	28.44
3.	Residual value assignable to TMA (1) minus (2)	53.44
4.	Consumption of TMA	1.41 kg per kg of the drug
5.	Desirable price of TMA (3 ÷ 4)	37.90
6.	Actual price of TMA	131.21

Note (A) Data pertains to a developing country

Note (B) Conversion cost includes utilities, direct wages, consumable stores and maintenance, depreciation and overheads as in note (c) below

Note (C) Weight assigned to TMA is 100% as other raw materials which are indigenous account for about 5% of the total cost of raw materials

Note (D) Please see below.

Itemwise Details of Conversion Cost

S. No.	Item	$/kg
1.	Utilities	2.72
2.	Wages and Salaries	0.77
3.	Repairs, maintenance and stores	2.82
4.	Factory overheads	7.78
5.	Administrative overheads	12.78
6.	Depreciation	1.53
		28.44

TABLE NO. 13

Impact of Pricing Scheme on Prices of intermediates used in bulk drug manufacture

(Summary of Tables 7 to 12)

Name of drug	Intermediate required for manufacture	Price of intermediate in the international market (US$ per Kg)	Desirable price of intermediate based on pricing scheme (US$ per Kg)	International market price of intermediate compared to desirable price
1. Ampicillin	6APA	A) 75.90	A) 64.05	A) + 18.5 %
		B) 77.50	B) 59.49	B) + 30.0 %
		C) 75.90	C) 68.13	C) + 11.0 %
	D Alphaphenyl Glycine	A) 29.74	A) 24.63	A) + 20.5 %
		B) 28.75	B) 21.78	B) + 32.0 %
		C) 29.74	C) 26.50	C) + 12.0 %
2. Ethambutol	D 2 Aminobutanol	42.0	26.45	+ 58.8 %
3. Sulpha - methoxazole	Isoxamine	63.97	46.93	+ 36.0 %
4. Trimethoprim	TMA	131.21	37.9	+ 246.0 %

28. The steep escalation in the prices of intermediates as for instance in the case of Chloramphenicol and Trimethoprim leads us to the conclusion that it would be cheaper to import certain essentail drugs than to manufacture the same from imported intermediates. This will naturally force the developing countries to close down the drug production units as it actually happened in some developing countries in the recent past. Otherwise they can only continue to operate under Government protection.

The closure of production units will bring in its trail many disadvantages to the developing countries. First such a closure will create unemployment and serve as disincentive to the industrialization process in these countries. Secondly, the country becomes dependent on imports expending valuable foreign exchange and limits its ability to supply drugs. Restarting of production units may take considerable time, as for example, in the case of antibiotics based on fermentation, it may take two years for resuming production operations. Last but not least, due to a reduction in the number of producers, the prices of bulk drugs suddenly go up as it happened in several cases in the past, thus aggravating the drug supply position in the developing countries.

29. There are yet other situations wherein the big manufacturers curtail production owing to a fall in the demand for some drugs, as happened in the case of Chloroquine Phosphate for which 99 percent market is in the developing countries. The latter who have been dependent all along on imports from developed countries found themselves in a very difficult situation, when this drug was not available in adequate quantity in the international market and thereby they could not effectively control malaria. This highlights the need for establishing bulk drug production in developing countries.

30. In view of above, it is essential to have a mechanism to ensure that the intermediates required for the manufacture of essential bulk drugs are available at reasonable prices. It is in this context that the pricing scheme

for intermediates has been evolved which has been elaborated above.

31. It is also necessary that the Governments of developing countries take measures to support the indigenous pharmaceutical industry on account of its strategic value.

32. As the pharmaceutical industry is well established in some of the developing countries, technical cooperation amongst the developing countries will facilitate the transfer of technology and thus promote the growth and development of this industry.

33. It is also imperative that the developing countries strengthen their research and development base to develop technology especially when it is not forthcoming from traditional sources.

PRICING SCHEME FOR BULK DRUGS

34. In order to secure stability for the domestic prices of the formulations made out of bulk drugs, it is necessary that bulk drug prices are stable during a certain period of time. With a view to avoid wide fluctuations in the prices of bulk drugs, it is desirable to enter into long ter contracts based on an escalatory formula. Such an arrangement would become feasible if the suppliers of bulk drugs could agree upon bench mark prices for the bulk drugs and escalatory formulae for neutralizing the escalations in the more important of these inputs going into the manufacture of these bulk drugs, which are purchased from the chemical industry at large.

35. The suggested price escalation formulae for the selected essential drugs are given table 14. The indicatory bench mark price for the bulk drug is based on the yearly average price preceding the contract. The escalatory formulae have been suggested for the important intermediates and raw materials used in the process of manufacture.

36. For example, Acetyl Salicylic Acid is manufactured in two stages. In the first stage Phenol is converted into Salicylic Acid and in the second Salicylic Acid is subjected to Acetylation with Acetic Anhydride to produce Acetyl Salicylic Acid. Since raw material costs account for nearly 90 percent

TABLE 14

Indicatory bench mark prices (CIF) for suggested bulk drugs and suggested price escalation formula

SNO	Drug	Indicatory bench mark price (CIF) $/KG	Suggested price escalation formula	Remarks
1.	Acetyl Salicylic Acid	1.88	For 50% increase in phenol price, bulk price could increase by 15%. For 40% increase in acetic anhydride price, bulk drug price could increase by 15%.	Indicatory bench mark price based on yearly average of 78-79 imports of 319 M/T of bulk drug
2.	Ampicillin Trihydrate	77.92	For 1% increase in price of 6APA, Ampicillin price could increase by 1/2%. For 2.5% increase in price of D Alpha Phenyl Glycine, ampicillin price could increase by 1/2%.	Indicatory bench mark price based on yearly average of 79-80 purchase of 25 M/T by National Purchase Organization
3.	Chloroquine Phosphate	28.35	For 10% increase in price of EMME, bulk drug price could increase by 3%. For 6% increase in price of Novaldiamine, bulk drug price could increase by 1.5%. For 12% increase in price of metachloroaniline, bulk drug price could increase by 1.5%.	Indicatory bench mark price based on 80-81 purchase of 25 M/T by National Purchase Organization

TABLE 14 (cont'd)

Indicatory bench mark price (CIF) for selected bulk drugs and suggested price escalation formula

SNO	Drug	Indicatory bench mark price (CIF) $/KG	Suggested price escalation formula	Remarks
4.	INH	5.01	For 10% increase in gamma picoline price, INH price could increase by 4%. For 10% increase in Hydrazine hydrate price, INH price could increase by 2%	Indicatory bench mark price (CIF) based on yearly average 79/80 import prices; imports covered 28 M/T
5.	Ethambutol	39.40	For every 1% increase in d 2-Aminobutanol, prices of ethambutol could increase by 1.3%	Indicatory bench mark price (CIF) based on yearly average of 79/80 imports by National Purchasing Organization of 32 M/T
6.	Tetracycline	29.40		Indicatory bench mark price (CIF) based on 80/81 import of 40 M/T made by National Purchase Organization

Note: The escalatory formulae are based on domestic raw material prices (India) and landed cost of imported intermediates; and on domestic fair selling prices based on cost study carried out in a developing country.

of variable cost of production of Acetyl Salicylic Acid, the pricing scheme for this drug is linked to the prices of Phenol and Acetic Anhydride as can be seen from table 14. Similar is the case with Ampicillin Trihydrate, Chloroquine Phosphate, INH, Ethambutol and Tetracycline.

ANALYSIS

37. In the pricing schemes described for intermediates as well as bulk drugs, the main principles have been outlined. Although the relative prices of raw materials, intermediates, bulk drugs and conversion costs may undergo some changes from time to time and based on the efficiency of manufacturing process and yields, the principles hold good and these schemes can be used as the basis for deciding fair prices for intermediates and bulk drugs.

38. The following factors may be taken into consideration with a view to improve the situation relating to the supply of bulk drugs required for formulation by the developing countries:

- to undertake indigenous production of bulk drugs to meet the requirements
- to enter into a satisfactory licencing arrangement
- not to include in the licencing agreement a clause binding the licencee to purchase bulk drug from the licensor
- to promote technical co-operation amongst the developing countries particularly those who produce bulk drugs and possess technology for the same
- to establish a committee to monitor availability and prices and give information to developing countries.

39. In the course of the Global Preparatory Meeting, it was suggested that UNIDO prepares and regularly updates a directory of sources of supply of essential drugs and their intermediates, both in developed and developing countries, to be circulated among developing countries. This could serve as a useful source of information.

40. It is also desirable that the requirements of at least essential bulk drugs and their intermediates are made known to the pharmaceutical industry in developed countries as well as developing countries engaged in bulk drug manufacture to enable them to plan production properly. This will also interest several competent drug manufacturers and will generate competition. It is well known that certain manufacturers stop production of certain basic drugs or intermediates due to lack of demand in the international market based on inaccurate information.

41. It has been suggested that a joint committee representing both developed and developing countries be set up under the auspices of UNIDO to discuss the pricing schemes for bulk drugs and intermediates and this could be discussed at the First Consultation.

ANNEX I

ACETYL SALICYLIC ACID

A. PRODUCTION

Name of country, Producer and quantity produced are given in Table I.

Consumption

Name of the region and country and consumption are given in Table II.

Forecast of World consumption

Year	1980	1985
Quantity in metric tons	34,500	40,000

based on estimated average annual growth of 3%

Patent

Ger. Pat 236,196 (1908 to Boehringer). Patent expired. However, Dow Chemical has recently patented a process which is reported to increase operating efficiency and produce finer crystals.

Price

Price in the international market (average) in May 1980 - US$ 2.1/kg

B Industrial Profile

Based on the data received from a developing country for the manufacture of Acetyl Salicylic acid from Salicylic Acid and Acetic anhydride in 1979.

B (i) Outline of the manufacturing process

Acetyl Salicylic Acid is prepared by acetylation of Salicylic Acid with Acetic Anhydride and a small quantity of Sulphuric Acid 98 percent. About 100 percent excess of Acetic Anhydride over the theoretical amount is added to get hard tabular crystals (it is important because Acetyl Salicylic Acid is directly compressed into tablets without granulation) as well as stable product, Economic operations require the recoverty of Acetic Acid and excess of Acetic Anhydride.

Preparation of Salicylic Acid sublimed - Salicylic Acid technical grade is produced by reacting Pehnol with Caustic Soda to produce Sodium Phenate. Carbondioxide is introduced under pressure to react with Sodium Phenate at 170°C to 190°C and converted to Sodium Salicylate.

B (II) Availability of intermediates and raw materials

The two important intermediates are Salicylic acid and Acetic anhydride;in addition to the developed countries some of the advanced developing countries also produce these materials. No problem in the availability of these intermediates has been reported.

B (III) Plant capacity

Based on the experience of a developing country, the plant capacity recommended in 1979 is 1200 M/T per year.

B (IV) Investment

Based on the experience of a developing country in 1979, the investment for a capacity of 1200 M/T is $4.0 million.

B (V) Requirement of different intermediates and other raw materials per kg of the finished product. (F.P.)

Raw material	Requirement per Kg of the F.P. in kg	Price per Kg in $	Cost in $ per kg of F.P.
Acetic anhydride	0.78	1.3	1.0
Salicylic acid	0.88	1.68	1.48
Caustic Soda (lye)	0.054	0.426	0.023
Other raw materials	-	-	0.09
			2.59

B (VI) Cost breakdown for the bulk drug

Item	Cost for 1200 M/T in thousand $	As percentage of Total cost
Raw material	3100.0	77.5
Wages	127.5	3.19
Utilities	100.0	2.5
Depreciation	400.0	10.0
Maintenance	127.5	3.19
Overhead	145.0	3.62
	4000.0	100.00

Cost per ton: $3333.33

B (VII) Cost of intermediates and other raw materials as percentage of the total cost.

Total cost of raw materials	US$ 2.59	(A)
Total cost of production	US$ 3.33	(B)
A as percentage of B	77.77	

B (VIII) Cost Breakdown of Acetylsalicylic Acid Formulation

Dosage form - Tablet
Strength - 300 mg per tablet
Pack size - 1500 tablets in a tin container

Item	Cost per pack in US$	As percentage of cost
Acetylsalicyclic Acid	1.725	63.44
Other raw materials	0.094	3.46
Conversion cost *	0.56	20.6
Packaging cost *	0.1	3.68
Packaging materials	0.24	8.82
Ex factory cost	2.719	100.10

* includes direct wages, utilities, depreciation, maintenance and general overhead.

TABLE I

PRODUCTION OF ACETYL SALICYLIC ACID DURING 1977

Country	Producers	Production in metric tons
Australia	Monsanto	500
France	Rhone-Poulenc	3800
Federal Republic of Germany	Bayer, Hoechst	2000
Spain	Quim. Farm. Bayer	500
USA	Dow Chemical, Monsanto, Norwich Pharmaceutical, Sterling Drug	14000
UK	Grasser Salicylates, Monsanto	4200
Czechoslovakia	SPOFA	100
DDR	VEB Chem. Pharm. Werk	200
Poland	POLFA	750
Rumania	Uzina de Medicamente	1000
Yugoslavia	Bayer Pharma Jugoslavia	100
Argentina	Quim. Farm. Platense	1000
Brazil	Sydney Ross	600
Colombia	Industria Quimica Andina, Sydney Ross	400
India	Alta Laboratories, Southern Medico	1000
Mexico	Lepetit, Salicylates de Mexico	1750
South Africa	Fine Chemicals Epping Industria Norichem Silverton	500
Turkey	Bayer Türk Kimya Sanayü	400
	Total world production	33,250 tons

PRODUCTION OF ACETYL SALICYLIC ACID IN DEVELOPING COUNTRIES DURING 1979

Country	Producers	Production in metric tons
Argentina	Quimica Farmaceutica	
	Platense	
	Sudamfos	
Brazil	The Sydney Ross Co.	
Colombia	Industria Quimica Andina	
	The Sydney Ross	
Egypt	Nasar Co.	reported to be 500 tons
India	Alta Laboratories	1321
Mexico	Dow Quimica Mexicana	
	Saliclatos de Mexico	

TABLE II

CONSUMPTION OF ACETYLSALICYLIC ACID DURING 1977

Region and Country	Consumption in metric tons
North America	
Canada	750
United States	12,750
Subtotal	13,500
Latin America	
Argentina	1,100
Brazil	850
Chile	175
Columbia	325
Mexico	400
All others	650
Subtotal	3,500
Western Europe	
France	1,250
Italy	1,500
Scandinavia	250
Spain	750
Federal Republic of Germany	1,750
United Kingdom	3,000
All others	1,000
Subtotal	9,500
Asia	
India	1,250
Indonesia	250
Japan	400
Pakistan	250
Philippines	250
South Korea	100
Thailand	300
Turkey	400
All others	800
Subtotal	4,000
Africa	1,750
Oceania	750
TOTAL	33,000

ANNEX II

AMPICILLIN

A. Production

Name of the country producer and quantity produced are given in table I.

Consumption

Name of the region and country and consumption are given in Table II

Forecast of World consumption

Year	1980	1985
Quantity in metric tons	2,840	3,300

based on estimated average annual groth of 3%

Patent

U.S. Patent - 2,985,648 (1961)
British Patent- 902,703 (1962 to Beecham)
U.S. Patent - 3,079,307 (1963 to Bayer)
U.S. Patent - 3,140,282 and 3,157,640 both 1964 to Bristol-Myers

Practically all patent protection has expired.

Price

Price in the international market (average) in May 1980-US$86.50 per Kg.

B. Industrial Profile

Based on the data received from a developing country for the manufacture of Ampicillin trihydrate starting from 6APA in 1979.

B (i) Outline of manufacturing process

Ampicillin is a semisynthetic penicillin and the process comprises of two stages.

1) Production of 6APA (6-Aminopenicillanic acid) by removal of the side chain of Penicillin G.
2) Acylation of 6 APA to produce Ampicillin.

6APA can be produced by chemical process or by enzymatic process. Chemical method will be considered here.

Penicillin G is converted to Penicillin G dimethyl silyl ester by reacting with Dimethyl dichlorosilane. Dimethyl chloro silyl ester is treated first with Phosphorus Penta chloride and then with Butanol to produce the Dimethyl silyl imino ether derivative. Imino ether derivative is hydrolysed to give 6APA. The method requires anhydrous conditions and low temperature (about - 40°C).

Enzymatic production of 6APA presents various problems. Specialization is required for the processing, production, extraction and recovery of the enzyme. Requires fermentation infractructure with a methodology and equipment quite different from what is normally required for chemical synthesis.

Cost of raw materials exluding the enzyme is minimal but the capital goods and service requirements are substantial.

Since the diffusion of enzymatic technology is still limited, its cost is high compared to the technology by chemical method.

There is greater potential of products elaborated with enzymatic reaction to cause secondary reactions and hypersensitivity.

B (ii) Availability of intermediates and raw materials

The important intermediates are 6APA, Phenyl glycine chloride hydrochloride and Dimethyl dichloro silane. No problem in the availability of these intermediates has been reported.

B (iii) Plant capacity

Based on the experience of a developing country the minimum plant capacity recommended in 1979 is 12 M.T. per year.

B (IV) Investment

Based on the estimate made in 1979 by a developing country the investment for a capacity of [illegible] M/T is $0.33 million.

B (V) Requirement of different intermediates and other raw materials per Kg of the finished product (F.P.)

AMPICILLIN

Raw material	Requirement per kg of the F.P. in Kg	Price per Kg in $	Cost in $ per Kg of F.P.
6APA	0.683	105	71.7
Phenyl glycine chloride hydrochloride	0.665	37.5	24.93
Dimethyldichlorosilane	0.529	16.25	8.6
Methyl chloride	4.197	1.4	5.88
Isopropylalchohol	6.891	0.66	4.55
Dimethylaniline	0.388	3.21	1.24
Other materials			8.1
			125.00

B (VI) Cost breakdown of bulk drug

Item	Cost for 12 tons in thousand $	As percentage of total cost
Raw material	1500.00	87.83
Wages	21.48	1.25
Utilities	24.00	1.41
Depreciation	33.24	1.95
Maintenance	21.84	1.28
Overhead	107.28	6.28
	1707.84	100.00

Cost per ton: $142320

B (VII) Cost of intermediates and other raw materials as percentage of total cost.

Total cost of raw material	$125.0	(A)
Total cost of production per kg	$142.320	(B)
A as percentage of B	87.8	

B (VIII) Cost breakdown of Ampicillin Trihydrate formulation

Dosage form - Capsule
Strength - 250 mg. per capsule
Pack size - 4 capsules in vial

Item	Cost per pack in $	As percentage of cost
Ampicillin trihydrate	0.163	57.19
Other raw materials	0.031	10.9
Conversion cost 1/	0.011	3.86
Packaging materials	0.061	21.40
Packaging cost 1/	0.019	6.65
Ex factory cost	0.295	100.00

1/ Includes direct wages, utilities, maintenance, depreciation and general overhead.

TABLE I

PRODUCTION OF AMPICILLIN DURING 1977

Country	Producers	Production in Metric tons
Belgium	Beecham	150
Finland	Fermion	100
Germany (Fed.Rep.of)	Bayer	180
Italy	Archifar, Bristol, Farmitalia, Glaxo Instituto Biochimico Italiano, I.S.F.	570
Israel	Inkapharm, Plantex	20
Japan	Banyu, Meiji-Seika, Takeda, Toyama, Toyo Jozo, Yamanouchi	290
Netherlands 1/	Gist-Brocades	50
Portugal	Atral-Cipan	15
Spain	Antibioticos, CEPA, GEMA, LISAC Laboratorios Fher	115
USA	Beecham, Biocraft, Bristol-Myers, Squibb, Wyeth	585
UK	Beecham	200
Argentina	Squibb and other manufacturers	80
Brazil	Bayer, Quimasa-Bristol	70
India	Alembic, Hindustan Antibiotic, Ranbaxy	10
Mexico 2/	Beecham-Orsabe, Benvenides, Fermic, Fersint, Laboratories Sanfor, Quinonas	30
Korea	Chong Kun Dan, Dong Shin, Dong Wha, Seoul Pharmaceuticals.	40
Singapore	Beecham	100
Taiwan	Not known	20
Turkey	FAKO	20
Peru	SINQUISA	10
Sweden	Astra	30
World total production		2,600 tons

1/ There are reports of significantly larger production: Ampicillin production is relatively small, concentrates more on 6APA.

2/ Mexico's production in 1977 was low. Total production is reported to have exceded 100 tons in 1978.

TABLE I (CONTINUATION)

PRODUCTION OF AMPICILLIN IN DEVELOPING COUNTRIES DURING 1979

Country	Producers	Production in metric tons
Argentina	Laboratories Bago Microsuies Argentina	Reported to be 100 tons
Brazil	Bayer do Brasil Companhia Brasileira de Antibioticos Industria Farmaceuticas Fontura Wyeth Laboratorios Beecham Quimica Industrial Santo Amaro Quimica Lorenzini Sintequim	
India	Hindustan Antibiotics Ranbaxy	12.2
Singapore	Beecham	
Mexico	Centro Industrial Bioquimico Eurolatin Farmaceutical Fermentaciones y Synthesis Fermic Kemika Industrial Orsabe Quinonas de Mexico Richter (America)	
Peru	SINQUISA	

TABLE II

CONSUMPTION OF AMPICILLIN DURING 1977

Region and Country	Consumption in metric tons
North America	
United States	360
Canada	40
Subtotal	400
Latin America	520
Western Europe	
France, Italy, Germany	440
All others	560
Subtotal	1000
Asia	
Japan	220
All others	300
Subtotal	520
Africa and Oceania	160
TOTAL	2600

CHLOROQUINE PHOSPHATE ANNEX III

A. PRODUCTION

Industry structure in Western countries is made up of very few but large volume producers who produce for captive (20 percent of total) consumption and sale of bulk and formulated tablets to third parties.

Name of the country, producer and quantity produced are given in Table I.

World's production in 1980 is estimated to be 1500 tons

Consumption

Name of the region and country and consumption are given in Table II.

Forecast of World Consumption

Year	1980	1985
Quantity in metric tons	1200	1500

based on estimated average annual growth of 5%.

Patent

German patent - 683692 (1939)
U.S. patent - 2233970 (1941)
Patents expired long ago.

Price

Price in the international market (average) in may 1980 - US$ 30 per kg.

B. Industrial Profile

Based on data received from a developing country for the manufacture of chloroquine phosphate starting from Novoldiamine and EMME in 1979.

B (I) Outline of manufacturing process.

1. Chloroquine is produced by the condensation of 4.7 dichloro-quinoline with Novol diamine. 4.7 Dichloro-quinoline is treated with molten phenol, the condensation with Novoldiamine then can be carried out at a low temperature. Chloroquine diphosphate salt is directly produced in the original reaction mixture with the addition of Phosphoric acid.

2. Manufacturing process for 4.7 dichloroquinoline. Metachloroaniline is reacted with diethyl ethoxy methylene malonic ester to produce chloroxyquinoline. This is treated with Phosphorous oxychloride to produce 4.7 dichloroquinoline.

B (II) Availability of intermediates and raw materials

Novoldiamine and Ethoxymethylene malonic ester are the two important intermediates. No availability constraints in the import of these intermediates. The availability, however, is potentially vulnerable since there are only few producers in the world.

B (III) Plant capacity

Based on the experience of a developing country the minimum economic plant capacity recommended in 1979 is 25 M/T per year.

B (IV) Investment

As per estimate made in 1979 in a developing country the investment for a plant capacity of 25 MT is $18 million.

B (V) Requirement of different intermediates and other raw materials

Per kg of the finished product (F.P.)

CHLOROQUINE

Raw material	Requirement per kg of F.P. in kg	Price per kg in $	Cost in $ per kg of F.P.
Ethoxy methylene malonic ester	0.75	13.08	9.81
Novoldiamine	0.41	120.88	8.56
Metachloroaniline	0.40	12.21	4.88
Acetone	1.12	1.2	1.34
Other raw materials			4.11
			28.70

B (VI) Cost breakdown of bulk drug

Item	Cost for 25 M/T in thousand $	As percentage of total cost
Raw materials	718.00	63.8
Wages	31.00	2.76
Utilities	76.00	6.76
Depreciation	130.00	11.56
Maintenance	52.00	4.63
Overhead	118.00	10.49
	1,125.00	100.00

Cost per ton: $45,000

B (VII) Cost of raw materials as percentage of total cost

Total cost of raw materials	US$ 28.70	(A)
Total cost of production	US$ 45.00	(B)
A as percentage of B	63.78	

B (VIII) COST BREAKDOWN OF CHLOROQUINE PHOSPHATE FORMULATION

Dosage form - Tablet
Strength - 250 mg. per tablet
Pack size - 100 tablets in strips of 10 tablets

Item	Cost per pack in US$	As percentage of cost
Chloroquine phosphate	1.288	82.78
Other raw materials	0.073	4.69
Conversion cost *	0.056	3.6
Packaging cost *	0.06	3.86
Packaging materials	0.079	5.07
Ex factory cost	1.556	100.00

* includes direct wages, utilities, depreciation, maintenance and general overhead.

Table I

PRODUCTION OF CHLOROQUINE DURING 1977

Country	Producers	Production in metric tons
France	Rhone-Poulenc	300
Federal Rep. of Germany	Bayer A.G.	125
U.K.	I.C.I. Sterling Drug, Fawdon	350
Hungary	Medimpex	150
India	Bayer (India), Bengal Immunity	25
People's Rep. of China		100
	Total world production	1,050

PRODUCTION IN DEVELOPING COUNTRIES DURING 1979

Country	Producers	Production in metric tons
Bangladesh	I.C.I. Bangladesh	10
India	Bayer (India) Suneeta Laboratories	42.8

Table II

CONSUMPTION OF CHLOROQUINE DURING 1977

Region and Country			Consumption in metric tons
North America			2
Latin America			100
Western Europe			3
Asia			
India		350	
All others		250	
	Subtotal		600
Africa			340
Oceania			5
		TOTAL	1,050

DI-ETHYL CARBAMAZINE

A. Production

Names of the producers are given in Table I

Consumption

Country	Consumption in metric tons
ASEAN countries	100.0 (Estimated 1982)
India	37.0 (Estimated 1982)

Patent

US patent 2467893:2467895 (1949 to American Cyanamide)

Price

Price in the international market (average) in May 1980-US$21 per Kg.

B. Industrial profile

B (i) Outline of manufacturing process

1-methylpiperazine is reacted with diethylcarbamoyl chloride in presence of a base to get diethylcarbamazine base which is subsequently converted into citrate by addition of citric acid. Di-ethyl carbamoyl chloride is produced by reacting diethylamine with phosgene.

B (ii) Availability of intermediates and raw materials

No problem in the availability of the intermediate N. Methyl piperazine has been reported.

B(iii) Plant capacity

Based on the experience of a developing country the minimum economic plant capacity recommended in 1979 is 15 M.T. per year.

B (IV) Investment

As per 1979 estimate of a developing country the investment for a plant capacity of 15 M/T is $0.5 million.

B (V) Requirement of different intermediates and other raw materials per Kg of the finished product (F.P.)

DIETHYLCARBAMAZINE

Raw material	Requirement per Kg of F.P. in Kg	Price per Kg in $	Cost in $ per Kg of F.P.
Methy piperazine	0.30	27.0	8.1
Diethylamine	0.510	3.46	1.77
Citric acid	0.640	3.38	2.16
Other raw materials			2.30
			14.33

B (VI) Cost breakdown of the bulk drug

Item	Cost for 15 M/T in thousand $	As percentage of total cost
Raw materials	215.00	62.32
Wages	5.7	1.64
Utilities	15.00	4.34
Depreciation	50.00	14.5
Maintenance	30.00	8.7
Overhead	29.3	8.5
	345.00	100.0

Cost per ton: $23000

B (VII) Cost of intermediates and other raw materials as percentage of total cost.

Total cost of raw material	$14.33	(A)
Total cost of production	$23.0	(B)
A as percentage of B	62.3	

B (VIII) Cost breakdown of Diethycarbamazine formulation

Dosage form - Tablet

Strength - 50 mg. per tablet

Pack size - 1000 tablets in a tin

Item	Cost per pack in US$	As percentage of cost
DEC	1.32	62.86
Other raw materials	0.17	8.1
Conversion cost 1/	0.395	18.81
Packaging cost 1/	0.10	4.76
Packaging materials	0.115	5.47
Ex factory costs	2.10	100.00

1/ Includes direct wage, utility, depreciation, maintenance and overhead.

TABLE I

Names of the major producers of Di-ethyl Carbamazine

Aceto Chemical Co. Inc., U.S.A.
Lederle Laboratories, U.S.A.
Roussel Corp., France
Ward Blenkinsop and Co., Ltd. U.K.
Wander Chemie A.G. Switzerland

Producers in the developing countries

India

Burroughs wellcome
UNI-UCB
India's production in 1979 - 24.26 tons

ANNEX V

ETHAMBUTOL

A. Production

Names of the producers are given in Table I

Consumption

Country	Consumption in metric tons	
ASEAN countries	97.0	(estimated 1982)
Arab countries including Egypt	10.0	(estimated 1980)
Bangladesh	0.75	(estimated 1980)
India	90.0	(Estimated 1982)

Patent

US Patents	3,297,707 (1966)
Year of introduction	1967

Price

Price in the international market (average) in May 1980 - US$43 per kg.

B. Industrial profile

Based on the data received from a developing country for the manufacture of Ethambutol from 2 Aminobutanol in 1979.

B (i) Outline of manufacturing process

d-2 aminobutanol is reacted with ethylene dichloride in presence of a base to get ethambutol which is subsequently converted into hydrochloride.

B (ii) No problem in the availability of the intermediate 2 Aminobutanol has been reported.

B (iii) Plant capacity

Based on the experience of a developing country the minimum economic plant capacity recommended in 1979 is 15 M.T. per year.

B (IV) Investment

Based on the estimate made in 1979 by a developing country the investment for a plant capacity of 15 M.T. is US$163,500.

B (V) Requirement of different intermediates and other raw materials per kg of the finished product. (F.P.)

Raw Material	Requirement per Kg of FP in Kg	Price per Kg in US$	Cost in US$ per Kg of FP
2 aminobutanol	1.10	54.02	59.42
Isopropanol (lit./kg.)	4.48	2.13	9.54
Ethylene dichloride	0.45	0.70	0.315
Sulphuric acid	2.69	0.35	0.94
Sodium hydroxide	0.72	0.335	0.24
Other materials			0.975
			71.43

B (VI) Cost of breakdown of bulk drug

Item	Cost for 15 M.T. in 1,000 US$	As percentage of the total cost
Raw material	1071.45	87.39
Wages	44.85	3.66
Utilities	7.50	0.61
Maintenance	22.65	1.84
Depreciation	16.35	1.34
Overhead	63.30	5.16
	1226.10	100.00

Cost per ton: US$81740

B (VII) Cost of intermediates and other raw materials as percentage of the total cost.

Total cost of raw material	US$71.43	(A)
Total cost of production	US$81.74	(B)
A as percentage of B	87.39	

B (VIII) Cost Breakdown of Ethambutol Formulation

Dosage form - tablet

Strength - 200 mg per tablet

Pack size - 10 tablets in a bottle

Item	Cost per pack in US$	As a percentage of total cost
Ethambutol	0.187	77.59
Other raw materials	0.008	3.32
Conversion cost 1/	0.006	2.49
Packaging cost 1/	0.019	7.88
Packaging material	0.021	3.72
Ex factory cost	0.241	100.00

1/ Includes direct wage, utility, depreciation, maintenance and overhead.

TABLE I

NAMES OF MAJOR PRODUCERS OF ETHAMBUTOL

Lederle Laboratories, USA

Medimpex-Chinoin, Hungary

Lederle-Novalis, France

PRODUCERS IN THE DEVELOPING COUNTRIES

Brazil

Cyanamid Quimica do Brasil

India

Themis

Venezuela

Subsidiary of Cyanamid

ISONIAZID

A Production

Names of the producers are given in Table I

Consumption:

Country	Consumption in metric tons
ASEAN countries	100.0 (estimated 1982)
Andean countries	237.0 (estimated 1980)
Arab countries including Egypt	100.0 (actual 1977-78)
Bangladesh	28.50 (estimated 1980)
India	375.0 (estimated 1982)

Patent

US patent 2,830,994 (1958) issued to distillers. Patent expired.

Price

Price in the international market (average)in May 1980 - US$ 6 per kg.

B. Industrial Profile

Based on the data received from a developing country for the manufacture of Isoniazid starting from Gama picoline in 1979.

B (I) Outline of manufacturing process

Gama picoline is oxidised with sulphuric acid and magnesium oxide to Nicotinic acid. Isoniazid is produced from Nicotinic acid and hydrazine hydrate.

Isoniazid can also be produced by reacting 4-cyano-pyridine with hydrazine hydrate.

B (II) Availability of intermediates and raw materials

Important intermediates are Gama picoline and Hydrazinehydrate. No problem in their availability has been reported.

B (III) Plant capacity

Based on the experience of a developing country plant capacity recommended in 1979 is 100 M/T per year.

B (IV) Investment

As per 1979 estimate made in a developing country the investment for a capacity of 100 M/T is $2.5 million.

B (V) Requirement of different intermediates and other raw material per kg of the finished product (F.P.)

ISONIAZID

Raw material	Requirement per kg of F.P. in kg	Price per kg in $	Cost in $ per kg of F.P.
Gamapicoline	0.896	5.42	4.86
Isonicotonic acid amide	0.692	8.66	6.0
Hydrazinehydrate	2.267	8.7	2.0
Caustic soda (lye)	4.01	0.29	1.16
Other raw materials			0.72
			14.74

B (VI) Cost breakdown of bulk drug

Item	Cost of 100 M/T in thousand $	As percentage of total cost
Raw material	1,474.00	62.75
Wages	168.00	7.15
Utilities	130.00	5.53
Depreciation	250.00	10.64
Maintenance	125.00	5.32
Overhead	202.00	8.61
	2,349.00	100.00

Cost per ton: $ 23490

B (VII) Cost of intermediates and other raw materials as percentage of total cost

Total cost of materials	$ 14.74	(a)
Total cost of production	$ 23.49	(B)
A as percentage of B	62.75	

B (VIII) COST BREAKDOWN OF ISONIAZID FORMULATION

Dosage form - Tablet
Strength - 50 mg. per tablet
Pack size - 1000 tablets in a tin

Item	Cost per pack in US$	As percentage of cost
Isoniazid	1.348	65.66
Other raw materials	0.09	4.38
Conversion cost *	0.375	18.26
Packaging cost *	0.1	4.88
Packaging materials	0.14	6.82
Ex factory cost	2.053	100.00

* includes direct wage, utility, depreciation, maintenance and overhead.

TABLE I

Name of major producers of Isoniazid

A.B. Bofors,	Sweden
Bayer A.G,	Fed.Rep.of Germany
Carlo Erba,	Italy
Farmitalia,	Italy
Merck,	Darmstadt
Parke Davis,	USA
Rhone-Poulenc,	France
E.R. Squibb,	USA

Producers in the developing countries

Argentina

Gierrado Ramon and C.I.A.
Lepetit

India

Bio-Evans
Chemo Pharma
Pfizer
Suneeta Laboratories

India's production in 1979 - 82.76 tons.

SULPHADIMIDINE

A. Production

Names of the producers are given in Table I

Consumption

Country	Consumption in metric tons
Arab countries including Egypt	100.0 (estimated 1980)
Bangladesh	22.5 (estimated 1980)
India	625.0 (estimated 1982)

Patent

British patent - 546,158 (1942 to Ward Blenkinsop)
US patent - 2,407,966 (1946 to Sharp and Dohme)
British patent - 552,887 (1943 to I.C.I.)
US Patent - 3,119,818 (1946 to 1st Chemioterap. Ital)

Price

Price in the international market (average) in May 1980-US$ 10 per Kg.

B. Industrial Profile

Based on the data received from a developing country for the manufacture of Sulphadimidine from Acetanilide and Guanidine nitrate in 1979.

B (i) Outline of manufacturing process

Acetanilide is converted into acetylsulphanilylchloride as usual by reaction with chlorosulphonic acid. The resultant compound is subsequently reacted with guanidine nitrate, to produce acetylsulphaguanidine. This component is refluxed with acetyl acetone to produce actylsulphadimidine which is subsequently hydrolised with alkali to produce sulphadimidine.

B (ii) Availability of intermediates and raw materials

Important intermediates are Guanidinenitrate and Methyl isobutylketone. No difficulty in their availability has been reported.

B (iii) Plant capacity

A developing country is now producing in a plant capacity of 500 M.T. per year. Based on their experience a plant capacity of 50 M.T. per year should be economically viable or still better is a multipurpose plant.

B (IV) Investment

As per the estimate of a developing country in 1979, investment for a plant capacity of 500 M.T is US$ 10 million.

B (V) Requirement of different intermediates and other raw materials per Kg of the finished product. (F.P.)

Manufacture of sulphadimidine from guanidine nitrate

Raw material	Requirement per Kg of FP	Price per Kg in $	Cost in $ per Kg of FP
Guanidine nitrate	0.96	2.29	2.2
Methyl isobutylketone	1.6	1.36	2.2
Acetanilide	1.24	1.95	2.42
Caustic Soda flaked	1.79	0.335	0.6
Acetylacetone	0.8	9.49	7.59
Chlorosulphonic acid	4.5	0.22	0.99
			16

B (VI) Cost breakdown of bulk drug

Item	Cost for 500 MT in thousand US$	As percentage of total cost
Raw material	8000.0	81.2
Wages	60.0	0.62
Maintenance	300.0	3.05
Utilities	300.0	3.05
Depreciation	1000.0	10.15
Overhead	190.0	1.93
	9850.0	100.00

Cost per ton: $19,700

B (VII) Cost of raw material as percentage of total cost

Total cost of raw material	US$ 16	(A)
Total cost of production	US$ 19.7	(B)
A as percentage of B	81.2	

B (VIII) Cost breakdown of sulphadimidine formulation

Dosage form - tablet
Strength - 500 mg per tablet
Pack size - 1000 tablets in a tin

Item	Cost per pack in US$	As percentage of cost
Sulphadimidine	9.85	84.9
Other raw materials	0.533	4.59
Conversion cost 1/	0.81	6.98
Packaging cost 1/	0.10	0.86
Packaging materials	0.31	2.67
Ex-factory cost	11.603	100.0

1/ Includes direct wages, utility, depreciation, maintenance and general overhead.

TABLE I

NAMES OF MAJOR PRODUCERS OF SULPHADIMIDINE

Beecham Research Laboratories, UK

I.C.I. UK

Medimpex- Alkaloida, Hungary

May and Baker, UK

PRODUCERS IN THE DEVELOPING COUNTRIES

Egypt

NASAR Co.

India

I.D.P.L.

Mexico

Julian de Mexico, S.A. Laboratories

Production of India in 1979 - 383.2 tons.

Production of Egypt during 1977-78 has been reported to be 64 tons.

TETRACYCLINE

A. Production

Name of the country, producer and quantity produced are given in Table I

Consumption

Name of region and country and consumption are given in Table II

Forecast of World consumption

Year	1980	1985
Quantity in metric tons	2,180	2,130

Estimated average annual growth is zero

Patent

Production by Streptomyces Viridifacines. U.S. patent 2,712,517;2886,595 (1955,1959) both to Bristol labs.

Production by S. aureofacines. U.S. patent 3,005,023; 3,019,173 (1961, 1962) both to American Cyanamid.

Purification, U.S. patent 3,301,899 (1967) to Bristol-Myers)

Price

Price in the International market (average) in May 1980 - US$ 37.55 per Kg

B. Industrial Profile

Based on the data received from a developing country for the manufacture of Tetracycline in 1979

B (1) Outline of manufacturing process

Tetracycline is produced by fermentation using culture of specific strains of S. Viridifacines. At the end of the fermentation the broth is acidified and the micro-organism is removed by filtration using rotary vacuum precoat filters. The crude base is precipitated, filtered and dried in fluid bed drier.

To obtain the hydrochloride the crude base is dissolved in Butanol and Hydro-chloric acid is added. After filtration of the solution the Tetracycline hydrochloride is precipitated by raising the temperature to about 40°c. The product is centrifuged, washed, dried and packed.

Tetracycline is also produced by reductive dehalogenation of chlortetracycline which is produced by fermentation using specific strains of S. aureofacines.

B (II) Availability of intermediates and raw materials

In addition to the developed countries many of the advanced developing countries produce most of the raw materials required for the production of Tetracycline

B (III) Plant capacity

Based on the experience of a developing country minimum plant capacity recommended in 1979 is 30 M/T per year

B (IV) Investment

Based on the estimate of 1979 in a developing country the investment for a plant capacity of 30 M/T is $3.0 million.

B (V) Requirement of different intermediates and other raw material per kg of the finished product (F.P.)

TETRACYCLINE

Raw material	Requirements per kg of F.P. in kg	Price per kg in $	Cost in $ per kg of F.P.
Lard oil	0.56	1.8	0.10
Hyflosupercel	5.59	0.75	4.20
Strach	2.94	0.45	1.32
Ground nut oil	3.20	1.25	4.0
Oxaclic acid	2.42	1.13	2.75
Methylisobutyl Ketone	2.39	2.53	6.05
Arquad	1.93	4.5	8.68
Other raw materials			29.99

B (VI) Cost breakdown of bulk drug

Item	Cost for 30 m/T in thousand $	As percentage of total cost
Raw materials	900.00	48.25
Wages	52.31	2.80
Utilities	425.00	22.79
Depreciation	300.00	16.09
Maintenance	90.00	4.83
Overhead	97.69	5.24
	1,865.00	100.00

Cost per ton: $62166

B (VII) Cost of intermediates and other raw materials as percentage of total cost

Total cost of materials	$29.99	(A)
Total cost of production	$62.166	(B)
A as percentage of B	48.24	

B (VIII) COST BREAKDOWN OF TETRACYCLINE FORMULATION

Dosage form - capsule

Strength - 250 mg per capsule

Pack size - 100 capsules

Item	Cost per pack in US$	As percentage of cost
Tetracycline	1.78	52.04
Other raw materials	1.09	31.87
Conversion cost *	0.25	7.32
Packaging cost *	0.02	0.58
Packaging materials	0.28	8.19
Ex-factory cost	3.42	100.0

* includes direct wages, utilities, maintenance, depreciation and general overhead.

TABLE I

PRODUCTION OF TETRACYCLINE IN 1979

Country	Producers	Production in metric tons
United States	American Cyanamid Bristol-Myers Pfizer ING	460
Argentina	Pfizer	40
Brazil	American Cyanamid Pfizer Quimasa	205
France	Pfizer Massy (Paris)	
	Soc. Pointet-Grirard	180
Ireland	Proter (Aand D) Ltd Squibb	270
Italy	American Cyanamid Diaspa Lepetit Pierrel Proter	580
Spain	American Cyanamid	
	Antibioticos	55
U.K.	Pfizer	180
India	IDPL Cyanamid Synbiotics	100
Japan	Pfizer Taito Meiji	60
Korea	Chong Kung Dang Pfizer	50

PRODUCTION OF TETRACYCLINE IN DEVELOPING COUNTRIES IN 1979

Country	Producers	Production in metric tons
Argentina	Pfizer	
Brazil	Quimica Industrial Santo Amaro Pfizer Quimica Cyanamid Quimica do Brasil	
India	IDPL Cyanamid Synbiotics	
Mexico	Fermic Cyanamid de Mexico	

India's total production in 1979 -

Tetracycline Salt - 125.3 tons

Tetracycline base - 8.33 tons

CONSUMPTION OF TETRACYCLINE IN 1977

Region and Country	Consumption (metric tons)
North America	
United States	780
Latin America	
Argentina	90
Brazil	200
All others	175
Subtotal	465
Western Europe	
France	90
Germany	110
United Kingdom	90
All others	150
Subtotal	440
Asia, Africa, and Oceania	
India	100
Japan	80
Korea	40
Malaysia	35
Taiwan	100
Thailand	40
All others	100
Subtotal	495
TOTAL	2,180

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Lisbon, Portugal, 1-5 December 1980

THE PRICING AND AVAILABILITY OF INTERMEDIATES AND BULK DRUGS

Corrigendum

Page	Line	For	Read
20	17	(C)	NOTE (C)
25	8	table 10	table 11
27	2	SULPHAMETHAXAZOLE	SULPHAMETHOXAZOLE
	22	note (c)	note (D)
28	19	note (c)	note (D)
31	16	ter	term
33	21	Prices(India)and	prices and
36	26	recoverty	recovery
38	17	100.10	100.00
40	10	Nasar Co.	Nasr Co.
42	4	country producer	country, producer
45	16	0.295	0.285
50	20	120.88	20.88
53	8	Medimpenx	Medimpex
67	13	Gierrado	Gerardo
71	9	NASAR Co.	NASR Co.
73	Last entry		2.89
			Total 29.99

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