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**FEASIBILITY STUDY**

**ON**

**THE ESTABLISHMENT OF A MULTI PURPOSE PLANT  
FOR CHEMICAL**

**PROJECT NO UC/PHI/89/074  
CONTRACT NO 91/179**

**on behalf of**

**UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANISATION  
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**THE ESTABLISHMENT OF A MULTI PURPOSE PLANT  
FOR CHEMICAL SYNTHESIS**

**FEASIBILITY STUDY**

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## SECTION 1

### EXECUTIVE SUMMARY

#### 1.1 PROJECT BACKGROUND AND HISTORY

1.1.1 The aim of this feasibility study is to provide the Government of the Philippines with a basis for rational decision making concerning the introduction and installation of a development orientated multi-purpose chemical plant for chemical synthesis.

1.1.2 The United Nations Development Organisation (UNIDO) commissioned Manderstam Consulting Services to prepare a feasibility study to investigate the technical feasibility, commercial profitability and economic viability of the project proposal, as per the terms of reference presented at Appendix 1-1.

1.1.3 The field work which formed much of the basis of this appraisal was undertaken in November 1991, and the assistance and cooperation received from all those concerned in the Philippines is hereby gratefully acknowledged.

1.1.4 The initiator of this project is the Ministry of Health in the Philippines Government at San Lazaro Compound, Rizal Avenue, Santa Cruz, Manila, Philippines, telephone: 711 6771/711 6105.

#### 1.2 PROJECT BACKGROUND

1.2.1 The drug industry is an important sector in the Philippines. Drugs are produced, imported and distributed in a free market system. The main manufacturing activity is formulation and packaging of final dosage forms from imported materials.

1.2.2 In order to have high quality pharmaceutical products more affordable and acceptable, a National Drug Policy (NDP) was enunciated. One of the four pillars of NDP is the development of the national capability to manufacture intermediate and basic chemicals so that the Philippines is not totally reliant on foreign services.

1.2.3 The introduction and installation of a development orientated multi purpose chemical pilot plant in the Philippines has been identified as an important element in this strategy for the development of the upstream integration of the indigenous pharmaceutical industry.

1.2.4 At the time of this study, only one organisation, Chemfields, was carrying out the synthesis of pharmaceuticals in the Philippines. Chemfields, a company owned jointly by United Laboratories (40%) and the Philippines government (60%) manufactures semi synthetic penicillins from imported intermediates.

1.2.5 The concept of this pilot plant is to develop expertise in chemical synthesis and identify products and processes at greater than laboratory scale production, thus facilitating the possibility of later establishment of specialist full scale production plants.

1.2.6 The Terms of Reference for the project are given in Appendix 1-1 and the most important features of the multi purpose pilot plant are to provide facilities to:

- introduce and develop the experience of chemical synthesis of fine chemicals and pharmaceuticals
- provide the range of equipment for adequate scaling up facilities and for research and development
- provide some limited capacity in production of several pharmaceutical chemicals, fine chemicals or their intermediates (e.g. in semi-synthetic antibiotics)
- provide sufficient facilities and capacity to incorporate development of additional upstream integration or introduction of new products
- provide a training facility
- develop the atmosphere for progressive advancement in scientific skills from innovation to accomplishment.

1.2.7 The project proposals emphasise the training and development objectives of the multi purpose pilot plant. However the plant is to be designed from the outset to produce products which will be sold in bulk quantities to domestic downstream companies on a competitive price and quality basis against the alternative sources of imported products.



1.2.8 It is fully expected that it will be difficult for the plant to be financially viable and meet statutory approvals set against the objectives of training and development. As such, support in terms of both manufacturing infrastructure from existing facilities and also readily accessible market have been identified and assumed from the outset of our analysis.

1.2.9 We have assumed that the ready access to the market place will be achieved by collaboration with United Laboratories. Manufacturing infrastructure requirements have been assumed by siting the proposed multi products pilot plant at the existing Chemfields production facility (40% owned by United Laboratories). Alternatives with respect to marketing and manufacturing strategies are discussed but none are obviously as attractive as those involving United Laboratories. However, despite representations at senior level we were unable to obtain details of United Laboratories strategic thinking to confirm our assumptions.

1.2.10 The original project proposals provided a preliminary list of 10 products to which further products have been considered on the basis of our market examination with priority being given to paracetamol and isoniazid.

The key parameters for product selection were:

**Medical Acceptability** - To be compatible with the objectives of the Department of Health.

**Manufacturing Compatibility** - To ensure that all products could be made in a multi product plant.

**Technical Considerations** - A review of other factors which could prevent local manufacture (eg. patent restrictions).

**Reference to Unilab** - An assessment of the requirements of Unilab in terms of tonnage and price sensitivity.

**Profitability Potential** - A negative screen to eliminate serious loss makers.

1.2.11 The project is designed solely to contribute to the chemical manufacturing sector in the Philippines. As such it is not intended to cater for the bulk of the domestic market, much less have a surplus for export. In the longer term, however, it is believed that experience developed in this plant will lead to a series of larger specialist units.

1.3 MARKET

1.3.1 Based on a detailed assessment of product alternatives, this study concentrated on the potential for producing ten pharmaceuticals :

Ethambutol	Nifedipine
Ibuprofen	Paracetamol
Isoniazid	Pyrazinamide
Mefenamic Acid	Sulfamethoxazole
Metronidazole	Trimethoprim

At present a total of some 304 tons of these items appear to be imported into the Philippines.

1.3.2 All of these drugs are classified in the National Drug Formulary, and most are listed as essential for both private and public health care, with particular reference to the treatment of tuberculosis, respiratory and other infections and diarrhoea. Paracetamol has been included as this is the single most important drug currently in use in the Philippines. It was further confirmed that all ten drugs listed are off-patent, and are therefore available for manufacture.

1.3.3 It is further estimated that United Laboratories are currently responsible for approximately 60% of these imports, but its share of the market per individual product varies widely. Whereas it clearly dominates the markets for Ibuprofen, Isoniazid and Paracetamol, it has little or no share in those for Metronidazole, Pyrazinamide and Sulfamethoxazole/Trimethoprim.

1.3.4 Our projection of future demand has been based on three principal elements : continued population growth, the trend to higher expenditure on health care and drugs, and relevant changes in morbidity rates. Given the growth factors identified for each individual product, demand is thus expected to increase as follows :

Tonnes	Base	1995	2000	2005
Ethambutol	8.8	10.7	12.8	15.1
Ibuprofen	25.2	30.3	36.0	42.3
Isoniazid	28.4	34.6	41.5	48.8
Mefenamic Acid	20.0	24.0	28.5	33.5
Metronidazole	2.0	2.4	2.9	3.4
Nifedipine	0.2	0.2	0.3	0.3
Paracetamol	192.0	230.8	274.1	322.4
Pyrazinamide	11.5	14.0	16.8	19.8
Sulfamethoxazole	12.8	15.5	18.7	22.2
Trimethoprim	3.3	4.0	4.8	5.7
Total	304.2	366.5	436.4	513.5

1.3.5 It is anticipated that the market for the pilot plant would be limited to United Laboratories and to those indigenous manufacturers who would be prepared to support the development of local production expertise, notwithstanding the fact that they may have to pay a 20% premium over and above world market prices.

1.3.6 Based on our assessment of Unilab's share of the market for each product, and the extent to which it could reasonably be expected to source its requirements from a local supplier, production has been limited to 52.5 tonnes of five products in the initial instance :

	Unilab Total Demand	Local Purchase	Sales to Unilab	Sales to Others	Total Sales
Ethambutol	2.2	50%	1.1	-	1.1
Ibuprofen	27.3	40%	11.2	-	11.2
Isoniazid	20.8	40%	8.1	-	8.1
Mefenamic Acid	5.5	25%	1.4	1.1	2.5
Paracetamol	150.0	20%	30.7	1.9	32.6
	<u>205.8</u>		<u>52.5</u>	<u>3.0</u>	<u>55.5</u>

The above figures would give the pilot plant an overall market penetration of just under 17% by reference to the 1995 figures.

1.3.7 Projected sales revenues, calculated by reference to forecast sales and the prices which have been assumed for each product, may be summarised as follows :

	1995 *	1996 - 2004
Ethambutol	P 936,000	P 1,287,000
Ibuprofen	P 6,989,000	P 9,318,000
Isoniazid	P 3,013,000	P 4,001,000
Mefenamic Acid	P 1,087,000	P 1,430,000
Paracetamol	P 4,570,000	P 6,078,000
	<u>P 16,595,000</u>	<u>P 22,114,000</u>

\* based on 75% capacity utilisation

1.3.8 The overall production schedule (see Appendix 3-10) is based on 75% of 1995 sales figures and thereafter the production schedule is held constant at 1995 sales tonnage:-

<u>Product</u>	<u>Output (Tonnes/Year)</u>					
	1995	1996	1997	1998	1999	2005
Paracetamol	24.45	32.6	32.6	32.6	32.6	32.6
Isoniazid	6.07	8.1	8.1	8.1	8.1	8.1
Ethambutol	0.825	1.1	1.1	1.1	1.1	1.1
Mefenamic Acid	1.875	2.5	2.5	2.5	2.5	2.5
Ibuprofen	8.4	11.2	11.2	11.2	11.2	11.2
<b>TOTAL</b>	<b>41.62</b>	<b>55.5</b>	<b>55.5</b>	<b>55.5</b>	<b>55.5</b>	<b>55.5</b>

1.3.9 The production schedule is based on working an average 2 shifts per 8 hour day, 5 days per week, 47 weeks per year. Production would be based on a series of campaigns whereby only one product is manufactured exclusively for a period of weeks as set out below.

	<u>Batch (kgs)</u>	<u>Batches per day</u>	<u>Duration of Campaign (weeks)</u>
Paracetamol	260	2	12.5
Isoniazid	100	1	16.2
Ethambutol	100	1	2.2
Mefenamic Acid	100	1	5.0
Ibuprofen	100	2	11.2

1.3.10 The following table summarises our computations of annual production in tonnes.

	Shifts	Batches/day	Tonnage 5 days/week	Tonnage 6 days/week	Tonnage 7 days/week	+15%
Paracetamol	3	4	65.20	78.24	91.28	104.97
Isoniazid	3	2	16.20	19.44	22.68	26.08
Ethambutol	3	1½	1.65	1.98	2.31	2.65
Mefenamic Acid	3	4	10.00	12.00	14.00	16.10
Ibuprofen	3	4	22.40	26.88	31.36	36.06
		(with additional Reactor B	----- 115.45	----- 138.54	----- 161.63	----- 185.87
				A		B

A = Feasible Normal Plant Capacity = 138.54 Tonnes/Annum  
 B = Nominal Maximum Plant Capacity = 185.87 Tonnes/Annum

#### 1.4 MATERIALS AND INPUTS

1.4.1 There are no chemicals produced in the Philippines which could be used in the manufacture of the pharmaceuticals considered.

1.4.2 The annual supply requirements of the main feedstocks and intermediates include some 27 items which are not available in the Philippines and must be imported.

1.4.3 Large price variances were found in the quoted prices for all the imported chemicals, most notably the key ingredients specific to each process. The conclusion drawn is that there is often a large elasticity available between production cost and selling prices of these intermediates which can often deter new manufacturing operations from entering the market.

1.4.4 To manufacture the recommended pharmaceuticals would require a supply of utilities as follows:

Power	:	100KW
Cooling Water	:	25 tonnes/day
Steam	:	0.8 tonnes/day

1.5 LOCATION

1.5.1 The preferred location and that assumed in this study is Chemfields factory, south of Manila in the Calabarzon region, in that the following advantages are foreseen:

- Unilab own 40% of Chemfields and provide all management and labour.
- Unilab can provide the largest single source access to the market as discussed.
- Chemfields site already has the infrastructure for a small chemical factory: administration, power supplies, waste disposal, solvent recovery and experienced workforce exist to act as a nucleus.
- Chemfields own 27 hectares to the rear of the factory as shown on the proposed site layout, see Appendix 5-1, and could easily accommodate an extension requiring approximately 4,000m<sup>2</sup>.
- Easy access to Metro Manila and the University at Los Banos.

1.6 PROJECT ENGINEERING

1.6.1 The aim of the project is to produce a modern, flexible pilot plant capable of producing a range of pharmaceuticals to internationally acceptable standards of quality and productivity.

- 1.6.2 For the pharmaceuticals proposed for manufacture, a conceptual design for a multi purpose plant on a pilot plant scale has been prepared, followed by a preliminary engineering design in sufficient detail to allow a cost estimate to be made to +15%.
- 1.6.3 The chemical syntheses are achieved by multi stage batch operations. The proposed plant consists of a number of reaction vessels, condensers, pumps, feed tanks, centrifuge/filters, driers and receivers manufactured principally in stainless steel, plastic and mild steel (glass lined). The main items are interconnected to facilitate their multi purpose roles.
- 1.6.4 There are no important patents still active for the processes considered. However, the practical details of the manufacturing process are still commercial secrets. Not all international manufacturers of these products manufacture them all and it is not conceivable to have a separate technical partner for each of the pharmaceuticals to be manufactured. A compromise may be possible whereby know-how packages can be negotiated against limited production/competition guarantees.
- 1.6.5 The ideal civil engineering requirements consist of a process building of 900m<sup>2</sup> and a warehouse of 1,300m<sup>2</sup>. However, in order to reduce the capital costs, these requirements may be reduced to just the process building with storage requirements being provided within the process building or within the existing Chemfields facilities. The process building would be clear span portal construction with proprietary cladding complete with extraction fans. All floors should be acid resistant.
- 1.6.6 The plant design is intended to meet internationally acceptable quality levels to the equivalent of United States (USP) or British Pharmacopoeia (BP) standards. However achieving and monitoring such standards set against a development and training rationale could well prove to be a fundamental obstacle.
- 1.6.7 The environmental impact of the proposed plant in the region is not likely to lead to any significant short or long term problems. Waste water treatment is required and it has been anticipated that this will be provided by the existing Chemfields factory.

1.7 **MANPOWER**

1.7.1 Various technical and commercially trained personnel are required for such an undertaking. The technologies are new to the Philippines and adequate training is of paramount importance.

1.7.2 An abbreviated organisation structure is shown below:

General Manager

Production and Projects Chemical Engineering Process Maintenance Labour	Administration Finance and Accounts Warehouse Drivers	Quality and Technical Services Chemistry Sales	Training and Development
--	--	--	-----------------------------

1.7.3 The manpower requirements which we estimate to be appropriate in this project are given in below. The workforce numbers 43 and is based on there being a degree of flexibility between functions, eg process operators should be able to carry out simple chemical tests in a shift laboratory. This theme is the basis of the envisaged training programmes.

<u>POSITION</u>	<u>NUMBER</u>	<u>TYPE OF WORK</u>
General Manager	1	days
Senior Managers		
Chemical Engineers	2	shifts (2 x 1)
Chemists	2	shifts (2 x 1)
Administrator	1	days
Training and Development	1	days
Middle Management		
Process Superintendents	3	shifts (2 x 1 + spare)
Maintenance Foreman	1	days
Warehouse Foreman	3	shifts (2 x 1 + spare)
Sales Liaison	1	days

<u>POSITION</u>	<u>NUMBER</u>	<u>TYPE OF WORK</u>
Technicians and Administration		
Chemists	6	
Operators	6	
Storemen	3	
Maintenance	3 (average)	shifts (2 x 1 + 1 on average)
Administration	5	days
Unskilled		
Drivers	2	shifts (2 x 1)
Labour	2	shifts (2 x 1)
	--	
<b>TOTAL</b>	<b>43</b>	

1.8 **IMPLEMENTATION SCHEDULE**

1.8.1 On the basis that approval to proceed is given by the end of the third quarter of 1992 and award of contracts are made by the end of the third quarter of 1993, production could begin in the first quarter of 1995 reaching full production by the end of 1996.

1.9 **FINANCIAL EVALUATION**

1.9.1 The initial investment cost of the proposed pilot plant has been estimated at a total of P 233.2 million, equivalent to approximately US\$ 9 million. Only 40% of this total would be payable in foreign currency :

<b>Initial Fixed Investment Costs</b>	
- Structures/Civil Works	: P 116,247
- Machinery and Equipment	: P 65,981
	<hr/>
	P 182,228
 <b>Pre-Production Expenditures</b>	 : P 35,149
 <b>Working Capital Requirement</b>	 : P 15,796
	<hr/>
<b>Total</b>	<b>: P 233,173</b>
	<hr/> <hr/>



- 1.9.2 The financing arrangements proposed would result in an acceptable debt : equity ratio of 0.99 : 1 at project implementation, and are summarised as follows :

<b>Equity Capital</b>	
- Project Promoters	: P 70,332
- Financial Agencies	: P 46,888
<b>Long-Term Borrowings</b>	
- Foreign Currency	: P 45,542
- Local Currency	: P 70,411
<b>Current Liabilities</b>	
- at full capacity	: P 1,266
<b>Total</b>	: <u><u>P 234,439</u></u>

- 1.9.3 It has been assumed that the local project promoters would wish to retain an overall majority interest, consequently the participation of external financial institutions/agencies has been limited to 40%.

- 1.9.4 Expenditures on raw material inputs and utilities have been calculated by reference to clearly specified usage and cost figures per individual input, and provide the basis for estimating the unit cost of each of the products to be manufactured. Comparison of these unit costs with the anticipated selling prices highlights the fact that the project would produce both Mefenamic Acid and Paracetamol at a gross loss :

per kg	Input Cost	Sales Price*	Gross Margin	% Margin
Ethambutol	284	1,170	886	76%
Ibuprofen	340	832	492	59%
Isoniazid	338	494	156	32%
Mefenamic Acid	591	572	( 19)	( 3%)
Paracetamol	211	187	( 24)	(13%)

\* inclusive of a 20% premium

- 1.9.5 On the basis of the 10-year financial projections prepared, the proposed pilot plant would not appear to be a feasible proposition :

- a) The project would record an operating loss in each year, due to the fact that the estimated input costs in respect of Paracetamol in particular exceed the selling price assumed. Accumulated losses would exceed the equity capital by the third year of operation, at which point the plant would be technically bankrupt.

- b) By the end of the 10-year period, the accumulated losses would total nearly P 263.9 million, and the cumulative cash shortfall would amount to P 220.6 million.

1.9.6 An alternative scenario was prepared in order to assess the impact of excluding Paracetamol from the production programme, and increasing the output of Ethambutol, Ibuprofen and Isoniazid to a level which would satisfy all Unilab's estimated requirements. Unfortunately, the results of this analysis were not encouraging :

- a) Although the pilot plant would make operating profits, these would not be sufficient to cover financial costs and depreciation. Sales would have to increase by a further 75% to enable the project to achieve break-even.
- b) By the end of the 10-year period, accumulated losses would total nearly P 155 million, and the cash shortfall would exceed P 112.6 million.
- c) The internal rate of return on total investment was calculated at -8.1%, and that on equity capital at -13.3%.

1.9.7 Three further analyses were then prepared to ascertain what changes would be necessary to enable the project to break-even. These confirmed that sales prices would have to increase by 36% over and above those assumed, or the cost of all direct factory inputs would have to be reduced by 50%. Alternatively, a 21% increase in sales prices, combined with a 21% reduction in the cost of factory inputs, would bring about the same result.

1.9.8 A further analysis was prepared after considerations on the capital cost estimates. These showed a very high component for warehousing, offices and lecture rooms. Secure warehousing is important when chemicals are concerned and the original estimate was based on a stand-alone basis. However, if the Chemfields site is used, warehousing facilities could be obtained from Chemfields since the amounts involved would not be large. On this basis, capital costs would be reduced by P46.5 million.

1.9.9 With the reduced capital demand, if the Philippines market for Ethambutol, Ibuprofen and Isoniazid at the 1995 demand level were to be entirely supplied by the pilot plant then the operating profits would rise to P18 million, and a positive cash surplus could be recorded in year 10.

1.10 ECONOMIC ANALYSIS

1.10.1 Notwithstanding the fact that the proposed multi-purpose pilot plant is not intended to be a commercial venture, the prospects for its implementation and operation appear to be no better than marginal. In addition, it is considered that this would depend on a combination of four factors in particular :

- successful negotiation of grant monies to fund a significant proportion of the capital costs;
- exclusion of Paracetamol from the production programme;
- an increase in selling prices or, alternatively, direct subsidisation of the production costs; and
- a reduction in input costs.

1.10.2 It is anticipated that the plant would employ a total of 43 members of staff, at an annual wage and salary cost of approximately P 5.6 million. However, none of the chemicals used in the production process could be obtained from local sources of supply and, as a result, utilisation of domestic resources would be limited to utilities and such sundry consumable items as protective clothing and office supplies.

1.10.3 However, the pilot plant would fulfil an important function, in that it would provide access to extensive training facilities on an on-going basis, and would thereby serve to develop local expertise and experience in this particular field.

1.11 CONCLUSIONS AND RECOMMENDATIONS

1.11.1 A range of pharmaceuticals were considered for batch production in a multi purpose pilot plant scale manufacturing facility.

1.11.2 Based on a Market Survey and an assessment of Unilab's share of the market we believe a multi purpose pilot plant could supply on an annual basis:

	<u>Tonnes</u>
Ethambutol	1.1
Ibuprofen	11.2
Isoniazid	8.1
Mefenamic Acid	2.5
Paracetamol	32.6

representing an overall market penetration of about 17%.

- 1.11.3 No chemicals used in the preparation of these pharmaceuticals are produced in the Philippines and some 27 items would have to be imported.
- 1.11.4 The best location for such a plant would be on Chemfields site adjacent to their plant and using common services such as electricity and water supplies, waste treatment facilities, warehousing and security.
- 1.11.5 A multi purpose plant would employ an additional 43 people when it reached full production in 1996.
- 1.11.6 On the basis of a completely independent manufacturing plant the total cost would be P233.3 million of which some 40% would need to be in foreign currency. However, by siting the plant on the Chemfields site and sharing common support facilities, the capital cost would be reduced by P46.5 million.
- 1.11.7 On the foregoing basis, the pilot plant would make an operating profit of P7.4 million when operating at 95% capacity and would not be a viable commercial operation.
- 1.11.8 If the Philippines market for Ethambutol, Ibuprofen and Isoniazid at the 1995 demand level were to be entirely supplied by the pilot plant then the operating profits would rise to P18 million, and a positive cash surplus could be recorded in year 10.
- 1.11.9 Given the strategic value of such a project to the Philippines nation, the building of a multi purpose pilot plant scale manufacturing units for pharmaceuticals is worthy of serious consideration in that it would:
- result in establishing a core of experienced personnel in fine chemicals manufacture
  - form a basis for research into alternative pharmaceutical products manufacture
  - introduce a degree of independence into the supply of pharmaceuticals to the Philippines market
  - form the basis from which pharmaceutical manufacture in the Philippines could be expanded and made more profitable, thus attracting more investment.

## SECTION 2

### PROJECT BACKGROUND AND HISTORY

#### 2.1 PROJECT BACKGROUND

##### 2.1.1 Strategy for Upstream Integration in the Pharmaceutical Industry

The drug industry is an important sector in the Philippines. Drugs are produced, imported and distributed in a free market system. The main manufacturing activity is formulation and packaging of final dosage forms from imported materials. Almost all the raw materials for pharmaceutical production are imported.

In order to have high quality pharmaceutical products more affordable and acceptable, a National Drug Policy (NDP) was enunciated. One of the four pillars of NDP is the development of the national capability to manufacture intermediate and basic chemicals so that the Philippines is not totally reliant on foreign services, thereby avoiding the detrimental effects of such dependence.

The introduction and installation of a development orientated multi purpose chemical pilot plant in the Philippines has been identified within this strategy for the development of the upstream integration of the indigenous pharmaceutical industry.

##### 2.1.2 The Pharmaceutical Industry in the Philippines

The Philippines has a large and active industrial sector with approximately 250 companies engaged in the compounding of pharmaceutical chemicals and the production of final dosage forms. However, almost all pharmaceutical chemicals are imported. The only chemicals made in the Philippines are semi-synthetic penicillins manufactured from imported intermediates by Chemfields, a company owned jointly by United Laboratories (40%) and the Philippines government (60%).

The country has a pool of qualified pharmacists and chemical engineers and there are a number of biotechnology facilities centred around the University of the Philippines at Los Banos. There is however little opportunity for them to gain experience in the manufacture of fine chemicals and intermediates.

The concept of this pilot plant is to develop expertise and identify products and processes at greater than laboratory scale production, thus facilitating the possibility of later establishment of specialist full scale production plants.

2.1.3

Terms of Reference

The Government of the Philippines is to be provided with a rational decision making basis for assessing the technical and financial feasibility of establishing a multi purpose pilot plant for chemical synthesis.

The Terms of Reference for the project are given in Appendix 1-1 and the most important features of the multi purpose pilot plant are to provide facilities to:

- introduce and develop the experience of chemical synthesis of fine chemicals and pharmaceuticals
- provide the range of equipment for adequate scaling up facilities and for research and development
- provide some limited capacity in production of several pharmaceutical chemicals, fine chemicals or their intermediates (e.g. in semi-synthetic antibiotics)
- provide sufficient facilities and capacity to incorporate development of additional upstream integration or introduction of new products
- provide a training facility
- develop the atmosphere for progressive advancement in scientific skills from innovation to accomplishment.

2.1.4

Manufacturing Philosophy

The terms of reference emphasise the training and development objectives of the proposed multi purpose pilot plant. However the plant is to be designed from the outset to produce products which will be sold in bulk quantities to domestic downstream companies on a competitive price and quality basis against the alternative sources of imported products.

Within the framework of the project objectives, there therefore exists a threefold balance between contradictory requirements;

- a) the implied inefficiencies of small scale production from a non dedicated plant,
- b) the need to make a positive contribution not only to the domestic requirements and supply of pharmaceuticals but also to overhead and labour absorption in running the plant,

- c) the need to meet national and statutory pharmaceutical requirements for approval for human consumption set against a training and development objective.

In summary therefore, it is fully expected that it will be difficult for the plant to be financially viable and meet statutory approvals set against the objectives of training and development and as such, support in terms of manufacturing infrastructure from existing facilities and readily accessible market have been identified and assumed from the outset of our analysis.

We have assumed that the ready access to the market place will be achieved by collaboration with United Laboratories. Manufacturing infrastructure requirements have been assumed by siting the proposed multi products pilot plant at the existing Chemfields production facility (40% owned by United Laboratories). Alternatives with respect to marketing and manufacturing strategies are discussed but none are obviously as attractive as those involving United Laboratories.

2.1.5

#### The Role of United Laboratories (Unilab)

Unilab dominates the pharmaceutical manufacturing sector in the Philippines. It is several times larger than the largest multinationals and it has a wide spread of interests across most of the generic drugs. There are a number of other Filipino owned manufacturing companies but they are relatively small and underfunded compared with Unilab.

However, Unilab expertise is largely in the compounding of drugs and, in particular, the marketing of final dosage forms. (It operates via six or seven subsidiaries, each with their own range of drugs and often competing with each other). It has gained experience in manufacturing intermediates by its partial ownership of Chemfields but it has not shown enthusiasm in developing this side of the business.

Chemfields has been established for about ten years and the capacity has been gradually increased over that period. We are not able to find out if it has operated profitably over that time but it is probably profitable now as further expansion is planned.

Despite representations at senior level we were unable to obtain details of United Laboratories strategic thinking to confirm our assumptions.

2.1.6

Product Selection

The terms of reference provided a preliminary list of 10 products to which further products were to be added on the basis of our market examination with priority being given to paracetamol and isoniazid.

The key parameters for product selection were:

**Medical Acceptability** - To be compatible with the objectives of the Department of Health.

**Manufacturing Compatibility** - To ensure that all products could be made in a multi product plant.

**Technical Considerations** - A review of other factors which could prevent local manufacture(eg. patent restrictions).

**Reference to Unilab** - An assessment of the requirements of Unilab in terms of tonnage and price sensitivity.

**Profitability Potential** - A negative screen to eliminate serious loss makers.

2.1.7

Geographical Level of Involvement

The project is designed solely to contribute to the chemical manufacturing sector in the Philippines. As such it is not intended to cater for the bulk of the domestic market, much less have a surplus for export. In the longer term, however, it is believed that experience developed in this plant will lead to a series of larger specialist units.

2.2

PROJECT PROMOTER

The initiator of this project, together with previous UNIDO studies, is the Ministry of Health in the Philippine Government, whose address is:-

San Lazaro Compound, Rizal Avenue, Santa Cruz, Manila, Philippines, telephone 711-6771/711-6105



2.3

PROJECT HISTORY

2.3.1

The United Nations Industrial Development Organisation (UNIDO) has for some years co-operated with the Ministry of Health in the Philippines towards identifying and establishing a locally based pharmaceutical industry.

2.3.2

Working in close conjunction with the Philippine Government, UNIDO has produced previous studies of the pharmaceutical industry in the Philippines with the objective of pinpointing the areas most likely to yield successful results.

2.3.3

A major examination of the pharmaceutical industry was carried out under the auspices of UNIDO by a team of experts between 1987 and 1989 resulting in the following reports.

- "Assessment of the agricultural raw materials for drug preparation in the Philippines" (W Padolina, UNIDO, 14 September 1988)
- "Assessment of Research and Development in Biotechnology and Biochemistry in relation to development of Pharmaceutical Industry in the Philippines" (W Padolina, UNIDO, 19 September 1988)
- "Medicinal Plants and Essential Oils - Philippine experience" (W Padolina, UNIDO 19 September 1988)
- "State of Science and Technology in the Philippines" (W Padolina, UNIDO, 5 October 1988)
- "Fermentation Processes, Manpower Training, Suggestions for New Biotechnology in the Philippines" (H Bungay, 19 December 1988)
- "Semi-synthesis of Antibiotics" (R Sciaky, UNIDO, 16 February 1989)
- "Environment and Possibility of Pharmaceutical Industry in Philippines and Upstream Integration" (K Ivanov et al, UNIDO, 9 March 1989)
- "Manufacture of Antibiotics through Fermentation" (V Gallo, UNIDO, 17 April 1989)

2.3.4

The specific report which led to this feasibility study for a multi product pilot plant was "Philippines Pharmaceutical Industry Development Study" DP/PHI/87/019, Dr W N Walker, UNIDO, 25th July 1988.

This study identified the problems in establishing a fine chemical industry in the Philippines and suggested the establishment of a multi-purpose pilot plant as a catalyst for such an industry.

2.3.5 Manderstam Consulting Services

The present study has been completed for UNIDO on behalf of the Philippine Ministry of Health by Manderstam Consulting Services of London.

### SECTION 3

#### MARKET AND PLANT CAPACITY

##### 3.1 BACKGROUND

##### 3.1.1 Original Selection of Products

3.1.1.1 The 10 pharmaceuticals listed in the Terms of Reference at Appendix 1-1 were used as the starting point for our analysis of the proposed multi-products pilot plant. These products had been selected on the basis of the preliminary study referred to in Section 2.3.4, and are as follows :

<u>Name of Drug</u>	<u>Treatment</u>
Ethambutol	Tuberculosis
Furazolidone	Diarrhoea
Glaphenine	Pain conditions
Ibuprofen	Inflammations
Isoniazid	Tuberculosis
Mefenamic Acid	Muscular pains/inflammations
Metronidazole	Infections
Pyrazinamide	Tuberculosis
Sulfamethoxazole )	Taken in combination for the
Trimethoprim )	treatment of Pneumonia

3.1.1.2 The present study further examines this original list, and the criteria used for their selection.

##### 3.1.1.3 National Drug Requirements

The main drug requirements of both the public and private sectors were ascertained, listed and compared, and suitable products for chemical synthesis were identified. A preliminary list was then drawn up of those drugs regarded as important for national health (Appendix 3-1 refers). Seven of the pharmaceuticals identified appear as priority products.

##### 3.1.1.4 National Health Priorities

The five predominant sicknesses in the Philippines and their respective incidence in 1988 are as follows :-

#### Morbidity Rate per 100,000

Bronchitis	1,293.4
Diarrhoea	1,063.3
Influenza	981.6
Pneumonia	343.8
Tuberculosis	311.8

Source : Philippines Health Statistics

The pharmaceuticals listed are instrumental in treating all of these conditions.

The Department of Health has also established its own list of medical priorities :

Tuberculosis  
Malaria  
Schistosomiasis (Bilharziasis)  
Leprosy  
Diarrhoea  
ARI (Respiratory Infections)

The ten drugs identified are vital to the treatment of tuberculosis, diarrhoea and ARI. However, the drugs used to treat the remaining three priorities are not made by chemical synthesis.

The incidence and trend of the notifiable diseases most closely linked to these priorities were examined, and details are given in Appendix 3-2. It is clear that progress in reducing the morbidity rate has been slow, and this reinforces the original choice of ten drugs.

3.1.1.5 **Drug Consumption**

Import figures for all drugs in 1987, as per the Philippines Pharmaceutical Development Study carried out in that year, were analyzed and the twenty most important products were ranked in order of volume (Appendix 3-3 refers). All ten drugs listed in the Terms of Reference fell into this category at the time of initial selection.

3.1.2 **Additional Product Possibilities**

3.1.2.1 A further examination was then carried out to confirm the completeness of the original product selection, as a result of which three additional drugs have been included in the listing :

<b>Name of Drug</b>	<b>Treatment</b>
Paracetamol	Ulcers, pain relief
Nifedipine	Hypertension
Salbutamol	Asthma

3.1.2.2 As is apparent from the list of pharmaceutical imports set out in Appendix 3-3, Paracetamol (or acetaminophen) is the single most important drug currently in use in the Philippines. Owing to its importance world-wide, it tends to be produced on a large scale in continuous process plants, and cannot be manufactured economically in a limited capacity batch plant.

3.1.2.3 However, the Terms of Reference highlight the omission of Paracetamol and, given that these also specify that the purpose of the proposed pilot plant is to develop indigenous expertise in the chemical synthesis of fine chemicals and pharmaceuticals, the inclusion of this product was considered to be appropriate.

3.1.2.4 A sample survey of pharmacists, doctors, manufacturers and Department of Health officials was undertaken in order to identify any other important omissions and, without exception, all respondents nominated Nifedipine and Salbutamol. Certain other drugs suggested were not included, either because they cannot be produced by chemical synthesis, or because they were nominated by fewer than 50% of survey respondents.

3.1.2.5 Finally, the Bureau of Food and Drugs (BFAD) has carried out an assessment of the most important drugs for the general health of the population, the objective of which is to make these drugs available as widely as possible and at the least possible cost. Full details are presented at Appendix 3-4, from which it may be noted that Paracetamol, Nifedipine and Salbutamol all appear on the priority list.

3.1.3 Screening Criteria

3.1.3.1 The preliminary listing of thirteen candidate drugs was then screened by reference to the following criteria in order to eliminate any drugs which did not conform to the objectives of the project as set out in the Terms of Reference at Appendix 1-1 :

- Medical acceptability
- Suitability for purchase by United Laboratories
- Manufacturing compatibility
- Profitability potential
- Technical considerations

3.1.3.2 Medical Acceptability

To ensure that the drugs listed were compatible with the objectives of the Department of Health, they were all checked against the National Drug Formulary (NDF). The classification and use of each drug as per the latter is detailed in Appendix 3-5.

Neither Furazolidone nor Glaphenine appear on the NDF and further investigation confirmed that :

- a) Furazolidone was originally included in the NDF by the National Drug Committee as a complementary drug for anti-diarrhoea treatments. However, therapeutic practice has since moved away from the use of anti-diarrhoea agents, and now emphasises fluid replacement.
- b) Glaphenine has been the subject of local reports of anaphylaxis and, although there has been no documented study, the National Drug Committee is no longer recommending its inclusion in the NDF.

On the basis that these two drugs would therefore not receive official endorsement, it was decided that they should be eliminated from the list.

#### 3.1.3.3 Suitability for Purchase by United Laboratories

The Terms of Reference specify that the interests of United Laboratories should be considered, given that this company "is a potential buyer of the proposed products".

United Laboratories has a wide spread of interests in the generic drugs business, and is the largest domestic manufacturer of drugs in the Philippines. Management expressed an interest in the local sourcing of all the drugs listed, but were not prepared to give an order of priority. In the absence of any specific guidance from United Laboratories, their relative interest in each drug was thus calculated by reference to their share of total imports by volume. Such details as were available for the years 1988 to 1990 are presented at Appendix 3-6.

Based on imports over this period, Unilab's domestic sourcing requirements would include the following (in assessed order of importance) :-

- Paracetamol
- Ibuprofen
- Isoniazid
- Mefenamic Acid
- Sulfamethoxazole
- Ethambutol
- Pyrazinamide
- Trimethoprim
- Nifedipine
- Salbutamol

This is further examined in Section 3.4.4.

#### 3.1.3.4 Manufacturing Compatibility

All the products in question are basically compatible in terms of process route, equipment and utilities (Section 3.8 refers).

3.1.3.5 **Profitability Potential**

The Terms of Reference state that the proposed pilot plant should be financially self-sustained, even though its scale is such that certain chemicals would have to be produced in batches which are less than optimal in economic terms. However, should the assessment of manufacturing costs show any product to be a major loss generator, serious consideration might have to be given to its exclusion from the manufacturing programme.

3.1.3.6 **Technical Considerations**

The patent status of each drug was examined, and it was confirmed that, with the exception of Salbutamol, all the products in question were off patent and available for manufacture.

In addition, the final dosage form of each drug was checked to ascertain whether its manufacture would be practicable in the Philippines. Once again, with the exception of Salbutamol, all the drugs were commonly available in the form of tablets or capsules. However, Salbutamol is an anti-asthma drug which is normally administered by direct inhalation, and virtually all requirements are supplied in a variety of specialist packs. In view of the fact that these final dosage forms are neither made nor packaged in the Philippines, this was taken as further justification for excluding Salbutamol from consideration.

3.1.4 **Final Choice of Products**

3.1.4.1 On the basis of our assessment of each of the product alternatives, it was concluded that the present study should concentrate on ten pharmaceuticals :

Ethambutol  
Ibuprofen  
Isoniazid  
Mefenamic Acid  
Metronidazole  
Nifedipine  
Paracetamol  
Pyrazinamide  
Sulphamethoxazole  
Trimethoprim

3.2 **DATA AND ALTERNATIVE PROJECTION METHODS**

3.2.1 **Data Required for Market Study**

3.2.1.1 The data required may be classified as follows :

- a) Clinical data on mortality rates, acceptable drugs and current medical practice are required in order to assess the product mix; and

b) Market information is required to relate the volume of production to the size of the market.

3.2.1.2 However, the Terms of Reference do emphasise that the objectives of the pilot plant include the introduction and development of expertise in the field of chemical synthesis, and that it would have an education and training function. Unlike a normal commercial plant, marketing considerations would thus be of secondary importance.

3.2.1.3 **Mortality and Morbidity Rates**  
Morbidity statistics are collected on an on-going basis by the Department of Health. There is probably an element of under-reporting in these statistics, owing to variations in the coverage of the public health service, which is gradually being corrected. However these variations would not have a significant effect on the trend from year to year.

Reported rates for certain relevant notifiable diseases are set out in Appendix 3-2. Unfortunately, there is no direct correlation between morbidity and individual drug consumption as doctors tend to use a variety of different drugs for treatment of the same complaint. However, the general trends indicate continuing demand for the respective drugs.

3.2.1.4 **Acceptable Drugs**  
Reliable lists of acceptable drugs and advice on treatment regimes were obtained from official or professional sources such as BFAD and the Philippines Medical Association.

3.2.1.5 **Current Medical Practice**  
Advice on current medical practice was rather more subjective, but we found few inconsistencies in the advice we received. Most reliance was placed on the DOH medical staff, on the basis that they were likely to be the most up-to-date in their knowledge, and best placed for translating this knowledge into practice.

3.2.1.6 **Import Statistics**  
Market data can come from a variety of sources but, from previous experience, we have found that the most accurate information is contained in import statistics. Unfortunately, detailed records could not be obtained from the National Statistics Office as they were in the process of moving offices, but contemporaneous monthly import statistics are compiled by Business Statistics Monitor. We have a high degree of confidence in the reliability of these figures (Appendix 3-6 refers).



However, there is an element of illegal importation which cannot be accurately quantified. Our informal estimate is that the official figures are understated by 5% in the case of most drugs, and by as much as 10% in that of such products as Ethambutol and Isoniazid which are available from a large number of suppliers. In view of the underlying uncertainty, no specific provision has been made in this regard.

3.2.1.7 **Private Sector Demand**

Private sector demand figures collated by a commercial research company, IMS, could be used to confirm the supply data, but for the fact that previous experience has shown that the sampling methods used result in the market being considerably underestimated. For example, a cross-check of the full list of pharmaceuticals being imported indicated that the IMS figures record between 30% and 75% of the known market for each drug. Given the extent of this variation, the IMS figures do not constitute a reliable basis for calculating the size of the market.

3.2.1.8 **Public Sector Demand**

Public sector demand was quantified by examining DOH central purchases, as well as the drug consumption of a sample of 500 hospital beds over a three-month period. Although we have full confidence in these figures, the fact that public drug purchases vary substantially from year to year, and also account for only 10% to 15% of total demand, make them too limited to be of any real use in verifying supply statistics (Appendix 3-7 refers).

3.2.1.9 **United Laboratories**

As United Laboratories are to be considered as a potential customer of the proposed plant, we requested figures relating to their actual and anticipated levels of consumption. This was refused on the grounds of commercial confidentiality, and we have therefore used import records as a substitute means of calculating the company's market share.

3.2.1.10 **General Market Data**

Other information used to forecast growth in demand included trend data from imports, private sector demand, population forecasts and economic forecasts.

3.2.2 Alternative Methods of Data Evaluation

3.2.2.1 The Terms of Reference stress that production from this plant is intended to supply no more than a small part of the total requirements of the market for the pharmaceuticals identified. As a result, we have concentrated on arriving at a good approximation of the market by using the import statistics available.

3.2.2.2 However, data on demand was used to check these figures wherever possible and to highlight any anomalies.

3.3 DETERMINATION OF DEMAND AND MARKET SIZE

3.3.1 The Overall Market

3.3.1.1 Appendix 3-6 details the imports of all the relevant drugs for 1990, together with such limited information as was available regarding imports of Ethambutol and Isoniazid in 1988 and 1989. Based on this, we estimate that the market for the ten products in question currently exceeds 300 tonnes per year. This total may be broken down as follows :

Ethambutol	:	8.8 tonnes	*
Ibuprofen	:	25.2 tonnes	
Isoniazid	:	28.4 tonnes	*
Mefenamic Acid	:	20.0 tonnes	
Metronidazole	:	2.0 tonnes	
Nifedipine	:	0.2 tonnes	
Paracetamol	:	192.0 tonnes	
Pyrazinamide	:	11.5 tonnes	
Sulfamethoxazole	:	12.8 tonnes	
Trimethoprim	:	3.3 tonnes	
Total	:	<u>304.2 tonnes</u>	

\* 3-year average

3.3.2 United Laboratories Demand

3.3.2.1 United Laboratories is the largest drug manufacturer in the Philippines with an estimated 20% share of the total market for pharmaceuticals. As an indigenous company, it can source its drugs independently of any international affiliations, hence the fact that the Terms of Reference specifically mention Unilab as "a potential buyer of the proposed products".

3.3.2.2 Given that management was unwilling to release sales figures to us, we have had to estimate their annual requirement for each of the relevant drugs by analyzing the import statistics available for the 3-year period from 1998 through to 1990. These figures are detailed in Appendix 3-6, but Unilab's average demand and market share are summarised below for ease of reference :

Drug	Imports	Market Share
Ethambutol	2.1 tonnes	24% *
Ibuprofen	24.8 tonnes	98%
Isoniazid	19.9 tonnes	70% *
Mefenamic Acid	4.0 tonnes	20%
Nifedipine	0.08 tonnes	40%
Paracetamol	128.6 tonnes	67%
Pyrazinamide	0.8 tonnes	7%
Sulfamethoxazole	2.1 tonnes	16%
Trimethoprim	0.4 tonnes	12%
	<hr/> 182.78 tonnes <hr/>	<hr/> 60% <hr/>

\* 3-year average

3.3.2.3 It is therefore clear that, whereas Unilab dominates the market for certain products, notably Ibuprofen, Isoniazid and Paracetamol, it has very little or no share in that for others, such as Metronidazole and Pyrazinamide. It may also be noted that its apparent strength in Nifedipine is slightly misleading, in that this is a very low volume product.

#### 3.4 EVALUATION OF DATA RESULTS

##### 3.4.1 Size and Composition of Demand

3.4.1.1 The import statistics set out in Appendix 3-6 highlight the wide disparity in the volumes of the fine chemicals under review. Paracetamol completely dominates the market in terms of quantity, primarily because it is such a widely known drug which is available without prescription to treat a range of symptoms. Ethambutol, Ibuprofen, Isoniazid and Mefenamic Acid are also classed as major drugs, but the other products listed represent small quantities in manufacturing terms.

3.4.1.2 Similarly, Unilab's potential demand figures clearly indicate that the only products which would justify manufacture on an industrial scale are Paracetamol Ibuprofen and Isoniazid. The requirement for Mefenamic Acid is very much smaller, whilst that for the other drugs specified could probably be adequately supported by laboratory production.

3.4.1.3 However, the pattern of demand for each of the drugs in question varies considerably :

- **Ethambutol** is an anti-tuberculosis drug used both as a single component and in combination in a wide variety of drugs. The market is dominated by the multinational companies, particularly Lederle, but Unilab has nevertheless secured a 24% share.
- **Ibuprofen** is an important anti-inflammatory drug used in the treatment of arthritis and other muscular disorders. Two of the five brands on the market are owned by Unilab and, in total, these account for well over 90% of the market.
- **Isoniazid** is another anti-tuberculosis drug used both as a single component and in combination in many products. The Unilab companies have five major brands in the market and have secured a 70% share of the market in total. Most of the rest of the market is supplied by the multinationals.
- **Mefenamic Acid** is an analgesic and antipyretic, the market for which is dominated by Parke Davis and Warner Lambert. However, Unilab has a 20% market share, and other indigenous companies also import this drug independently.
- **Metronidazole** is used for the treatment of serious infections, and this market is totally dominated by Rhone Poulenc. We found no evidence of any presence by Unilab or other indigenous companies.
- **Nifedipine** is used for hypertension, and total imports are small in volume terms. Unilab has a 40% share of the market by weight, but only 14% in terms of value. Most imports are brought in by Asian companies as opposed to multinationals.
- **Paracetamol** is a general purpose painkiller which is imported by a wide variety of multinationals as well as local companies. The Unilab subsidiary companies are in a very strong position, supplying up to two thirds of the total market demand.
- **Pyrazinamide** is an anti-tuberculosis drug which is mostly used as a single component. The market is dominated by Ciba Geigy, Cyanamid and Lederle, but other main suppliers include regional Asian companies. Unilab has a 7% share of the market.

- Sulfamethoxazole and Trimethoprim are usually used in combination (known as Cotrimoxazole) for the treatment of respiratory tract infections. Roche dominates the market for clinical application, but there is also some demand for veterinary purposes. Unilab has a 15% share of the overall market.

3.4.2 Demand Projections

3.4.2.1 An accurate market projection is not critical in the context of the proposed pilot plant, although it is important to ascertain that demand for the products in question will continue to grow in real terms over the next decade.

3.4.2.2 Our projection of future demand has accordingly been based on three principal elements :

- Population growth
- The trend to higher expenditure on health care
- Relevant changes in morbidity rates

These elements are discussed in full in Appendix 3-8.

3.4.2.3 Based on the growth factors identified, demand for the ten products in question is expected to increase at the following annual percentage rates :

Drug	1991-1995	1996-2000	2001-2005
Ethambutol	4.05%	3.7%	3.3%
Ibuprofen	3.75%	3.5%	3.3%
Isoniazid	4.05%	3.7%	3.3%
Mefenamic Acid	3.75%	3.5%	3.3%
Metronidazole	3.85%	3.7%	3.5%
Nifedipine	3.65%	3.7%	3.6%
Paracetamol	3.75%	3.5%	3.3%
Pyrazinamide	4.05%	3.7%	3.3%
Sulfamethoxazole )			
Trimethoprim )	3.95%	3.8%	3.5%

3.4.2.4 Applying these growth rates to identified demand would result in the following market projections from 1990 through to the year 2005 :

Tonnes	Base	1995	2000	2005
Ethambutol	8.8	10.7	12.8	15.1
Ibuprofen	25.2	30.3	36.0	42.3
Isoniazid	28.4	34.6	41.5	48.8
Mefenamic Acid	20.0	24.0	28.5	33.5
Metronidazole	2.0	2.4	2.9	3.4
Nifedipine	0.2	0.2	0.3	0.3
Paracetamol	192.0	230.8	274.1	322.4
Pyrazinamide	11.5	14.0	16.8	19.8
Sulfamethoxazole	12.8	15.5	18.7	22.2
Trimethoprim	3.3	4.0	4.8	5.7
Total	304.2	366.5	436.4	513.5

### 3.4.3 Maximum Potential Market

3.4.3.1 The potential customers for the output of this proposed pilot plant fall into four groupings :

- Multinational manufacturers of pharmaceuticals;
- Korean and Taiwanese regional drug companies;
- United Laboratories; and
- Other indigenous manufacturers.

3.4.3.2 It is highly unlikely that a relatively small-scale pilot plant would be able to contain its production costs to a level which would enable it to effectively compete against the specialised large-scale producers. In addition, given that the output of the proposed project would account for no more than a small part of the market, the government would not be prepared to afford it protection through the introduction of high tariff barriers or other restrictions on free trade.

3.4.3.3 Both the multinationals and the regional Asian drug companies tend to source their requirements from their parent companies, not least because this enables them to take advantage of certain economies of scale. There would be no incentive for them to purchase from a local source of supply, particularly if the product was to prove to be more expensive.

3.4.3.4 Indigenous manufacturers could probably see the longer-term value of developing chemical production facilities in the Philippines but, with the exception of United Laboratories, these are small and underfunded. It is therefore unlikely that they would be prepared to pay a premium over and above world market prices for their raw material inputs in order to support such a project.

3.4.3.5 However, United Laboratories has already contributed to an extension of domestic production through its investment in Chemfields, and it is believed that it would consider sourcing a proportion of its overall drug requirements from the proposed plant. The extent of this is discussed further by individual product in Section 3.4.4.

3.4.4 **Anticipated Market Penetration**

3.4.4.1 **Ethambutol**

There are 28 brands of Ethambutol available in the market, 8 of which are single components. Both the leading brands are owned by Lederle, but the third and fourth brands by value are owned by Unilab via two subsidiary companies, Biomedis and United American.

The total market for this product is estimated at just under 9 tonnes, rising to 11 tonnes by 1995. Unilab's share is currently put at 24%, but this is expected to reduce to 21% by 1995, equivalent to 2.2 tonnes. Given the relatively strong brand position identified, it has been assumed that Unilab would be prepared to source a maximum of 50% of its requirements from the pilot plant.

3.4.4.2 **Ibuprofen**

Two of the five brands of Ibuprofen on the market are owned by Unilab, operating as Therapharma and Biomedis.

The total market is estimated at about 25 tonnes and is expected to exceed 30 tonnes by 1995. Unilab is the dominant force in the market but, given that no other indigenous company brings in supplies, it is possible that some of Unilab's imports are not for its own use. Its market share is thus likely to be eroded to 90% by 1995, when it is anticipated that it could source about 40% of its total requirement of 27.2 tonnes from a domestic supplier.

3.4.4.3 **Isoniazid**

Although there are 57 brands of Isoniazid available, all but two are in combination as opposed to single components. Ciba Geigy, Lederle and Merrell Dow own the three leading brands, but Unilab owns five of the top ten brands via its Westomont, United American and Pediatrica subsidiaries.

It is estimated that the market totals about 28 tonnes, increasing to nearly 35 tonnes by 1995. Unilab's share currently amounts to 70% of this, but competition from domestic producers could result in a reduction to 60% by 1995, equivalent to 20.8 tonnes. Nevertheless, based on its strong brand position, it

has again been assumed that Unilab would be able to source up to 40% of its requirements from a local supplier.

**3.4.4.4 Mefenamic Acid**

There are 18 brands of Mefenamic Acid available, and we estimate the total market at 20 tonnes, rising to 24 tonnes by 1995. Warner Lambert accounts for 40% of this, and Unilab for a further 20% to 23% despite the fact that it does not market a well-known brand. A number of indigenous compounders import on their own account, and together probably account for another 20% of the market.

It is anticipated that both Unilab and the indigenous compounders, such as Doctors and Drugmakers, would be prepared to source up to 25% of their total material requirements from the pilot plant.

**3.4.4.5 Metronidazole**

Although there are 13 different brands of this product available, Rhone Poulenc dominates the imports and, presumably, supplies many of the other multinational firms with their requirements. Unilab does not import this drug at all.

In view of the fact that the market for Metronidazole is very limited in both scope and size, at no more than 2 tonnes on current estimates, it is considered that it should not be introduced at the development stage.

**3.4.4.6 Nifedipine**

Of the five brands currently available, Bayer owns three and has a very strong market position. The Unilab brand is produced by Therapharma.

In addition to being limited in terms of scope, the market for Nifedipine is very small at only 200 kg per year. Once again, it is therefore recommended that this product should be excluded from the initial stages of project development.

**3.4.4.7 Paracetamol**

The total market for paracetamol is estimated at over 190 tonnes, and is expected to increase to nearly 231 tonnes by 1995. The Unilab share of the market is put at two thirds of this at the present time and whilst some erosion is likely it should still amount to 65% in 1995, equivalent to some 150 tonnes. The multinational companies have a limited presence only, whilst the demand of the other indigenous firms does not exceed 10 or so tonnes.



Given that this is a highly competitive market where product margins are comparatively low, it is doubtful that Unilab would be prepared to pay a premium on more than a fifth of its overall requirement. However, it might be possible to sell an additional limited tonnage to other indigenous companies, particularly if the DOH made their Rural Health Unit contracts conditional upon local sourcing.

3.4.4.8 **Pyrazinamide**

The market for this product is dominated by the brands owned by Ciba Geigy, Lederle and Pascual, all of which are in a very strong position. The Unilab brand is produced by Medichem Pharma, and accounts for about 7% of the total market of 11 tonnes, equivalent to 800 kg.

As with both Metronidazole and Nifedipine, the size and scope of the market for Pyrazinamide is such that this would not be an appropriate product for inclusion at the development stage.

3.4.4.9 **Sulfamethoxazole and Trimethoprim**

The market comprises a total of 28 different brands, but is dominated by Roche and, to a lesser extent, by Wellcome. Many of the other multinationals are also represented, and the three Unilab brands, produced by Medichem, United American and Pediatrica, are not particularly strong in the face of this competition.

In addition, the Unilab brands are already selling at about half the price of the brand leader, and it is anticipated that the companies concerned would be reluctant to source locally as opposed to buying as competitively as possible on the international market.

3.4.4.10 **Summary of Market Penetration by Product**

On the basis of the foregoing, it is estimated that the pilot plant would be able to supply 52.5 tonnes of five different products to United Laboratories in 1995

:

Product	Total Market	Unilab Share	Unilab Demand	Local Purchase	Unilab Sales
Ethambutol	10.7	21%	2.2	50%	1.1
Ibuprofen	30.3	90%	27.3	40%	11.2
Isoniazid	34.6	60%	20.8	40%	8.1
Mefenamic Acid	24.0	23%	5.5	25%	1.4
Metronidazole	2.4	-	-	-	-
Nifedipine	0.2	40%	0.1	-	-
Paracetamol	230.8	65%	150.0	20%	30.7
Pyrazinamide	14.0	7%	0.9	-	-
Sulfamethoxazole	15.5	16%	2.2	-	-
Trimethoprim	4.0	12%	0.4	-	-
<b>Total</b>	<b>366.5</b>		<b>209.4</b>		<b>52.5</b>

In addition, it could supply 3 tonnes of Mefenamic Acid and Paracetamols to other indigenous companies, thereby giving it an overall market penetration of just under 17% by reference to the 1995 figures :

Product	Total Demand	Unilab Sales	Other Sales	Total Sales	% Market Share
Ethambutol	10.7	1.1	-	1.1	10.3%
Ibuprofen	30.3	11.2	-	11.2	37.0%
Isoniazid	34.6	8.1	-	8.1	23.4%
Mefenamic Acid	24.0	1.4	1.1	2.5	10.4%
Paracetamol	230.8	30.7	1.9	32.6	14.1%
<b>Total</b>	<b>330.4</b>	<b>52.5</b>	<b>3.0</b>	<b>55.5</b>	<b>16.8%</b>

However, provision has been made for all sales to be limited to 75% of the figures specified above in 1995 only, in order to take account of any shortfall in production during the first year of operation. It may be noted that this would result in a reduced total of 41.6 tonnes, giving an initial market penetration of 12.6%.

For the purpose of the financial projections, it has been assumed that the above tonnages would thereafter remain constant throughout the 10-year project period, with the result that market penetration would reduce to 12% by the year 2005.

3.5 **ADDITIONAL DATA REQUIRED AND ALTERNATIVE STRATEGIES**

3.5.1 **Additional Data**

3.5.1.1 **Government Policy**

The attitude of the government is supportive in general terms, in that current policies with regard to health give priority to the drugs identified. However, some action may have to be taken to ensure an adequate supply of properly qualified staff to man the proposed pilot plant.

3.5.1.2 **Tariff Policy**

At the present time, bulk chemicals are subject to a tariff of 3%, whereas the tariff on bulk mixtures is set at 10%. It is understood that the Drug Association is planning to apply for a reduction in the level of customs duties payable on bulk antibiotics, and also on some other important pharmaceuticals.

In our opinion, the pilot plant would not be able to apply for specific protection in the form of increased tariffs on the products in question, on the basis that production capacity, and hence market share, would necessarily be limited.

3.5.1.3 **Licensing Procedures**

Any drug produced for human consumption would have to be approved by the Philippines government prior to its introduction onto the market. BFAD already has an inspectorate for compounders, and an extension of this could be used for licensing purposes.

Current licensing procedures are very strict and do not provide for the experimental nature of a pilot plant. The authorities have yet to formulate a policy in this regard, and it is clear that guidelines should be drawn up well in advance of project implementation.

3.5.2 Alternative Marketing Strategies

- 3.5.2.1 The marketing situation is unusual in that it must be accepted at the outset that the cost of the bulk pharmaceuticals produced by the pilot plant would be higher than that of the equivalent imported product. As no product differentiation would be possible, the plant would have to either sell to a buyer who would be prepared to pay a premium over and above the market price, or to subsidise output to the extent of the difference between that market price and the total cost of production.
- 3.5.2.2 As has already been noted in Section 3.4.3.3, neither the multinationals nor the regional drug companies are likely to be prepared to purchase their raw material inputs at a non-competitive price. The only potential customers would thus be Unilab and/or other domestic compounders in the Philippines.
- 3.5.2.3 The preferred solution would be for Unilab to accept responsibility for the entire output of the plant, which would then be transferred to the downstream manufacturing concerns at cost. In effect, Unilab would be investing in future production expertise at the expense of short-term profitability, and this could prove to be unpalatable. We perceived no interest in this type of venture in the course of our discussions with the company, and its acceptance might be subject to an approach at the highest level.
- 3.5.2.4 With regard to the other domestic manufacturers, these are all much smaller than Unilab and, in general, are under-capitalised. It is unlikely that they would anticipate investing in the country's future production capability, but they might be interested in purchasing relatively small quantities of chemicals which would otherwise have to be sourced from the international market. Preliminary reactions indicated that there would be an upper limit on the premium they would be prepared to pay for a local product, equivalent to not more than 20% over and above the import price.
- 3.5.2.5 One further alternative strategy which might work in conjunction with sales to domestic manufacturers would be for the Department of Health to place central orders for drugs at a high enough price to allow for the higher cost of raw materials. However, the problem with this is that very few of the drugs in question are purchased for the RHU programme, whilst the larger hospitals have their own budgets for drug purchases.

3.6 SELECTED MARKETING STRATEGY

3.6.1 Overall Marketing Strategy

3.6.1.1 On balance, we consider that the most realistic of the three alternative strategies outlined above would be for United Laboratories to negotiate an involvement in the pilot project, and to guarantee the purchase of a substantial proportion of the output.

3.6.1.2 In adopting this proposal, we have assumed that drug prices would be set at a premium of not more than 20% over and above the average prices paid by Unilab for the imported equivalent. This would not only enable Unilab to cost their involvement in the proposed plant, but would also provide an incentive for operational efficiency.

3.6.2 Individual Product Strategies

3.6.2.1 Strategy Selected

The plant would sell its entire output of Ethambutol, Ibuprofen and Isoniazid to United Laboratories. About 56% of its production of Mefenamic Acid and 94% of that of Paracetamol would also be reserved for supply to Unilab, with the balance being sold to other domestic compounders on a first come, first served basis.

3.6.2.2 Product Pricing

As noted above, it has been assumed that prices would be set at a level not more than 20% higher than those charged for imported products :

	Landed Price per kg	Domestic Price per kg
Ethambutol	\$ 38.00	\$ 45.00 = P 1,170
Ibuprofen	\$ 27.00	\$ 32.00 = P 832
Isoniazid	\$ 16.00	\$ 19.00 = P 494
Mefenamic Acid	\$ 18.50	\$ 22.00 = P 572
Paracetamol	\$ 6.00	\$ 7.20 = P 187

3.6.2.3 Product Promotion

It is estimated that total expenditure on technical literature, product promotion and entertainment would not exceed P 300,000 per annum.

3.6.2.4 **Organisation of Sales and Distribution**  
 In view of the very limited customer base, it would not be necessary to employ a sales team as such. However, provision has been made for the recruitment of a client liaison officer, who would be responsible for all the public relations aspects of the project's activities, and for operation of a limited delivery service. On this basis, it is anticipated that annual expenditure on sales/distribution would total about P 400,000.

3.6.2.5 **Commissions/Discounts**  
 All product prices have been quoted on an ex-factory basis, net to the customer. For the purpose of this study, it has been assumed that commissions/discounts would not be allowed but, in reality, sales to Unilab in particular would be subject to negotiation.

3.7 **ESTIMATE OF SALES REVENUES AND COSTS**

3.7.1 **Sales Revenues**

3.7.1.2 Details of sales revenues, calculated by reference to forecast sales and the prices assumed for individual products, are as follows :

	1995	1996 - 2004
Ethambutol	P 936,000	P 1,287,000
Ibuprofen	P 6,989,000	P 9,318,000
Isoniazid	P 3,013,000	P 4,001,000
Mefenamic Acid	P 1,087,000	P 1,430,000
Paracetamol	P 4,570,000	P 6,078,000
Total	<u>P 16,595,000</u>	<u>P 22,114,000</u>

3.7.2 **Sales and Distribution Costs**

3.7.2.1 Expenditure directly related to sales and marketing has been calculated at a total of P 700,000 per year, broken down between manpower, product promotion and travel/transport as follows :

Manpower	:	P 220,000
Product Promotion	:	P 300,000
Travel/Transport	:	P 180,000
Total	:	<u>P 700,000</u>

3.8 **PRODUCTION PROGRAMME**

3.8.1 **Data and Alternatives**

3.8.1.1 **Project Start Date**

Section 9 sets out the project implementation schedule from which it is assumed that the plant would commence production in January 1995.

3.8.1.2 **Sales Forecast**

The starting point for compiling the production programme is the projected sales for 1995, para. 3.4.4.10 of the market section refers and is reproduced below.

Table 3.8.1.2

Product	Total Projected Sales (Tonnes per annum)
Ethambutol	1.1
Ibuprofen	11.2
Isoniazid	8.1
Mefenamic Acid	2.5
Paracetamol	32.6
Total	<hr/> 55.5 <hr/>

3.8.1.3 **Production Schedule Data**

For the purpose of establishing the production schedule it has been assumed that actual production in 1995 would be limited to 75% of the forecast sales in 1995 in recognition of likely production and organisational familiarisation requirements in this first year of operation.

Thereafter it has been assumed that annual production would be a constant 55.5 tonnes as shown in table 3.8.1.2. The foregoing assumption is justifiable in the light of the orientation of the multi purpose pilot plant towards training and development where indeed the marginal cost of production may well be negative and that increasing production quantities, commensurately increases the cost of operation.

3.8.1.4 **Production Capacity Data**

Set against this rather conservative production schedule is the great flexibility afforded by a multi purpose plant such that products and quantities can be changed very quickly with no further capital expenditure and at short notice in the light of subsequent production and market experience. It will be demonstrated in section 3.9.2 that an ultimate

capacity of 138 tonnes per annum could be achieved with the plant as proposed.

**3.8.1.5 Manufacturing Route**

The manufacturing route for the 5 selected products is discussed in section 6. However, there is a similarity in that all manufacturing routes require batch processing of a number of intermediates by a series of consecutive steps in separate reactors to produce the final product.

**3.8.1.6 Manufacturing Options**

This sequenced batch processing presents a number of basic manufacturing options:

- Provision of 5 separate dedicated processing lines; one for each product;
- Provision of one process line enabling each of the products to be processed in the same equipment in 'campaigns' lasting from say one week to several months.

**3.8.1.7 Dedicated Processing Lines**

Dedicated processing lines require less storage for raw materials and products, are easier to operate but offer no flexibility and incur larger capital and space requirements.

**3.8.1.8 Multi Purpose Campaign Type Processing Lines**

Campaign production requires a smaller and less expensive process plant which has greater operational flexibility in meeting short term market fluctuation in product and/or quantities.

However there are disadvantages in that there needs to be a greater stock holding of finished product. In addition there is the non productive time between campaigns during which the plant has to be thoroughly cleaned to prevent cross contamination. It is generally more difficult to operate this type of plant leading to the possibility of spoiling batches.

The campaign type of processing was selected on the basis that:

- a) all raw materials and products have shelf lives measured in years.
- b) the emphasis is on providing flexibility to develop these five products.
- c) there is the potential to develop more products with little further capital expenditure.



### 3.8.1.9 Selection of Manufacturing Priorities

Within the framework of campaign type manufacturing, it is necessary to select the order in which the campaigns are to be run. The criteria used to make this selection are:-

- a) The expressed priorities to manufacture paracetamol and isoniazid as given in the terms of reference (Appendix 1-1).
- b) The manufacturing complexity of the product selected. The manufacturing routes described in section 6 indicate that paracetamol is the simplest and shortest manufacturing process with 2 steps in the synthesis; and ibuprofen is the more complex and longest synthesis, requiring 5 steps.

On this basis the following order of annual manufacturing campaigns was selected:-

#### Tonnes/per annum

Paracetamol	32.6
Isoniazid	8.1
Ethambutol	1.1
Mefenamic Acid	2.5
Ibuprofen	11.2

It is of course possible to subdivide the campaigns. However the maximum campaign is 16 weeks for isoniazid, see Appendix 3-9. An allowance of 1 week has been assumed to clean the production line for the next product. In these circumstances sub-division of the campaigns was not proposed as cleaning time would take an increasingly higher percentage of the available time.

### 3.8.1.10 Batch Size Selection

The pilot plant envisaged within the terms of reference for this study forms an important step in scaling up a process from the laboratory scale development unit to a full scale dedicated production facility. The problems encountered with scaling up processes especially economic and engineering data regarding yields and operating efficiency are such that a pilot plant is seen as a precautionary half way step between the laboratory and full scale manufacture. A pilot plant can also be designed such that it is not totally redundant should the production move to full scale manufacturing in that other products can be investigated and useful training and development objectives can be achieved.

A full scale manufacturing facility may be expected to process batch sizes upwards of 300 to 500 kg for economic scale production whereas a laboratory scale

development unit may be expected to process batch sizes of between 1 and 10 kg.

As a consequence batch sizes in the range 100 to 300 kg were considered.

#### 3.8.1.11 Operating Philosophy

Process plants are normally operated continuously 24 hours a day with maybe 2 full shifts and third twilight shift.

A batch processing unit does not necessarily need to run continuously because of the very nature of the intermittent processing by batches. However it does make operational sense to synchronise production with the shifts wherever possible.

On this basis we have selected a philosophy of processing a batch of product per day.

For the purpose of establishing a production schedule we have assumed 5 days per week working two shifts per day, 8 hours per shift. This will leave surplus time available for training and product development activities.

#### 3.8.1.12 Batch Size Determination

On the basis of producing one batch per day, the batch size for each product was evaluated against the annual tonnage requirements and a reasonable duration for each campaign.

The following batch sizes were selected:

	Batch (kgs)	Duration of Campaign (weeks)
Paracetamol	260	12.5
Isoniazid	100	16.2
Ethambutol	100	2.2
Mefenamic Acid	100	5.0
Ibuprofen	100	11.2

#### 3.8.1.13 Storage Requirements

Sufficient storage of raw materials is required for 4 months stock holding.

Ideally, for finished product, storage requirements should be sufficient to hold a maximum of one year's production.

### 3.8.2 Selection of Production Schedule

3.8.2.1 The overall production schedule (see Appendix 3-10) is based on 75% of 1995 sales figures and thereafter the production schedule is held constant at 1995 sales tonnage:-

<u>Product</u>	<u>Output (Tonnes/Year)</u>					
	1995	1996	1997	1998	1999	2005
Paracetamol	24.45	32.6	32.6	32.6	32.6	32.6
Isoniazid	6.07	8.1	8.1	8.1	8.1	8.1
Ethambutol	0.825	1.1	1.1	1.1	1.1	1.1
Mefenamic Acid	1.875	2.5	2.5	2.5	2.5	2.5
Ibuprofen	8.4	11.2	11.2	11.2	11.2	11.2
TOTAL	41.62	55.5	55.5	55.5	55.5	55.5

3.8.2.2 Within this overall framework, the details of the production schedule with respect to each product/batch size/processing line/campaign duration are presented at Appendix 3-9.

The salient factors are:

Product	Batch Size	Shifts	Batches per day	Campaign	
				Output (Tonnes)	Duration (wks)
Paracetamol	260kg	2	2	32.6	12.5
Isoniazid	100kg	2½	1	8.1	16.2
Ethambutol	100kg	1½	1	1.1	2.2
Mefenamic Acid	100kg	1½	1	2.5	5.0
Ibuprofen	100kg	2	2	11.2	11.2

### 3.8.2.3 Quality Standards

The plant design is intended to meet internationally acceptable quality levels to the equivalent of United States (USP) or British Pharmacopoeia (BP) standards. However achieving and monitoring such standards set against a development and training rationale could well prove to be a fundamental obstacle.

At present in the Philippines the Bureau of Food and Drugs (BFAD) does not have a set of standards for the manufacture of most pharmaceuticals. It does inspect and regulate compounders but the only manufacturer in the Philippines at present is Chemfields. No definitive guidance can be given by BFAD at this time but it is likely that they will establish and develop a regulatory system based on USP or BP standards.

If this is the case it will be preferred to license a drug for distribution to the public once the method of large scale manufacture has been fixed. This final process would be on the master file and no deviation

would be permitted. The only alternative approval which would be allowed for drugs for human consumption would be for BFAD to establish an Ethics Committee for approval of smaller non-standard batches. However, even here, it is unlikely that they would give a general approval on the end product - they would insist on approval on a case by case basis. With small quantities this would be impractical.

3.8.2.4 **Waste Treatment**

The waste products from the processes consist of relatively small quantities of acids, alkalis, solvents and chemicals. These wastes are mainly water borne and treated by active sludge process, except toxic metals which have to be disposed of by specialist contractors. Solvent recovery facilities are incorporated within the design of the plant although solvent recovery facilities exist at the Chemfields site (see below). Airborne pollution is not regarded as a significant problem provided that dust is adequately vented and organic vapours are kept below the toxic threshold limit values.

For the purpose of evaluating this project we have assumed that the plant is to be located at the Chemfields existing site. The small quantities of waste could then be treated by the existing Chemfields waste treatment facilities and we have ascribed no cost to this provision other than the cost of tying in to these facilities.

3.8.2.5 **Production Losses and Wastage**

All production figures in the production schedule are net of losses in the production cycle.

3.9 **PLANT CAPACITY**

3.9.1 **Data and Alternatives**

3.9.1.1 Appendix 3-9 sets out the production schedule computation indicating the process times for each intermediate step.

3.9.1.2 Production levels can be increased over and above this schedule by the following factors.

- a) increase working week to 6 days/week
- b) increase working week to 7 days/week
- c) increase shift working to 3 shifts/day
- d) wherever possible by operating batches simultaneously
- e) engineering contingency designed in to the sizing of equipment at plus 15%.

3.9.1.3 Points a) to c) are self explanatory and point d) may be illustrated by taking paracetamol as an example:-

The production schedule calls for 2 batches/day from each reactors A and B of 4 hours duration per batch i.e each reactor is only operating for a total of 8 hours per day. Therefore it is entirely feasible to double their operating time to 16 hours per day overlapping the production batches and effectively doubling the output.

Reactor A	<u>Batch 1</u>	<u>Batch 2</u>	<u>Batch 3</u>	<u>Batch 4</u>	
Reactor B		<u>Batch 1</u>	<u>Batch 2</u>	<u>Batch 3</u>	<u>Batch 4</u>

20 hours

Total Output 4 batches.

3.9.1.4 On point e) the engineering contingency of +15% has been built into our sizing of the basic equipment to provide tolerance in the event of equipment under performing and also some flexibility for future expansion.

### 3.9.2 Determination of Feasible Normal Plant Capacity

3.9.2.1 The feasible normal plant capacity may be defined as the maximum continuously sustainable output. This we have assumed to be taken as:-

- working 6 days/week
- working 3 shifts per day
- operating batches simultaneously

3.9.2.2 The nominal maximum plant capacity may be defined as the maximum occasionally sustainable output. This we have assumed as:

- working 7 days/week
- working 3 shifts/day
- operating batches simultaneously
- operating equipment at +15% of rated capacity

3.9.2.3 The following table summarises our computations of annual production in tonnes taken from Appendix 3-9 for the base data.

	Shifts	Batches/day	Tonnage 5 days/week	Tonnage 6 days/week	Tonnage 7 days/week	+15%
Paracetamol	3	4	65.20	78.24	91.28	104.97
Isoniazid	3	2	16.20	19.44	22.68	26.08
Ethambutol	3	1½	1.65	1.98	2.31	2.65
Mefenamic Acid	3	4	10.00	12.00	14.00	16.10
Ibuprofen	3	4	22.40	26.88	31.35	36.06
		(with additional)				
		Reactor B	115.45	138.54	161.63	185.87
				A	B	

A = Feasible Normal Plant Capacity = 138.54 Tonnes/Annum  
 B = Nominal Maximum Plant Capacity = 185.87 Tonnes/Annum

## SECTION 4

### MATERIALS AND INPUT

#### 4.1 CHARACTERISTICS OF MATERIALS AND INPUT

##### 4.1.1 Classification of Requirements

4.1.1.1 The raw materials required are 27 imported chemicals, solvents and intermediates which are listed at table 4.1.3.

4.1.1.2 There is no local manufacture of any of these materials.

4.1.1.3 All materials can be purchased on the international market directly from manufacturers (for the speciality items) or from stock holders (for the more common materials). All materials are technical grade manufactured by specialist organic chemical companies such as Kodak Inc.; Du Pont Inc., USA; Bayer AG, Germany and ICI plc, UK.

##### 4.1.2 Material and Input Selection

4.1.2.1 The choice of the process route dictates the raw material requirements. There are many alternative routes available in these chemical syntheses.

4.1.2.2 Since the raw material costs represent a substantial proportion of the production cost, we have selected those routes which provide the lowest material cost input based upon information available in the public domain together with requirements for methods, procedures and equipment which are compatible with a new pharmaceutical business just starting up.

By way of example, the classical processing route for Ibuprofen requires a total processing time of 39 hours and the total raw material costs exceeds the present selling price. An alternative route was therefore selected, a route that has recently been adopted by manufacturers and the current international price reflects sourcing via this route.

4.1.2.3 There are some limited opportunities to use alternative solvents, mineral acids and alkalis.

## 4.1.3

Raw Material Requirement

The complete list of raw materials required for synthesis per batch and indicative prices are shown in table 4.1.3.

Table 4.1.3 RAW MATERIALS

	kg/batch	FOB NY \$/ton	CIF UK \$/ton
<u>ETHAMBUTOL HYDROCHLORIDE (100kg/batch)</u>			
+ 2 amino 1 butanol	77		1920
dichloroethane	285	358	
methanol	850	111	
caustic soda - 50% solution	470	350	
ethanol	650ltr	426/m <sup>3</sup>	
petroleum-ether 80-100 BP	400	281/m <sup>3</sup>	
<u>IBUPROFEN (100kg batch)</u>			
propylene oxide	77	1288	
1 butyl benzene	89	3800	
aluminium chloride	87	448	
carbon disulphide	20ltr (25.2kg)	420	
acetic acid	42	740	
sulphuric acid conc	200	85	
sodium dichromate	212	2464	
<u>ISONIAZID (100kg batch)</u>			
4 cyanopyridine	125	5690	
hydrazine hydrate	125	2800	
sodium hydroxide	2.5	350	
<u>NEPENTHIC ACID (100kg batch)</u>			
potassium o bromo benzoate	178	4780	
bis 2 methoxy ethyl ether	335		1920 max 3410
n-methyl morpholine	80		3340
dimethyl aniline	84		2150 max 3500
cupric acetate	6.7	6428	
hydrochloric acid conc	58	95	
<u>PARACETAMOL (260kg/batch)</u>			
sodium sulphite	1.2	552	
p amino phenol	257		5280 max 8190
acetic acid	150ltr	740	
acetic anhydride	270	1064	
sodium thiosulphate	0.7	1018	



4.1.4 Raw Material Prices

4.1.4.1 Large price variances can be found in the quoted prices for all these chemicals often reflecting not only the normal supply/demand fluctuations but commercial perceptions of who is making the purchase and for what reason. This applies most particularly to the key raw materials specific to the manufacture of a single product.

4.1.4.2 By way of example several prices were obtained for P-amino phenol the key material for Paracetamol:-

Price FOB NY as listed \$7,150/ton

Price CIF UK import statistic  
Nov 1991 \$8,190/ton max  
\$6,860/ton average  
\$5,250/ton min

The conclusion drawn is that there is a large elasticity available between the production cost and the selling price of the intermediates. Where possible the selling price is set to deter new manufacturing operations from entering the market.

4.1.4.3 Prices in the Philippines are subjected to increases in FOB costs through application of tariffs, freight and insurance charges (approximately 18% total).

4.1.5 Availability of Supply

4.1.5.1 Whilst supplies can be obtained direct from manufacturers, or through international commodity traders located in Europe, Japan or the USA, the probable best method would be to appoint a buying/shipping agent specialising in this type of commodity who would then group the supplies together for regular shipment to the Philippines by container.

4.1.5.2 All materials are generally available ex stock and supplied in 200kg sealed drums.

4.1.5.3 Some of the materials are hazardous and would carry a freight premium for carriage as deck cargo.

4.1.6 Specifications

These raw materials would be purchased to normal technical grade specifications of the major USA, European and Japanese suppliers.

#### 4.1.7 Utilities

4.1.7.1 Utility requirements are summarised below in table 4.1.7.1 expressed as quantities per batch.

Table 4.1.7.1

	Batch Size (kg)	Steam (tonnes)	Cooling Water	Electricity kWh	Plant Air	Nitrogen	Potable Water
Paracetamol	260	0.08	3.3	105	Negligible	Negligible	Negligible
Mefenamic Acid	100	0.04	2.1	165	"	"	"
Isorniazid	100	0.16	2.5	270	"	"	"
Ethambutol	100	0.12	6.4	110	"	"	"
Ibuprofen	100	0.12	6.4	425	"	"	"

4.1.7.2 The total maximum capacity requirement to provide for peak loads is estimated in table 4.1.7.2.

Table 4.1.7.2

<u>Steam</u>	<u>Cooling Water</u>	<u>Electricity</u>
0.8 tonnes/day	25 tonnes/day	100kW

4.1.7.3 For the purpose of evaluating this project all the above utilities have been assumed to be provided by Chemfields and as such no capital cost has been included for separate facilities. The cost of consumption and the capital cost of tying into these facilities has been indicated in our cost estimates.

#### 4.2 SUPPLY PROGRAMME

##### 4.2.1 Supply Programme Schedules

Appendix 4-1 sets out the fully detailed annual raw material and utility requirement to support the production schedules for each of the respective products. All inputs are identified by quantity per batch for years 1995 to 2015.

##### 4.2.2 Supply Programme Determination

Appendix 4-1 was generated directly from the production schedules (Appendix 3-10) after determination of:-

- a) component material requirements drawn from the production campaign requirements.
- b) component procurement and storage requirements.

4.2.3 Component Procurement and Storage Requirements

4.2.3.1 Imported Raw Materials

Stocks of imported materials need to be anticipated and Table 4.2.3.1 shows that about 4-5 months stock is necessary.

Table 4.2.3.1 Imported Ingredients: Basis for stock Policy

weeks	action
2	shortage of stock to be reported
1	order placement
4	delivery to port
4	shipping
2	clear customs and local delivery.

The imported raw materials are normally handled with a fork lift and stored in standard racking. Most products are supplied in metal drums of 200 litre capacity, 25 or 50 kg plastic sacks, or in cartons, drums and packs of various sizes.

## SECTION 5

### LOCATION AND SITE

#### 5.1 DATA AND ALTERNATIVES

##### 5.1.1 Criteria for Location

The criteria for location are considered to be:

- commercial interests
- economic viability
- geographic

##### 5.1.1.1 Commercial Interests

The objectives for the multi purpose pilot plant are set out in the terms of reference (Appendix 1-1) and the consequential contradictory requirements are examined in section 2.1.4, highlighting the need to produce commercially viable products sufficient to sustain the plant's training and development function.

From the outset it has been viewed as an essential first stage from pure laboratory/research scale activities to developing the next stage of full scale commercial operations for dedicated products.

It is therefore seen that commercial interests should primarily be served rather than academic requirements on the following counts:-

- a) To test technical and commercial viability of products prior to undertaking full scale investment and hence reduce consequential risk.
- b) To create and develop indigenous expertise in the production of pharmaceuticals which will provide a pool of expertise for exploitation of future commercial opportunities, not least creating a measure of technical independence from foreign support and licence packages.

It is highly desirable that such a pilot plant is closely associated with commercial interests both in terms of organisational support - providing easy movement of engineers to the plant and their subsequent redeployment within the organisation and also ready access to proven sales/distribution and marketing networks.

5.1.1.2 **Economic Viability**  
It is foreseen that it will be difficult to be financially viable in view of the implied inefficiencies of small scale production from a non-dedicated plant. It is therefore considered highly desirable in view of the small consumption of utilities and waste disposal requirements to share existing facilities at a larger existing production facility.

5.1.1.3 **Geographic**  
The following general considerations were also taken into account:-

personnel availability of pharmacists\*, bio-technologists\*, engineers, laboratory, instrument, plant maintenance technicians; access to University\*.

site industrial site\* with adequate infra structure; power, transport, roads, water, waste treatment.

location good access\* to and from ports, air ports, roads, work force\*, University\*, sales distribution networks, customers, national policy makers.

area Approximately 4,000m<sup>2</sup>.

(\* highly important)

5.1.2 **Possible Locations**

5.1.2.1 There are two possible alternatives:

- Location at the only existing pharmaceutical processing plant - Chemfields
- 'Greenfield' location adjoining the University of the Philippines at Los Banos.

5.2 **SELECTION OF LOCATION AND SITE**

5.2.1 **Chemfields**

The preferred location and that assumed in this study is Chemfields factory, south of Manila in the Calabarzon region, in that the following advantages are foreseen:-

- Unilab own 40% of Chemfields and provide all management and labour.

- Unilab can provide the largest single source access to the market as discussed in section 3.
- Chemfields site already has the infrastructure for a small chemical factory: administration, power supplies, waste disposal, solvent recovery and experienced workforce exist to act as a nucleus.
- Chemfields own 27 hectares to the rear of the factory as shown on the proposed site layout, see Appendix 5-1, and could easily accommodate an extension requiring approximately 4,000m<sup>2</sup>.
- Easy access to Metro Manila and the University at Los Banos.

#### 5.2.2 Los Banos

The Los Banos site has several small scale biotechnical enterprises but the location would mean that the pilot plant would need to be self sufficient in utilities and waste disposal. It is also seen not to have any direct commercial self interest in terms of existing and future product sales to the market without direct commercial involvement.

#### 5.3 COST ESTIMATES

A 4,000m<sup>2</sup> site is required costing 12,000,000 pesos.

There are no special payments for rights of way, easements or rents, all of which have been included in the price.

#### 5.4 LOCAL CONDITIONS

The region to the south of Metro Manila is a rural coastal plain which has, until recent times been utilised for the production of sugar cane and similar crops in small and medium sized farms and plantations.

The region has a tropical maritime climate and is close to the Pacific Ocean and the South China sea. The prevailing winds have a high humidity, ranging from 71% in March to 85% in September. The rainfall and temperature are also both consistently high for most of the year, the rainfall averaging 300-400 cm every year and the temperatures from a January average of 25.5 degrees to 28.8 degrees celsius in May.

The area is very suitable for the proposed industrial development; living conditions for workers are good in the region, other similar plants have already been located in the district and the general level of public and private resources is good.

5.5 ENVIRONMENTAL IMPACT

5.5.1 Impact

The environmental impact of the proposed plant in the region is not likely to lead to any significant short or long term problems.

Waste water treatment is required and it has been anticipated that this will be provided by the existing Chemfields factory.

5.5.2 Waste Treatment

The waste products from the processes consist of relatively small quantities of acids, alkalis, solvents and chemicals. These wastes are mainly water borne and can be treated by an active sludge process, except for toxic metals which have to be disposed of by specialist contractors. Solvent recovery facilities are incorporated within the design of the plant although solvent recovery facilities exist at the Chemfields site. Airborne pollution is not regarded as a significant problem provided that dust is adequately removed before venting and organic vapours are kept below the toxic threshold limit values.

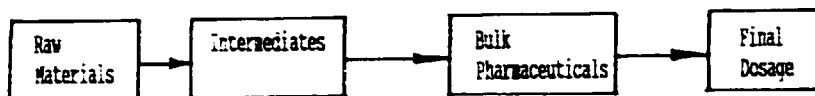
## SECTION 6.0

### TECHNOLOGY AND PROJECT ENGINEERING

#### 6.1 THE TECHNOLOGY

##### 6.1.1 General

- 6.1.1.1 The manufacture of pharmaceuticals is generally carried out in four stages as follows:



This project is concerned with the middle step, i.e. the conversion of intermediates to bulk pharmaceuticals.

- 6.1.1.2 The choice of the five products (Paracetamol, Mefenamic Acid, Isoniazid, Ethambutol and Ibuprofen) has been discussed and justified commercially and strategically in section 3. It is particularly noteworthy that all of these are out of patent protection and as generic pharmaceuticals/intermediates, their chemical production processes are in the public domain.

##### 6.1.2 Chemical Synthesis in Multi Purpose Batch Reactors

- 6.1.2.1 The five drugs are all made by the synthesis of organic chemicals in ways which are standard to the pharmaceutical, dyestuffs, photographic and fine chemicals industry.

- 6.1.2.2 All the products are manufactured in common equipment. The principal item of equipment is called a reactor which is used as a multi purpose vessel. The vessel is constructed from 316 stainless or glass lined steel. It has a jacket for heating and cooling as appropriate. Additional features can be incorporated, for example a condenser added to the reactor enables the reactor to be used as an evaporator or with other modifications, as a batch distillation unit. Similarly it can be used as an extractor by adding a solvent to the vessel contents, mixing and separating.

- 6.1.2.3 The basis of chemical synthesis is to add chemicals A, B, and C to the reactor in order for the chemicals to react together to provide the product we want.

For every organic synthesis there are a variety of possible routes. For example:

A + B -----> C + D -----> 'E' might be the classical way to synthesise 'E' from 'A', however it might be possible to purchase an intermediate, 'X' say, and react this with 'A' to produce 'E' in one



step. Obviously the cost and availability of raw materials will usually control the synthesis chosen.

6.1.2.4 The raw materials for each product, assuming a solvent recovery rate of 70%, are listed in Table 4.1.3 whilst the resulting outputs are recorded in Appendix 3-10. It is envisaged that the existing solvent recovery facilities at Chemfields will be used in accordance with 5.2.1. The chemical syntheses are achieved by multi stage batch operations and are illustrated in Appendix 6-1 which gives details of the process sequence together with durations.

6.1.2.5 The details of each configuration of equipment are represented on five flowsheets (one for each product) included at Appendix 6-2. These diagrams can be compared with the schedules in Appendix 6-1 to give a clear understanding of how the production operations will be carried out. The particulars of each process are described further as follows:-

### 6.1.3 Paracetamol

#### 6.1.3.1 Description

Paracetamol is a well established pharmaceutical having first been introduced in Germany in 1878 as an analgesic and antipyretic. At the present time well over 100 different brands are offered for sale worldwide in many different countries. The manufacturing processes used today use p-aminophenol as starting material.

Chemical Name: N-(4 hydroxyphenyl) acetamide

Molecular formula and weight:  $C_8H_9O_2N$ , 151

Pharmacopoeia references:

BP 1973, 340

USP 1975, 11

Martindale 26,245

#### 6.1.3.2 Process Route

SCIENTIFIC REFERENCES:

Ger. off 2121164, CA 76, 59199u

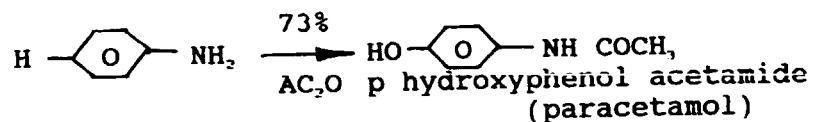
In a 3000 litre jacketed, agitated stainless steel reactor, 257kg para amino phenol is dissolved in 1500 litres of 10% acetic acid solution at at 95°C.

The mixture is maintained at 95°C and treated with 700g sodium thiosulphate, 1200g sodium sulphite and 10kg active carbon.

The mixture is pumped to a second 3000 litre reactor identical to the previous via a pan type filter having a capacity of 10 litres.

The acetic anhydride (270kg) is added to the filtered liquor and after 15 minutes the mix is heated to 85°C and filtered in a bowl centrifuge or pan filter to give 260kg of para hydroxy phenyl acetamide of 99% purity.

The filtrate is washed with water and dried in a batch fluidized bed drier of capacity 250 litres.



Reaction type: acetylation

Please see Appendix:      6-1 Reaction Schedule  
                                    6-2 Flow Diagram

The waste products from this process are aqueous with traces of acetic acid and related chemicals which are easily neutralised with alkali and treated in an activated sludge plant. The carbon should be sent to landfill.

No special sanitary procedures are foreseen at this stage for a teaching pilot plant for this product.

There are no oil soluble solvents used in this process available for recovery. The residual acetic acid is not recovered.

#### 6.1.3.3 Manufacturing Requirements

OUTPUT: 260 kg/batch, batch time 8 hours

##### RAW MATERIALS:

	kg
p-aminophenol	257
acetic acid 10%	150 litre (net)
sodium thiosulphate	0.7
sodium sulphite	1.2
acetic anhydride	270

##### UTILITIES:

steam - 1.5 bar g for vessel heating, drying  
water - recirculated water for vessel cooling to 20°C  
power - 30 kW installed, agitators, pumps, driers

EQUIPMENT:

<u>Item</u>	<u>No off</u>	<u>Capacity</u>	<u>Material/Type</u>
reactors	2	3 cu m	316 jacketed
condensers	2	1 sq m	316 or glass
pumps	2	3 cu m/hr	316, centrifugal
		2 bar	
feed tanks	2	750 l	316
		250 l	
filters	1	in line	316
centrifuge	1	bowl	316
		500 l	

6.1.4 Ethambutol Hydrochloride

6.1.4.1 Description

First introduced in 1967 in Europe and the USA by the Cyanamid Company as an antitubercular drug, this product is now manufactured in 30-40 brands worldwide and available in many countries of the world.

Chemical name: (R)-2, 2-(1,2-ethanediyldimino) bis-1-butanol dihydrochloride.

Molecular formula and weight:  $C_{10}H_{24}N_2O_2$ , 203.31

Pharmacopoeia references:

BP 1973, 191  
Martindale 26, 1868

6.1.4.2 Process Route

SCIENTIFIC REFERENCES

USP 3,297,707

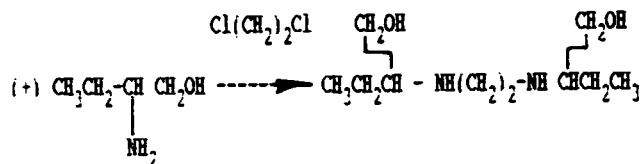
285kg dichloroethane is added to 77 kg 2-amino-1-butanol, and heated under reflux in a 2m<sup>3</sup> glass lined 316 stainless steel jacketed reactor to 84°C. After 30 minutes, 750 litres methanol and 240kg sodium hydroxide dissolved in 80 litres water are added.

The precipitated sodium chloride which results from this first stage is removed by centrifugation in a 500 litre 316 stainless steel centrifuge, and the solution is pumped into a batch distillation unit having a nominal capacity of 1m<sup>3</sup>. The still is electrically heated with a design pressure of full vacuum and 5 barg, and a design temperature of 300°C. The overhead air cooler/condenser has an area of 1m<sup>2</sup>.

Low boiling point components are removed at temperatures below 100°C at a pressure of around 30 mmHg. The product is then distilled under high vacuum at temperatures around 165 to 170°C and a pressure of

0.6 mmHg absolute. Electrical trace heating is used to prevent solidification of the distillate.

The overheads are pumped to a 2m<sup>3</sup> 316 stainless steel jacketed agitated crystalliser. 230 litres ethanol and 400 litres light petroleum solvent are added, and the material is cooled to 5°C using brine and left at this temperature for 8 hours. The resulting crystals are removed by centrifugation, and redissolved by heating in 300 litres ethanol in a second 2m<sup>3</sup> 316 stainless steel jacketed agitated crystalliser. Following chilling, the crystals are centrifuged, filtered in a 2m<sup>2</sup> filter, and dried in a 500 litre capacity fluidised bed drier.



(+) 2-amino -1-butanol (2)

ethambutol

All solvents are recovered for re-use after product recovery and distillation. Wastes are dissolved mineral salts in water and treated by the activated sludge process.

#### 6.1.4.3 Manufacturing Requirements

OUTPUT: 100 kg/batch, batch time 19 hours total.

##### RAW MATERIALS:

	kg
2-amino 1 butanol	77
dichloroethane	285
methanol	300 l
sodium hydroxide	240 in 80 l water
ethanol	230 l
light petroleum solvent	400 l

##### UTILITIES:

steam - 1.5 bar g for vessel heating, drying  
 water - treated water as raw material, recirculated  
           water for vessel cooling to 25°C  
 power - 35 kW installed for agitators, pumps,  
           centrifuge distillation and drier  
 compressed air  
 chilled water to 5°C

EQUIPMENT:

<u>Item</u>	<u>No off</u>	<u>Capacity</u>	<u>Material/Type</u>
reactors	3	2 cu m	316/glass lined steel jacketed
condensers	1	1 sq m	316 or glass
pumps	3	3 cu m/hr 2 bar	316
feed tanks	6		316, plastic
still	1	500 l, 1500 l/hr boil up rate, 250°C, 5 bar	316
centrifuge/ filter	2	500 l	316
drier	1	500 l	316

6.1.5 Mefenamic Acid

6.1.5.1 Description

Mefenamic Acid was first introduced as an analgesic by the Parke, Davis Company in Europe in 1963. About 14 mainly European brands are currently on the market.

Chemical name: 2-(2,3-dimethyl phenyl-amino) benzoic acid

Molecular formula and weight: C<sub>15</sub>H<sub>15</sub>O<sub>2</sub>N, 241

Pharmacopoeia references:

Merck Index 5617

PDR 1383

6.1.5.2 Process Route

SCIENTIFIC REFERENCES

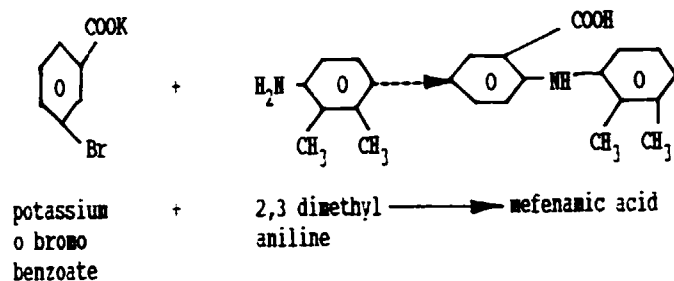
USP 3,138,636

178 kg potassium bromo benzoate, 335 kg bis 2 methoxy ethyl ether, 80 kg N ethyl morpholine, 84 kg di methyl aniline and 6.7 kg cupric acetate are batched, and charged into 2.0m<sup>3</sup> 316 stainless steel jacketed agitated reactor.

The reactants are agitated and heated under reflux to 140°C over 30 minutes, after which 58 kg concentrated hydrochloric acid is added. The solution is cooled to 20°C following the addition of 450 litres water.

The resulting crystals are centrifuged in a 500 litre capacity bowl centrifuge, and charged into a 2.0m<sup>3</sup> 316 stainless steel jacketed agitated crystalliser /reactor. 1000 litres bis 2 methoxy ethyl ether are added, and the mixture is heated to 100°C before being pumped via a 316 stainless steel in-line filter to a third 2.0m<sup>3</sup> 316 stainless steel jacketed agitated crystalliser/reactor.

Crystallisation takes place on cooling to 20°C. The crystals are centrifuged, washed and dried in a 316 stainless steel fluidised bed dryer.



All solvents are recovered for re-use after product recovery and distillation. Wastes are dissolved mineral salts in water, and treated by the activated sludge process.

#### 6.1.5.3 Manufacturing Requirements

OUTPUT: 100 kg/batch, batch time 11 hours total.

##### RAW MATERIALS:

	kg
potassium bromo benzoate	178
bis 2 methoxy ethyl ether	335
N ethyl morpholine	80
di methyl aniline	84
cupric acetate	6.7
hydrochloric acid, concentrated	58
water	450 l

##### UTILITIES:

steam - 5 bar g for vessel heating, drying  
 water - treated water as raw material, recirculated water for vessel cooling to 25°C  
 power - 20 kW installed for agitators, pumps, centrifuge distillation and drier  
 compressed air

EQUIPMENT:

<u>Item</u>	<u>No off</u>	<u>Capacity</u>	<u>Material/Type</u>
reactors	3	2 cu m	316 jacketed
condensers	2	1 sq m	316 or glass
pumps	3	3 cu m/hr	316
		2 bar	
feed tanks	5		316, plastic
centrifuge/ filter	2	500 l	316
drier	1	500 l	316
in line filter	1		316

6.1.6 Isoniazid

6.1.6.1 Description

Isoniazid is an antitubercular drug first introduced in 1958 and is now offered in 50-60 brands and manufactured in many different countries.

Chemical name: 4 pyridinecarboxylic acid hydrazide

Molecular formula and weight: C<sub>6</sub>H<sub>7</sub>N<sub>3</sub>O, 137

Pharmacopoeia references:

BP 1973, 256

USP 1975, 272

Martindale, 16, 1872

6.1.6.2 Process Route

SCIENTIFIC REFERENCES:

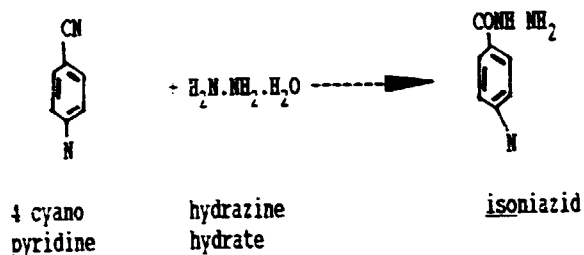
USP 2,830,994 and 2,596,069

125kg 4 cyano pyridine, 125kg hydrazine hydrate and 2.46kg sodium hydroxide are added to 375 litres water in a 1.0m<sup>3</sup> 316 stainless steel jacketed agitated reactor. The reactants are agitated and heated to 100°C, and maintained at this temperature under reflux for 7 hours.

The solution is cooled to 20°C and discharged to a 1.0m<sup>3</sup> 316 stainless steel jacketed crystalliser fitted with an anchor agitator via a 0.5m<sup>2</sup> in-line filter. The solution is then evaporated to dryness using low pressure steam under vacuum, and cooled to 20°C. 200 litres ethanol are added, and the solution heated to 60°C.

The solution is discharged into a further 1.0m<sup>3</sup> 316 stainless steel jacketed agitated crystalliser via a 0.5m<sup>2</sup> in-line filter, and cooled to 15°C. The resulting crystals are centrifuged, in a 500 litre capacity

bowl centrifuge, washed and dried in a 316 stainless steel fluidised bed dryer.



Waste products are dissolved mineral salts in water, and treated by the activated sludge process.

### 6.1.6.3 Manufacturing Requirements

OUTPUT: 100 kg/batch, batch time 18 hours total

#### RAW MATERIALS:

	<u>kg</u>
4 cyano pyridine	125
hydrazine hydrate	125
sodium hydroxide	2.46

#### UTILITIES:

steam - 2.5 bar g for vessel heating, drying  
 water - treated water as raw material, recirculated  
           water for vessel cooling to 25°C  
 power - 20 kW installed for agitators, pumps,  
           centrifuge and drier  
 compressed air

#### EQUIPMENT:

<u>Item</u>	<u>No off</u>	<u>Capacity</u>	<u>Material/Type</u>
reactors	3	1 cu m	316 jacketed
condensers	2	1 sq m	316 or glass
pumps	3	3 cu m/hr 2 bar	316
feed tanks	3		316, plastic
centrifuge/ filter	2	500 l	316
drier	1	500 l	316
in line filter	1		316
receiver	1	1 cu m	316



6.1.7 Ibuprofen

6.1.7.1 Description

Ibuprofen is an anti-inflammatory drug first introduced in the UK by the Boots Company in 1969. It is now offered for sale in 30-40 brands and manufacture in Europe, the USA and Japan.

Chemical name: alpha methyl-4-(2 methyl propyl) benzene acetic acid

Molecular formula and weight:  $C_{13}H_{18}O_2$ , 206

Pharmacopoeia references:

BP, 1975, A 26

Martindale, 26, 236

6.1.7.2 Process Route

SCIENTIFIC REFERENCE:

Japan 74,133,351, CA 82,139718z

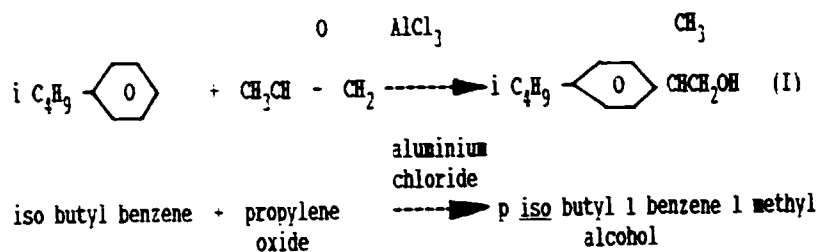
In the first step, a Friedel-Crafts reaction is carried out, in which iso butyl benzene is reacted with propylene oxide to give p iso butyl benzyl 1 methyl alcohol. In the second step, the p iso butyl benzyl 1 methyl alcohol is oxidised to ibuprofen using chromic acid.

100kg carbon disulphide, 77kg propylene oxide and 38.5kg iso butyl benzene are charged into a 0.5m<sup>3</sup> glass lined jacketed agitated reactor, A. In a second 1.0m<sup>3</sup> glass lined jacketed agitated reactor, B 100kg carbon disulphide, 38.5kg iso butyl benzene and 77kg anhydrous aluminium chloride are added, and cooled to -10°C. The contents of the first vessel A are added to the second vessel B over three hours, with the temperature being maintained between -10°C and -5°C, in a strongly exothermic reaction. The temperature is raised to 25°C, and the mixture is stirred for two hours. The catalyst is then dissolved using aqueous hydrochloric acid, and the aqueous phase is removed. The organic phase is removed and transferred to a 0.5m<sup>3</sup> 316 stainless steel jacketed agitated reactor C fitted with a condenser, where the solvent is removed by evaporation.

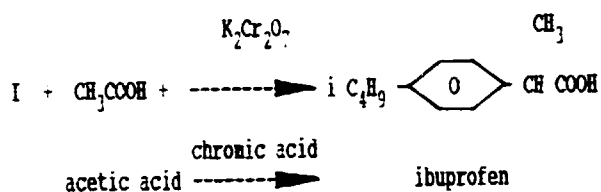
237kg potassium dichromate, and 200kg concentrated sulphuric acid are charged into a 1.0m<sup>3</sup> glass lined jacketed agitated reactor vessel, D and the contents of vessel C added. The mixture is agitated for one hour, then refluxed at 100°C for an hour, and then cooled to 5°C. 200 litres water and 200 litres organic solvent are added, and the aqueous phase removed. The material is dissolved by heating in 100 litres petroleum ether, and passed through an in-line filter

into a 1.0m<sup>3</sup> 316 stainless steel jacketed agitated crystalliser/reactor vessel E. The solution is cooled to 15°C and the resulting crystals are centrifuged in a 500 litre capacity bowl centrifuge, washed and dried in a 316 stainless steel fluidised bed dryer.

Step 1



Step 2



All solvents are recovered for re-use after product recovery and distillation. Wastes are dissolved mineral salts in water, and treated by the activated sludge process.

6.1.7.3 **Manufacturing Requirements**

OUTPUT: 100 kg/batch, batch time 13 hours total

RAW MATERIALS:

	kg
iso butyl benzene	89
propylene oxide	77
aluminium chloride	87
carbon disulphide	20
acetic acid	42
potassium dichromate	237
sulphuric acid concentrated	200

UTILITIES:

steam - 2.5 barge for vessel heating, drying  
water - treated water as raw material, recirculated water for vessel cooling to 25°C  
power - 45 kW installed for agitators, pumps, centrifuge and drier  
compressed air  
recirculated brine to 20°C  
vacuum

## EQUIPMENT

<u>Item</u>	<u>No off</u>	<u>Capacity</u>	<u>Material/Type</u>
reactors	1	500 l	glass lined, jacketed
	2	1 cu m	glass lined, jacketed
	2	500 l	316 jacketed
condensers	2	1 sq m	316 jacketed
pumps	5	3 cu m/hr	316
		2 bar	
feed tanks	6		316, plastic
centrifuge/ filter	1	500 l	316
drier	1	500 l	316
in line filter	1		316
receiver	1	1 cu m	316

## 6.2 EQUIPMENT

### 6.2.1 Major Items and Piping

6.2.1.1 In general, for this type of plant, the equipment consists of a number of reactors, vessels, receivers, filters, pumps, controls and ancillary items. The main items are inter-connected to facilitate their multi purpose roles.

6.2.1.2 In this study, we have based the proposed configuration of the plant on the requirements of the processes described above and as shown in Appendices 6-1 and 6-2. The additional needs for flexibility, training and product development have also been considered. Therefore, the number of selected plant items, which are summarised in Appendix 6-3, is a little in excess of the strict minimum needed for the operation of any one of the processes represented in Appendix 6-2. Any such duplication has been kept to a minimum consistent with the objectives of the project.

6.2.1.3 The reactor is typically located on the first floor (usually a steel framed 'mezzanine') so that the materials to be charged can be lifted to the second floor and tipped, pumped or fed into the vessel and discharged onto equipment installed on the ground floor.

6.2.1.4 Because of the multi-product, multi-purpose nature of the facility, care and creativity will be essential in the final detailed design of the interconnected piping. We have allowed for this in the estimate, noting that the pipework is small-bore and hence will

be relatively inexpensive to install (although, of course, most will be in stainless steel).

- 6.2.1.5 Because of the multi-purpose type of plant and the wide use of flammable solvents, all the processing area will be fitted with explosion proof electrical and other fittings and designated an explosion free area.

#### 6.2.2 Control and Instrumentation

The plant will be fully instrumented, using batch controllers for temperature, pressure, pH, weight and flowrate. The electronic control system should incorporate alarm signals, but in some cases additional hard-wired alarms will be necessary. Field mounted indicators will be provided where appropriate.

Although the control and instrumentation facilities will be fully developed and specified at the detailed design stage, it is envisaged that five small free-standing panels equipped with PLC capabilities and manual override would be appropriate to the project philosophy.

#### 6.2.3 Equipment Selection and Price

- 6.2.3.1 The equipment selection has been based on the rigorous requirements of the pharmaceutical industry; hence there is a predominance of stainless steel (316 grade) with some glass, glass lined and plastic items. This choice of materials is expensive but is essential and follows the normal practice for this type of project.

- 6.2.3.2 The costs of all major items are listed in the project estimate which is given in Section 9.

#### 6.3 SPARE PARTS AND MAINTENANCE

##### 6.3.1 Spare Parts

- 6.3.1.1 Commissioning spares are included in the estimate of capital cost. In addition, a further allowance of 2% of the initial value of the production and auxiliary equipment has been incorporated in the revenue forecasts to account for the consumption of miscellaneous spares throughout the appraised period of the project.

- 6.3.1.2 With regard to reactors and vessels, the above allowance includes the replacement of two such items per year. We feel that this is warranted in view of the nature of the materials being processed and,

especially, because of the use of glass-lined vessels. The latter are subject to a high frequency of damage and are costly.

6.3.1.3 Indeed, for this reason, and since these are long delivery items, we have added three reactors to the estimate of initial capital cost as 'capitalised spares'. In the same way, for spare pumps, one of each type have been capitalised.

6.3.1.4 Full details of the costings are provided in Appendix 10-8.

### 6.3.2 Maintenance

6.3.2.1 The cost of maintenance materials has been covered in 6.3.1 above. The labour costs related to maintenance are covered under the manpower assessment (see Section 8). Therein, we have indicated that a staff maintenance foreman plus three craftsmen/technicians will be required. It is foreseen that the latter is an average value and that some sharing with Chemfields - to cover peaks and troughs of activity - will be possible. These individuals, although costed, may not be on the staff of this project.

6.3.2.2 In line with modern thinking, we also envisage that labour will be flexible and that simple maintenance tasks may be carried out by others, for example the operators.

6.3.2.3 Full costing details are provided in Appendix 10-8.

## 6.4 PLANT LAYOUT

### 6.4.1 Location

6.4.1.1 The proposed location is by way of an extension of the existing Chemfields site as discussed in section 5.

### 6.4.2 Site Plan and Layout

6.4.2.1 The site plan showing the proposed positioning of the multi purpose pilot plant is given in Appendix 5-1. This places the plant close to the utilities units of the factory and the warehouse/training accommodation/offices adjacent to a large parking and manoeuvring area. The Chemfields laboratories, cafeteria, offices and so on are also close by.

6.4.2.2 The production facility is suggested as having an area of 900m<sup>2</sup> and the warehouse area of 1,300m<sup>2</sup>. As well as storage space, the latter includes the offices (12), laboratories, a lecture room, conference room, and rest rooms. The size of the production area is excessive for the presently proposed equipment which will occupy about 600m<sup>2</sup> of the 900m<sup>2</sup>. However, we feel that a considerable allowance should be made for expansion and also for training and unplanned development work.

6.5 CIVIL ENGINEERING AND CONSTRUCTION WORKS

6.5.1 The Process Building

6.5.1.1 The process building has been calculated from design criteria to demand 610m<sup>2</sup> area including production, local storage, circulation space, shift office and shift laboratory. The building is envisaged as a clear span portal construction with proprietary insulated roof and wall cladding. Environmental control equipment, eg the extractor fans should be capable of providing two air changes per hour.

As a teaching pilot plant, the building and roof would be clad externally with plastic covered steel sheets, and if the plant is either designated as a pharmaceutical plant or built on the Chemfields site, the internal walls would be fitted with plastic coated smooth finish panels for easy clean down.

It is unlikely the plant will be required to GMP Standards and this has not been assumed, except in the drying area.

The possibilities of cross contamination with other products manufactured at Chemfields are minimised by using a separate building away from the semi-synthetic penicillins, by controlling the air pressures in the buildings and by proper design of air and waste removal facilities.

The high humidity in the Philippines encourages the growth of moulds but this is not considered to be a problem for the main chemical processing areas since all the materials are contained within vessels. During material transfer and drying there is limited exposure of the product to the air which, if required, could be filtered to remove airborne pollution.

6.5.1.2 All electrical equipment must be flameproof; it is suggested that a rest room maintained at a small positive pressure should be provided for those of the workforce who smoke.

6.5.1.3 The floor of the operational area of the process building must be treated with acid resistant material and sloped and gullied to facilitate the cleaning of spillages and washing down. The run-off from this must be drained to the foul water system of Chemfields via an interceptor.

6.5.1.4 Although it is suggested that the steel structure of the building should be designed to accommodate a light duty gantry crane, we do not believe that the installation of such a crane is warranted for the scale of equipment proposed.

6.5.1.5 The reactor will be located and supported at first floor level and will provide an access for maintenance etc. A second floor platform shall also be provided to enable the materials to be taken to the vessel. The product discharge may be collected by equipment at ground floor level under the vessel by way of gravity.

The mezzanine floor shall comprise steel I, Z, or proprietary sections with an open mesh frame work and grill. The support structure around the vessel shall be supported by steel sections appropriate to the dead and imposed loadings.

6.5.2 The Warehouse/Offices

6.5.2.1 This has a total floor area of 1300m<sup>2</sup> with a two storey section at the front 400m<sup>2</sup> for the office accommodation including provision of a lecture room. The warehouse (900m<sup>2</sup>) should include a secure area for the storage of potentially hazardous feed materials with a flooring of acid resistant material. The same conditions apply to this building as to the process building with regard to environmental control and flameproofing. Entry to the office block must be via double fireproof doors.

6.5.2.2 There are some 27 raw materials for the five processes on which this project is based. Their usage ranges from 1.2kg to 3600 litres per 100kg batch. Therefore, at the first design stage care must be taken to assess the racking and other storage equipment required.

6.5.2.3 Finally, a 50m<sup>2</sup> concrete pad for the external storage of particularly toxic feedstocks (eg. cyanopyridine) should be sited at the side of the warehouse. This pad should be covered and fenced but unwallled.

6.6 UTILITIES, EFFLUENTS AND TRANSPORT

6.6.1 Utilities Requirement

6.6.1.1 The main utilities are electric power, steam and cooling water and are expected to be supplied on a chargeable basis by the existing Chemfields facilities. This should easily be possible because the requirements of the pilot plant are modest.

6.6.1.2 The utilities consumptions per batch were given in para. 4.1.7.1, Table 4.1.7.1 of which is repeated below.

Table 4.1.7.1

	Batch Size (kg)	Steam (tonnes)	Cooling Water	Electricity kWh	Plant Air	Nitrogen	Potable Water
Paracetamol	260	0.08	3.8	105	Negligible	Negligible	Negligible
Mefenamic Acid	100	0.04	2.1	165	"	"	"
Isoniazid	100	0.16	2.6	270	"	"	"
Ethambutol	100	0.12	6.4	110	"	"	"
Ibuprofen	100	0.12	6.4	425	"	"	"

6.6.1.3 Likewise we repeat Table 4.1.7.2 which gives the quantities to cope with peak loads.

Table 4.1.7.2

<u>Steam</u>	<u>Cooling Water</u>	<u>Electricity</u>
0.8 tonnes/day	25 tonnes/day	100kW

6.6.2 Waste Disposal

6.6.2.1 A semi-production scale plant such as this produces a range of pharmaceuticals in processes which are - to a greater or lesser degree - inevitably inefficient in their conversion of raw materials to finished products. There is thus some effluent produced most of which cannot be reused.

6.6.2.2 Because of the small scale of operation, the quantity of such waste products will be relatively small so that, for the time being it is suggested that the effluent system of the pilot plant could be connected to that of Chemfields in order to avoid wasteful duplication of systems. At a later date, the installation of neutralisation and settling equipment may be necessary to handle increased output if the plant is expanded.



6.6.3 Transport

6.6.3.1 Raw materials and product will generally be shipped in and out of the plant in drums of various capacities. When not being pumped, the same applies within the plant, eg movements to and from the warehouse. Again because of the scale of the operation, this level of activity will not be great and therefore it is expected that only two factory transports will be required. These are:

- a) one 0.5 ton capacity covered pick up truck
- b) one 300kg capacity fork lift truck

In the event of breakdown or the occasional need for a heavier vehicle, it is believed that a short term loan/hire from Chemfields would be possible.

6.6.3.2 A further three cars have been included in the estimate, one for the general managers, one for the sales co-ordinator, and one general purpose vehicle.

6.6.4 Where practical and possible, solvent is recycled for re-use after evaporation, drying and distillation. Chemfields existing facilities for distillation and storage have been assumed. All material consumptions have been based upon a 70% solvent recovery rate.

6.7 QUALITY CONTROL, SAFETY AND CLEANING

6.7.1 Good Manufacturing Practice (GMP), Product Licensing and Quality Control (QC)

6.7.1.1 A pharmaceutical product is defined as a medicinal chemical usually in its final dosage form. The active ingredient is the medicinally active compound used in a pharmaceutical preparation.

Good Manufacturing Practice is a set of rules affecting pharmaceutical product manufacture applied to ensure the quality, safety and efficacy of the product from the medical point of view. GMP rules lay down guidelines for manufacturing standards in pharmaceutical processes. Worker Health and Safety should be considered separately and in addition to the requirements for GMP.

A Product License is required before a pharmaceutical product can be sold. Amongst other things, the licensing procedure defines:-

- The production plant
- The input raw materials including the manufacturing route, and actual manufacturing plant for all active ingredients

- The specification of intermediates and final products
- In-process QC controls
- Physico-chemical verification of the process

Both the requirements of GMP and Product Licensing rules affect the multi purpose pilot plant, since purchasers of the plant products will require adherence to a defined manufacturing route. This is at odds with the other use of the pilot plant to develop and optimise commercial processes.

6.7.1.2 Quality should be the concern of all employees in a facility such as this pilot plant and this philosophy will be reflected in the training of the staff (see Section 8). Those particularly charged with the day to day control and maintenance of quality (of all materials - feedstocks, intermediates and products alike) are the chemistry team which consists of two senior managers and 6 technicians (i.e 1 and 3 per shift).

6.7.1.3 These will be distributed between a laboratory in the office building (the manager and one technician) and a shift laboratory in the process building (two technicians). The former will be particularly concerned with development work and training whereas the latter, working closely with the process superintendent, will check and report on daily production quality. It also envisaged that, with flexible working, the operators will be trained to perform simple tasks, thereby relieving the chemists of the more routine work.

6.7.1.4 The estimate includes almost \$46,000 for the laboratory equipment, an investment which will grow as the activities of the plant develop. The buildings estimate includes an allowance for building the laboratories.

6.7.1.5 It is expected that a teaching pilot plant will not be required to have a comprehensive need for QC facilities as the output is not to GMP Standards.

If pharmaceutical standards to GMP are required then chemical analysis of raw materials, intermediates and final product is required and could be supplied from existing facilities at Chemfields.

6.7.1.6 As mentioned in the building section 6.5.1.1, this plant would not normally be expected to produce to GMP Standards as a teaching pilot plant.

As a pharmaceutical plant, it would require the building's internal surfaces to be capable of easy cleaning, with smooth plastic coated, dust free surfaces. However, the facilities for the chemical

reactor area does not require this feature and this would only be required in the drying room.

6.7.2 Safety

6.7.2.1 As with quality, safety is everyone's concern. Safety will be ensured in four ways:

- a) by providing the necessary safety equipment, both portable and installed (eg. breathing equipment, fire extinguishers, smoke detectors and fire hydrants);
- b) by training and regularly retraining every member of staff in the essential safety precautions and procedures;
- c) by limiting intrinsic risks at the detailed design stage;
- d) by ensuring that operating staff strictly adhere to their instructions and data sheets.

The items 'miscellaneous utilities' in the cost estimate, see section 9, includes an allocation for equipment such as described above.

6.7.2.2 At the design stage, detailed considerations will need to be made to recognise and eliminate hazards, including fire, explosion and other potential accidents. In general:-

- Uncontrolled releases due to incorrect specification of equipment, equipment failure or procedural error should be prevented;
- Sources of ignition should be minimised, and the correct standard of explosion proof electrical equipment specified;
- The formation of flammable solvent/air mixtures in plant or equipment should be prevented;
- Consideration should be given to the control and prevention of runaway chemical reactions;
- Bulk storage of solvents should comply with acceptable standards of ventilation, handling and access for fire fighting;
- Chemicals stored in the warehouse should be properly segregated;
- The plant should be safe and operable for personnel.

Pressure vessels should be designed and tested to accepted international standards, such as ASME, with adequate provision for pressure relief. The fluidised bed dryer should incorporate a system in which the carrier gas nitrogen is recycled. Platforms and stairways should be designed with sufficient access and headroom, and escape routes provided. Safety showers should be provided, and potential hot and cold surfaces lagged to provide personnel protection. Emergency controls should be regularly tested, and the design should incorporate adequate instrumentation and alarm systems.

6.7.2.3 It will be the duty of management to ensure that all safety requirements are met and to develop, with external advice as necessary, a safety manual. The manual will describe the rules in place for permits to work in hazardous areas, for the use of sparking tools, and the undertaking of hot work, for the disconnection and reconnection of electrical supplies, and for entry in to vessels.

6.7.3 Cleaning Procedures

6.7.3.1 The cleaning of the building and equipment has already been dealt with under 6.5.1, 6.5.2 and 6.6.2. To comply with Quality Control standards in the industry, cleaning down of process equipment is required between batches. This is normally achieved using chemical cleaning agents or solvents, as appropriate, followed by rinsing with water or compatible solvent and, if necessary, drying with air.

6.7.3.2 Just as the quality of products is controlled, it will be essential to check effluents for the discharge of dangerous or flammable chemicals and to take immediate corrective action in the event of an abnormal occurrence.

6.7.3.3 When dealing with poisonous, corrosive and pharmaceutical materials, operator cleanliness is of paramount importance. The issue and regular laundering of overalls and the use, as appropriate, of protective clothing will be a crucial matter to be dealt with by senior management.

SECTION 7

PLANT ORGANISATION AND OVERHEAD COSTS

7.1 COST CENTRES

7.1.1 Appendix 7-1 sets out the breakdown of cost centres.

7.2 OVERHEAD COSTS

7.2.1 Appendix 7-1 also provides a breakdown of factory and overhead costs.

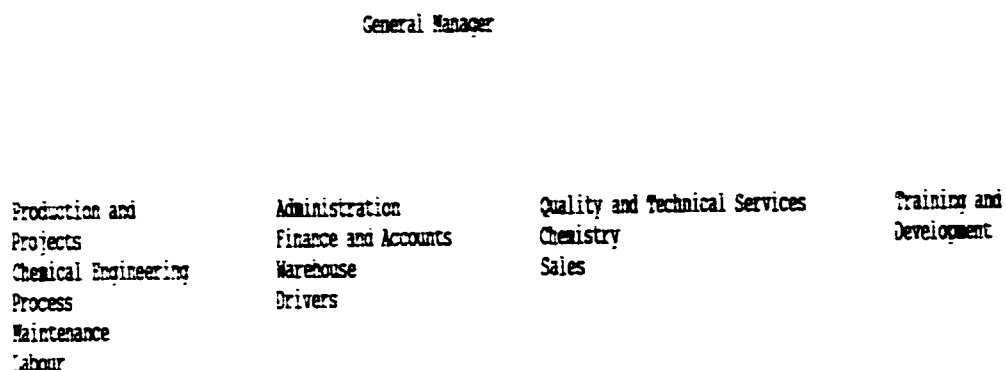
## SECTION 8

### 8.1 ORGANISATION AND MANPOWER

#### 8.1.1 Organisation Structure

8.1.1.1 An abbreviated organisation structure is shown below:

Figure 8.1.1.1



#### 8.1.2 Manpower Requirements

8.1.2.1 The manpower requirements which we estimate to be appropriate in this project are given in Table 8.1.2.1. The workforce numbers 43 and is based on there being a degree of flexibility between functions, eg process operators should be able to carry out simple chemical tests in a shift laboratory. This theme is the basis of the envisaged training programmes.

Table 8.1.2.1

<u>POSITION</u>	<u>NUMBER</u>	<u>TYPE OF WORK</u>
General Manager	1	days
Senior Managers		
Chemical Engineers	2	shifts (2 x 1)
Chemists	2	shifts (2 x 1)
Administrator	1	days
Training and Development	1	days
Middle Management		
Process Superintendents	1	shifts (2 x 1 + spare)
Maintenance Foreman	1	days
Warehouse Foreman	1	shifts (2 x 1 + spare)
Sales Liaison	1	days

<u>POSITION</u>	<u>NUMBER</u>	<u>TYPE OF WORK</u>
Technicians and Administration		
Chemists	6	
Operators	6	
Storemen	3	
Maintenance	3 (average)	shifts (2 x 1 + 1 on average)
Administration	5	days
Unskilled		
Drivers	2	shifts (2 x 1)
Labour	2	shifts (2 x 1)
	--	
<b>TOTAL</b>	<b>43</b>	

## 8.2 TRAINING REQUIREMENTS AND PATTERNS

### 8.2.1 Extent and Style of Training

8.2.1.1 The recruitment and training pattern prior to start-up is shown in Appendix 8-1 with the man weeks applying to each category; essentially this gives the manpower cost involved, i.e. a total of 180 man months divided as follows:

Table 8.2.2.1

<u>LEVEL</u>	<u>MAN MONTHS</u>
General Manager	12
Senior Managers	48
Middle Managers	40
Technicians	72
Unskilled Workers	8
	---
<b>TOTAL</b>	<b>180</b>

8.2.1.2 The philosophy here is that senior people are recruited before more junior staff and have longer training durations. This will enable them to become trainers in their turn, thus establishing an appropriate in-house tradition as well as an economic solution to the issue of training. This approach will carry through to the operational phase of the project and continue thereafter.

8.2.1.3 It is envisaged that the General Manager will take part in a bespoke course including 6 months overseas (preferable in the USA or the UK) at a cost of, say, \$50,000. Periods in a pharmaceutical plant, research institute and a business school could make up this programme. On his return, he would lead the recruitment effort and contribute to the training of his top people.

8.2.1.4 Other staff would attend purpose designed courses at the local University or other appropriate establishments. Experts would also be invited to the site to offer their skills. We estimate that about \$70,000 should be set aside for external charges to cover these programmes. However, at this stage, it is not possible to specify the courses more closely - their content depends to a large extent upon the qualification and experience of the new recruits, hence the need for technical assistance which is specified below.

8.2.1.5 Training in industrial chemical manufacture could be undertaken by Chemfields. If Chemfields are not involved with the project and did not contribute towards worker training, then the only alternative solution would be to recruit expatriates to set up in-house training courses.

The type of technical training required is summarised as follows:-

<u>Technology</u>	<u>Requirements</u>	<u>Provided By</u>
Chemistry	Theoretical, Practical	college/in-house
Engineering	Theoretical, Practical	college/in-house
Electrical	Theoretical, Practical	college/in-house
GMP	Theoretical, Practical	outside specialists
Chemical Processing	Practical	college/in-house
Chemical Engineering	Theoretical	college
Pharmacy	Theoretical	college

#### 8.2.2 Technical Assistance

8.2.2.1 For the above reasons, the details of the training plans and practice can only be determined during the pre start up year. For this purpose, we believe the skills and guidance of a foreign expert will be invaluable. The individual should be:

- a) Familiar with pharmaceutical production
- b) Preferably a chemical engineer or chemist
- c) A proven programme developer and instructor

It is likely he will be required as early as possible and carry through his assignment well into the first year of operation. We have therefore allowed \$120,000 to cover an 18 month assignment.



## SECTION 9

### IMPLEMENTATION SCHEDULING

#### 9.1 DATA AND ALTERNATIVES

9.1.1 The implementation programme for this project follows the standard requirement for a small sized bulk pharmaceutical plant and indicates 18 months from award of contract to commissioning the plant. Please see the bar chart which has been prepared (Appendix 9-1) to provide a summary of the main actions required.

9.1.2 The bar chart has been prepared under the following assumptions:-

- Approval to proceed is given by the end the third quarter of 1992
- The plant will start up in January 1995 and build up to full capacity in 1996
- The project will be placed with an engineering contractor for implementation to provide services on a 'turnkey' detailed design, supply and erection basis
- The contractor will be selected by open tender international tender before June 1993
- The contractor will be responsible for:-
  - any process licenses and process and plant guarantees
  - design, engineering, procurement, shipment, installation and commissioning
  - preparation of site
  - buildings and civil engineering design and construction
  - tying into utilities

#### 9.2 SELECTION OF PROJECT IMPLEMENTATION SCHEDULE

9.2.1 A company will have to be formed during 1992/3 initially employing a skeleton staff of 2 or 3 persons to re-confirm the engineering, financial, marketing and technical proposals. This work should be completed by the end of 1992 at which time, enquiries for the construction of the plant should be placed with contractors and the land allocated.

9.2.2

Once the tender has been awarded, say by June 1993, the contractor will assume his main responsibilities for construction but the new company will require the skeleton staff to monitor progress and to organise the recruitment and training of staff over the period 1992 to 1994. The main site preparation and building work will be in 1994 ready for equipment installation during 1994. Commissioning of equipment will take place over the 1994-5 period.

9.3

PROJECT COST ESTIMATE

The preliminary engineering design has been developed in sufficient detail to ensure that project costs (see Appendix 9-2) are accurate to +15%. Please refer to this Appendix for a complete discussion and analysis of the project cost estimates.

**SECTION 10**

**FINANCIAL EVALUATION**

10.1 **TOTAL INVESTMENT COSTS**

10.1.1 **Total Initial Investment Costs**

10.1.1.1 The total initial investment cost of the proposed pilot plant has been estimated at P 233.2 million, equivalent to approximately US\$ 9 million. Only 40% of this total would be payable in foreign currency :

Pesos '000	Foreign Currency	Local Currency	Total Cost
Initial Fixed Investment Costs	58,043	124,185	182,228
Pre-Production Capital Expenditure	29,987	5,162	35,149
Working Capital (at full capacity)	5,647	10,149	15,796
Total	<u>93,977</u>	<u>139,496</u>	<u>233,173</u>

10.1.1.2 Further details regarding the above cost estimates are presented in sections 10.1.2 to 10.1.4 inclusive.

10.1.2 **Initial Fixed Investment Costs**

10.1.2.1 The initial fixed investment cost may be broken down under two principal headings :

Pesos '000	Foreign Currency	Local Currency	Total Cost
Buildings/Civil Works	1,396	114,851	116,247
Machinery and Equipment			
- Production Machinery and Equipment	27,397	2,609	30,006
- Ancillary Production Equipment	20,029	2,003	22,032
- Auxiliary Equipment	9,221	1,312	10,533
- Vehicles	0	3,410	3,410
Sub-Total	<u>56,647</u>	<u>9,334</u>	<u>65,981</u>
Total	<u>58,043</u>	<u>124,185</u>	<u>182,228</u>

10.1.2.2 A detailed breakdown and explanation of the foregoing is presented at Appendix 10-1, but the following points may be highlighted for ease of reference :

- a) The prices quoted for purchase of the project vehicles and office furniture/equipment have been based on information obtained in the Philippines.
- b) The capital cost estimates in respect of the buildings and civil works, and the production and auxiliary machinery and equipment have been taken directly from the detailed project costing set out in Appendix 9-2, converted into Pesos.
- c) A provision has been made for payment of 10% customs duties on all imported items.
- d) All the cost estimates are quoted inclusive of an overall 10% contingency allowance.

10.1.2.3 Although it is anticipated that the initial investment cost would be phased over two years, approximately 82% would be incurred in 1994, the second year of project implementation :

1993	:	P 32,506,000	=	17.8%
1994	:	P 149,722,000	=	82.2%
		<u>P 182,228,000</u>		

10.1.2.4 Further details in this regard are set out in Appendix 10-2, which also splits each of the estimates into its foreign and local currency cost components.

10.1.3 Pre-Production Capital Expenditures

10.1.3.1 The pre-production capital expenditures relating to the project may also be broken down as follows :

Pesos '000	Foreign Currency	Local Currency	Total Cost
Pre-Investment Studies	533	0	533
Preparatory			
Engineering Studies	1,287	0	1,287
Management of Project			
Implementation	884	0	884
Detailed Engineering			
and Tendering	12,285	0	12,285
Supervision, Testing			
and Commissioning	4,472	546	5,018

Pesos '000	Foreign Currency	Local Currency	Total Cost
Recruitment and Staff Training	7,800	2,847	10,647
Arrangements for Supplies	0	195	195
Arrangements for Marketing	0	65	65
Build-up of Connections	0	260	260
Capital Issue Expenses	0	780	780
Contingency Allowance	2,726	469	3,195
<b>Total</b>	<b>29,987</b>	<b>5,162</b>	<b>35,149</b>

10.1.3.2 The costs quoted in respect of the first five items specified have been taken directly from the detailed project costing set out in Appendix 9-2, converted into Pesos. The remaining expenditures have been estimated by reference to the information available, and separate provision has been made for an overall contingency allowance of 10%.

10.1.3.3 It is expected that all but 15% of these costs would be incurred in the 2-year project implementation phase. However, provision has also been made for an expatriate training expert, specialising in chemical plant operation, safety and health, to be employed for an initial 18-month period thereafter, and for the cost of this to be capitalised :

1993	:	P 11,694,000	=	33.3%
1994	:	P 18,307,000	=	52.1%
1995	:	P 3,432,000	=	9.7%
1996	:	P 1,716,000	=	4.9%
		<u>P 411,183,000</u>		

10.1.3.4 Once again, further details in this regard are set out in Appendix 10-3, as is the split of the estimates into their foreign and local currency cost components.

#### 10.1.4 Working Capital Requirement

10.1.4.1 The working capital requirements of the project for the 10-year operational period from 1995 to 2004 inclusive are presented in Appendix 10-4, together with details as to how these have been calculated. However, the total initial investment cost includes provision for the net working capital requirement in 1996, given that the proposed plant would then be operating at 100% capacity utilisation :

<b>Current Assets</b>	
a) Accounts Receivable	: P 2,203,000
b) Inventory	
- Imported Materials	: P 4,990,000
- Spare Parts	: P 657,000
- Work-in-Progress	: P 1,684,000
- Finished Products	: P 6,434,000
b) Cash in Hand	: P 1,094,000
	<hr/>
Total Current Assets	: P 17,062,000
<b>Current Liabilities</b>	
a) Accounts Payable	: P 1,266,000
	<hr/>
<b>Net Working Capital</b>	: <u><u>P 15,796,000</u></u>

10.1.4.2 Based on the information set out in Appendices 10-2 to 10-4 inclusive, the investment costs incurred in each year of project implementation and operation from 1993 through to 2004 are summarised in Appendix 10-5 for ease of reference.

10.1.5 Total Assets Schedule

10.1.5.1 The initial asset value of the pilot plant has been estimated at a total of just over P 234.4 million :

Pesos '000	Foreign Currency	Local Currency	Total Cost
Initial Fixed Investment Costs	58,043	124,185	182,228
Pre-Production Capital Expenditure	29,987	5,162	35,149
Current Assets (at full capacity)	5,647	11,415	17,062
	<hr/>	<hr/>	<hr/>
Total	<u>93,677</u>	<u>140,762</u>	<u>234,439</u>

10.1.5.2 The build-up in the asset value in each year of project implementation and operation from 1993 through to 2004 is detailed in Appendix 10-6.

10.2 PROJECT FINANCING

10.2.1 Sources of Finance

10.2.1.1 The financing arrangements proposed for the multi-purpose pilot plant are as follows :

Pesos '000	Foreign Currency	Local Currency	Total Cost
Equity Capital			
- Project Promoters	0	70,332	70,332
- Financial Agencies	46,888	0	46,888
Long-Term Borrowings			
- Foreign Currency	45,542	0	45,542
- Local Currency	0	70,411	70,411
Current Liabilities (at full capacity)	1,247	19	1,266
Total	<u>93,677</u>	<u>140,762</u>	<u>234,439</u>

10.2.1.2 The financing plan has been formulated by reference to five main assumptions :

- a) The project would be required to conform to the standard guidelines set by the Central Bank of the Philippines with regard to suggested debt : equity ratios. Borrowings have therefore been limited to a maximum of 50% of the total requirement for project finance, the balance of 50% being covered by equity subscriptions by local promoters and external financial institutions or agencies.
- b) It is anticipated that, whilst the involvement of the latter would be welcomed, the government would wish to ensure that the local project promoters retained an overall majority interest of 60%. The participation of external partners in the share capital has accordingly been limited to 40%.
- c) 49% of the foreign currency investment in the initial assets of the project would be funded by medium term foreign currency loan facilities. These would bear interest at an average rate of 8% per annum, and would be repayable over six years (inclusive of a grace period of one year).
- d) Just over 50% of the local currency investment in the initial assets of the project would be funded by Peso loan facilities. These would bear interest at an average rate of 25% per annum, and

would be repayable over four years (inclusive of a grace period of one year).

- e) The balance of the working capital requirement would be covered by the provision made for current liabilities (that is, accounts payable).

10.2.1.3 On the basis of the foregoing, the debt : equity ratio would amount to an acceptable 0.99 : 1 at the outset.

10.2.1.4 The initial financing plan for the project is presented in Appendix 10-7, from which it may be noted that the prospective shareholders would be required to subscribe for their shares in full during 1993, and both the foreign and local currency loans would be drawdown in full by mid-1995.

10.2.1.5 Given the terms and conditions which have been assumed in respect of the foreign and local currency loans, and which are specified above, the annual financial costs may be estimated as follows :

Pesos '000	Forex Loan Facilities	Peso Loan Facilities	Total Interest
1995	3,643	17,603	21,246
1996	3,279	11,735	15,014
1997	2,550	8,802	11,352
1998	1,822	2,934	4,756
1999	1,093	0	1,093
2000	364	0	364

10.3 PRODUCTION COSTS

10.3.1 Total Production Costs

10.3.1.1 Separate schedules summarising total production costs under their individual cost headings, and itemising these in detail, are set out in Appendix 10-8a and 8b respectively. Comprehensive notes on the assumptions used in compiling these figures are included therein, but a number of points may be highlighted for ease of reference :

- a) Expenditures on raw material inputs and utilities have been calculated by reference to the detailed production schedule prepared, and specified usage and cost figures per individual input. In the case of imported materials, provision has been made for payment of 10% customs duties.



- b) It is anticipated that the project would employ a total of 11 direct production staff, and a further 13 laboratory and engineering staff.
- c) In recognition of the fact that the extent and cost of servicing needs would increase over time, a 5% compound growth factor has been built into the provision made for importation of replacement spare parts.
- d) Other factory overheads include provision for repairs and maintenance and expenditure on protective clothing and sundry consumable items (such as cleaning materials, lubricants, etc).
- e) It is anticipated that the project would employ a team of 7 senior managers, plus a further 10 administration and other personnel (including an accounts officer, secretarial and clerical staff, storekeepers and drivers).
- f) Administrative overheads include provisions in respect of the cost of insurance, office supplies, communications, land/property charges, licences, fees, travel/transport and sundry other items which are not separately specified, such as staff canteen and medical expenses.
- g) It is anticipated that the project would employ a sales liaison officer, who would be responsible for all public relations activities with both existing and potential customers.
- h) Other sales and distribution costs include product promotion and advertising, travel and transport.
- i) Full details of the financial costs assumed are set out in section 10.2.1.5 above.
- k) Depreciation in respect of the proposed investment has been calculated on a straight line basis in accordance with the following rates :
 

Buildings and Civil Works	:	5%
Production and Auxiliary Equipment	:	10%
Vehicles	:	20%
Pre-Production Capital Expenditures	:	20%

10.3.1.2 Total production costs in 1997, when the factory would be operating at an effective 100% capacity utilisation, may be summarised as follows :

Pesos '000	Foreign Currency	Local Currency	Total Cost
Direct Inputs			
- Raw Materials	14,969	0	14,969
- Utilities	0	224	224
Direct Manpower	0	1,340	1,340
Factory Overheads			
- Manpower	0	1,500	1,500
- Replacement Spares	1,314	0	1,314
- Other Overheads	0	863	863
Factory Costs	16,283	3,927	20,210
Admin. Overheads			
- Manpower	0	2,560	2,560
- Other Overheads	0	2,965	2,965
Sales/Distribution			
- Manpower	0	220	220
- Other Costs	0	480	480
Operating Costs	16,283	10,152	26,435
Financial Costs	3,279	11,735	15,014
Depreciation	0	19,781	19,781
Production Costs	19,562	41,668	61,230

### 10.3.2 Unit Costs

10.3.2.1 With regard to the unit costs of the various products to be manufactured, these have been estimated on the basis of the cost of their direct inputs only and are as follows :

#### Ethambutol

- Raw Materials : P 280.25 per kg  
 - Utilities : P 3.36 per kg

Total Input Cost : P 283.61 per kg

#### Ibuprofen

- Raw Materials : P 329.24 per kg  
 - Utilities : P 10.36 per kg

Total Input Cost : P 339.60 per kg

#### Isoniazid

- Raw Materials : P 331.39 per kg  
 - Utilities : P 7.04 per kg

Total Input Cost : P 338.43 per kg

<b>Mefenamic Acid</b>	
- Raw Materials	: P 586.89 per kg
- Utilities	: P 3.97 per kg
<b>Total Input Cost</b>	: <u>P 590.86 per kg</u>

<b>Paracetamol</b>	
- Raw Materials	: P 209.93 per kg
- Utilities	: P 1.13 per kg
<b>Total Input Cost</b>	: <u>P 211.06 per kg</u>

10.3.2.2 Comparison of these unit costs with the anticipated maximum selling prices highlights the fact that, on the basis of the cost and market information available, the project would, in fact, be unable to charge prices for either Mefenamic Acid or Paracetamol which would cover their input costs alone. Both these products would therefore be produced at a gross loss, although the gross margins on the other products would range from 32% on Isoniazid to a generous 76% on Ethambutol :

per kg	Input Cost	Sales Price	Gross Margin	% Margin
Ethambutol	284	1,170	886	76%
Ibuprofen	340	832	492	59%
Isoniazid	338	494	156	32%
Mefenamic Acid	591	572	( 19)	( 3%)
Paracetamol	211	187	( 24)	(13%)

#### 10.4 FINANCIAL EVALUATION

##### 10.4.1 Financial Projections

10.4.1.1 The projected net income statement in respect of the operations of the pilot plant over a 10-year period from 1995 to 2004 inclusive is presented at Appendix 10-9. The corresponding cash flow table for financial planning and the projected balance sheets are set out in Appendices 10-10 and 10-11 respectively.

10.4.1.2 Attention may be drawn to three principal points in connection with these financial projections :

- a) The pilot plant would record an operating loss in each of the ten years under review, due to the fact that input costs in respect of Paracetamol in particular exceed the selling price assumed.

- b) The accumulated losses would exceed the equity capital by the third year of operation, at which point the project would be technically bankrupt. By the end of the 10-year period, the accumulated losses would total nearly P 263.9 million, more than the total initial investment cost.
- c) The cash deficit on operations alone would average over P 43 million per annum. By the end of the 10-year period, the cumulative cash shortfall would total nearly P 220.6 million.

10.4.1.3 For the sake of completeness, the key financial ratios for the plant once full capacity utilisation has been achieved (in 1996) are detailed below :

Simple Rate of Return		
- Total Investment	:	(10.3%)
- Equity Capital	:	(33.4%)
Break-Even Analysis		
- % Increase in Sales	:	533.0%
Current Ratio	:	0.2
Debt Service Coverage Ratio	:	(0.4)

10.4.1.4 Appendix 10-12 details the cash flow tables in respect of both total investment and equity capital which form the basis for the internal rate of return analysis and computation of the net present value of the project :

Internal Rate of Return		
- Total Investment	:	(17.5%)
- Equity Capital	:	(22.9%)
Net Present Value @ 18%		
- Total Investment	:	( P 203.2 mn)
- Equity Capital	:	( P 199.2 mn)

10.4.2 Sensitivity Analysis

10.4.2.1 In order to assess the impact of including Paracetamol in the production programme, an alternative scenario was prepared based on the following assumptions :

- There would be no production of Paracetamol throughout the period under review;
- Production of Mefenamic Acid would be maintained at the same levels as projected in the base case; and

- The pilot plant would produce sufficient tonnages of Ethambutol, Ibuprofen and Isoniazid to satisfy all Unilab's estimated requirements in 1995 :

Ethambutol	:	2.2 tonnes
Ibuprofen	:	27.3 tonnes
Isoniazid	:	20.8 tonnes

All other assumptions made regarding sales prices and the costs of production have been left unchanged.

10.4.2.2 The results of this analysis may be briefly summarised as follows :

- a) The pilot plant would make an operating profit of approximately P 6.9 million when producing at its assumed maximum of 95% capacity utilisation. This would translate into a gross loss of P 28 million, reducing to P 6.5 million with effect from the year 2000.
- b) The accumulated losses would exceed the equity capital by the fifth year of operation, at which point the project would be technically bankrupt.
- c) By the end of the 10-year period, accumulated losses would total nearly P 155 million, and the cumulative cash shortfall would exceed P 112.6 million.
- d) Sales would have to increase by 75% to enable the pilot plant to achieve break-even.
- e) The internal rate of return on total investment was calculated at -8.1% and that on equity capital at -13.3%.

10.4.2.3 Three further analyses were then prepared to assess the sensitivity of this revised project to the factors most likely to have a direct impact on profitability and cash flow. In each case, the object of the exercise was to ascertain what changes would be necessary to enable the plant to break-even :

**Analysis I**

Sales prices would have to increase by a minimum of 36% over and above the levels assumed.

**Analysis II**

The cost of all direct factory inputs, including raw materials, utilities, manpower and other factory overheads, would have to be reduced by not less than 50% from the levels assumed.

### Analysis III

A 21% increase in sales prices, combined with a 21% reduction in the cost of all direct factory inputs would achieve the same result.

10.4.2.4 Projected financial statements in respect of Analysis III are set out in Appendix 10-13, but the following points may be highlighted for ease of reference :

- a) The pilot plant would make an operating profit of approximately P 19.4 million when producing at its assumed maximum of 95% capacity utilisation. This would initially translate into a gross loss but, with the elimination of financial costs, the plant would make pre-tax profits exceeding P 6 million per annum with effect from the year 2000.
- b) By the end of the 10-year period, accumulated losses would have reduced from a maximum of P 62 million to nearly P 39.5 million.
- c) The cumulative cash shortfall would peak at P 78.5 million in 1998 and, given the positive cash flow thereafter, an overall cash surplus would be recorded by the end of the project period.
- d) The internal rate of return on total investment was calculated at 0.2% and that on equity capital at -4.1%.

10.4.2.4 The foregoing serves to underline the fact that the proposed multi-purpose pilot plant would not be a commercially feasible proposition, even if Paracetamol were to be excluded from the production programme, and the underlying revenue and/or cost assumptions could be substantially improved.

10.4.2.5 Whilst it is appreciated that this is not intended to be a commercial venture, the Terms of Reference specify that the plant should be financially self-sustained. However, it is likely that this could only be achieved in circumstances whereby project implementation could be funded by grant and/or aid monies so as to eliminate financial costs; and the operations of the plant could be subsidised to the extent that it could then offer its product for sale at reasonably competitive prices.

### 10.5 FURTHER SENSITIVITY ANALYSES

Further sensitivity analyses were carried out based on assumptions aimed at reducing capital costs and increasing revenues.

10.5.1 Sensitivity Analysis IV

10.5.1.1 This alternative scenario was prepared based on reducing the non-production facilities to the minimum and on the following assumptions:

- The proposed warehouse, office accommodation and lecture theatre would be excluded, with the result that the civil engineering costs of the project would be reduced by P46.5 million (inclusive of the 10% contingency allowance). In the basic design of the process building and the warehouse, allowance was made for expansion. In the early years of the project the space could be sectioned off to permit storage of a substantial amount of feedstock and chemicals while temporary overflow space could be rented from Chemfields;
- There would be no production of Paracetamol throughout the period under review;
- The pilot plant would produce sufficient tonnages of Ethambutol, Ibuprofen, and Isoniazid to satisfy all Unilab's estimated requirements in 1995; and
- Production of Mefenamic Acid would be maintained at the same levels as projected in the base case.

All other assumptions made regarding sales prices and the costs of production have been left unchanged.

10.5.1.2 The revised initial investment cost of the pilot plant has thus been estimated at P188.6 million, equivalent to just over US\$7.25 million. 50% of this would be payable in foreign currency:

Pesos '000	Foreign Currency	Local Currency	Total Cost
Initial Fixed Investment Costs	58,043	77,710	135,753
Pre-Production Capital Expenditure	29,987	5,162	35,149
Working Capital (at full capacity)	6,645	11,050	17,695
	-----	-----	-----
Total	94,675	93,922	188,597
	=====	=====	=====

10.5.1.3 Given the reduction in the overall project cost, the financing arrangements proposed would then be amended as follows:

Pesos '000	Foreign Currency	Local Currency	Total Cost
Equity Capital			
- Project Promoters	0	57,040	57,040
- Financial Agencies	38,026	0	38,026
Long-Term Borrowings			
- Foreign Currency	55,152	0	38,026
- Local Currency	0	38,379	38,379
Current Liabilities (at full capacity)	1.497	37	1,534
	-----	-----	-----
Total	94,675	95,456	190,131
	=====	=====	=====

10.5.1.4 Projected financial statements (comprising net income and cash flow statements and balance sheets) in respect of Sensitivity Analysis IV are presented in Appendix 10-14. The following points may be highlighted for ease of reference:

- a) The pilot plant would make an operating profit of approximately P7.4 million when producing at its assumed maximum of 95% capacity utilisation. This would translate into a gross loss of approximately P20.4 million, reducing to P3.8 million as from the year 2000.
- b) The accumulated losses would exceed the equity capital by the sixth year of operation, at which point the project would be technically bankrupt.
- c) By the end of the 10 year period, accumulated losses would total nearly P110.4 million, but the cash shortfall would have reduced from a peak of P95.3 million in 2000 to just over P68 million.
- d) Sales would have to increase by 59% to enable the pilot plant to achieve break-even.
- e) The internal rate of return on total investment was calculated at -8.1% and that on equity capital at -13.6%.

10.5.1.5 Three further analyses were then prepared to ascertain what changes would be necessary to enable the plant to break-even:

**Analysis I**

Sales prices would have to increase by a minimum of 27% over an above the levels assumed.



### Analysis II

The cost of all direct factory inputs, including raw materials, utilities, manpower and other factory overheads, would have to be reduced by not less than 44% from the levels assumed.

### Analysis III

A 17% increase in sales price, combined with a 17% reduction in the cost of all direct factory inputs would achieve the same result.

## 10.5.2 Sensitivity Analysis V

10.5.2.1 The final scenario has been based on the assumption that production of Ethambutol, Ibuprofen and Isoniazid would be increased to the extent that the pilot plant would be able to satisfy the estimated requirements of the entire market in 1995. However, there would be no increase in the production of Mefenamic Acid and, once again, Paracetamol would be excluded:

Ethambutol	:	10.7 tonnes
Ibuprofen	:	30.3 tonnes
Isoniazid	:	34.6 tonnes
Mefenamic Acid	:	2.5 tonnes
Paracetamol	:	-

10.5.2.2 Projected financial statements in respect of Analysis V are set out in Appendix 10-15, but attention may be drawn to the following points in particular:

- a) The pilot plant would make operating profits of approximately P18 million when producing at this level of output. These would initially translate into gross losses but, with the elimination of financial costs, the project would make pre-tax profits of some P 7 million per annum with effect from the year 2000.
- b) By the end of the 10 year period, accumulated losses would have reduced from a maximum of P 43.5 million to just over P18.4 million.
- c) The cumulative cash shortfall would peak at P46.2 million in 1998 and, given the positive cashflow thereafter, a cash surplus would be recorded by the end of the project period.
- d) The internal rate of return on total investment was calculated at 01.% and that on equity capital at -4.2%

## SECTION 11

### ECONOMIC ANALYSIS

#### 11.1 OVERALL ASSESSMENT

##### 11.1.1 Prospects for Success

11.1.1.1 On the basis of the financial evaluation presented in Section 10, it is considered that the implementation and operation of this project would be dependent upon a combination of four factors in particular :

- the successful negotiation of aid or grant monies to fund a significant proportion of the capital costs anticipated;
- the exclusion of Paracetamol from the production programme;
- an increase in sales prices or, alternatively, the introduction of subsidies to enable the plant to price its product reasonably competitively; and
- a reduction in input costs.

11.1.2.2 The prospects for the proposed multi-purpose pilot plant would thus appear to be marginal at best.

#### 11.2 ECONOMIC ANALYSIS

##### 11.2.1 Employment

11.2.1.1 It is anticipated that the plant would employ a total of 43 members of staff, broken down as follows :

Management	:	7
Direct Production Staff	:	11
Laboratory/Engineering Staff	:	13
Administration/Other Personnel	:	10
Sales Personnel	:	2
		<hr/>
		43
		<hr/>

11.2.1.2 The total wage and salary cost has been estimated at approximately P 5.6 million per annum :

Management	:	P 2,000,000
Direct Production Staff	:	P 1,340,000
Laboratory/Engineering Staff	:	P 1,500,000
Administration/Other Personnel	:	P 560,000
Sales Personnel	:	P 220,000
		<hr/>
		P 5,620,000
		<hr/>

11.2.2 Domestic Resources

11.2.2.1 The project would be entirely dependent upon imported raw material inputs, given that none of the chemicals used in the production processes envisaged could be obtained from domestic sources of supply.

11.2.2.2 Utilisation of domestic resources would thus be limited to utilities and to such consumable items as protective clothing, cleaning materials, office supplies and the like. Total expenditure on these at full production has been estimated as follows :

		<u>Pesos</u>
Utilities	:	224,000
Consumables	:	200,000
Office Supplies	:	195,000
		<hr/>
		619,000
		<hr/>

11.2.2.3 In addition, the investment cost estimates assume that all the project vehicles and office furniture and equipment would be purchased from domestic suppliers. Provision has therefore been made for the vehicles to be replaced during the operational period, at an estimated cost of P 3.4 million.

11.2.3 Training and Expertise

11.2.3.1 However, the project should achieve what is perceived to be one of its most important functions, in that it would both introduce and develop local expertise and experience in this particular field. In the initial instance, some technicians would have to go overseas for relevant training, but thereafter the pilot plant would provide extensive training facilities within the Philippines on an on-going basis.

11.2.3.2 Although the spin-off benefits from this cannot be quantified, it would be fair to say that the project would have a positive impact in socio-economic if not in commercial terms.

**APPENDICES**

for

Feasibility Study on the Establishment of a Multi-purpose Pilot Plant  
for Chemical Synthesis1. BACKGROUND

The drug industry is an important sector in the Philippines. Drugs are produced, imported and distributed in a free market system. The main manufacturing activity is formulation and packaging of final dosage forms from imported materials. Almost all the raw materials for pharmaceutical production are imported.

In order to have high quality pharmaceutical products more affordable and acceptable, a National Drug Policy (NDP) was enunciated. One of the four pillars of NDP is the development of the national capability to manufacture intermediate and basic chemicals so that the Philippines is not totally reliant on foreign services, thereby avoiding the detrimental effects of such dependence. UNIDO recently implemented a UNDP-financed project entitled "Philippines Pharmaceutical Industry Development Study". In the course of its implementation, possible establishment of a multi-purpose pilot plant for chemical synthesis was investigated. The report elaborates the usefulness of the proposed pilot plant as follows:

The introduction and installation of a development orientated multi-purpose chemical pilot plant is viewed as the strategy in the development of the upstream integration of the pharmaceutical industry. Although production levels tend to be lower, the plant will provide a positive contribution not only to the domestic requirements and supply of pharmaceuticals but also to overhead and labour absorption in running the unit.

The findings were thus positive. On the basis of the preliminary investigation, the undertaking of further study was recommended. For easy reference, a copy of the project profile prepared is attached as annex to this TOR.

The most important features of the multi-purpose pilot plant are to provide facilities to:

- Introduce and develop the experience of chemical synthesis of fine chemicals and pharmaceuticals.
- Provide the range of equipment for adequate scaling up facilities and for research and development.
- Provide some limited capacity in production of several pharmaceutical chemicals, fine chemicals or their intermediates (e.g. in semi-synthetic antibiotics).
- Provide sufficient facilities and capacity to incorporate development of additional upstream integration or introduction of new products.
- Provide training facility.
- Develop the atmosphere for progressive advancement in scientific skills from innovation and accomplishment.

## OBJECTIVES

To provide the Government of the Philippines with a rational decision making basis for assessing the technical and financial feasibility of establishing a multi-purpose pilot plant for chemical synthesis by providing a detailed study on the proposed pilot plant, e.g. product mix, production facility, laboratory facility, optimum use of solvents, etc.

## 3. SCOPE OF CONSULTANCY SERVICE

The consultants are expected to prepare (a) a feasibility study report and (b) a separate report elaborating specific recommendations for future implementation of the pilot plant, including future technical assistance requirements, which will be used as a basis for elaboration of the project document to obtain future UNDP financing to implement the proposed pilot plant. The feasibility study report will be prepared in accordance with the UNIDO Manual for the Preparation of Industrial Feasibility Studies and will contain the following chapters:

- Executive Summary
- Project Background and History
- Market and Plant Capacity
- Material Inputs
- Location and Site
- Project Engineering
- Plant Organization and Overhead Costs
- Manpower
- Project Implementation
- Financial and Economic Evaluation

Specifically, the following aspects are to be clearly presented in the feasibility study report.

### 1. Market Study

- 1.1. Select products to be sold, bearing in mind that United Lab. Ltd. is potential buyer of the proposed products.
- 1.2. In conjunction with product mix determination, possibility of producing Paracetamol and Isoniazid as priority products should be reviewed. Note: The preliminary investigation as shown in the attached profile contain 10 different products. Paracetamol is not included.
- 1.3. Make projections of the demand for the proposed products in the country.
- 1.4. Determine the ex-factory price for each product - each price should be justified by details of the price build-up.

### 2. Plant Capacity

- 2.1. Select optimum initial and full production capacity for the proposed pilot plant, indicating: starting raw materials, type and quantity of intermediate products to be produced, number of steps for each product.
- 2.2. Determine a feasible production programme and the quantity to be produced of each of the product. Suggestions about campaign type of production or simultaneous production of several products should be given.

### 3. Raw Materials

- 3.1. Determine the annual requirements of the major raw materials to produce each product. It should be noted that CHEMFIELD'S should be considered as one of the major local raw material suppliers to this pilot plant. Indicate also other possible sources of suppliers of raw materials.
- 3.2. Indicate the quantity, specifications and prices.

## Location and Site

The location and site will be determined taking into account the the raw material supply and access to the market as well as the nature of the pilot scheme. Consultations with the Department of Health is indispensable.

## 5. Technology and Project Engineering

- 5.1. Outline the process flow and describe the selected technology for the proposed product indicating the time duration of the process.
- 5.2. List and specify the types and sizes of major machinery and equipment and justify the selection of items, indicating estimated price of each selected equipment.
- 5.3. Specify spare parts and maintenance requirements and their cost.
- 5.4. Select the most suitable physical plant layout, giving technical justification for the suggested layout.
- 5.5. Prepare equipment layout drawings.
- 5.6. Prepare functional chart for process and material flow, indicating working temperatures, PH, and process time.
- 5.7. Specify building and other civil works requirements. Indicate technical characteristics of the buildings and requirements based on GMP regulations.
- 5.8. Estimate utility requirement, indicating quantities and qualities per year/month/days etc. as well as peak consumptions.
- 5.9. Specify transportation facilities for raw materials and finished products.
- 5.10. Indicate the type and volume of effluents and the necessary treatment facilities before disposal.
- 5.11. Indication of quality control requirements (facilities, equipments, etc.) and cost estimation for the suggested quality control laboratories.
- 5.12. Indication of safety requirements for the production and quality control.
- 5.13. Cleaning procedures.

## 6. Plant Organization and Manpower Requirements

- 6.1. Prepare an organizational structure.
- 6.2. Estimate the manpower requirements with functional breakdown such as skilled, semi-skilled, unskilled, technical, managerial, etc.
- 6.3. Specify training requirements before the actual operation start-up as well as for future expansion of training programmes during the operation in view of the pilot scheme.
- 6.4. Determine the nature of training, duration and location of the training programmes.
- 6.5. Identify technical assistance requirements for foreign experts and their duration and timing of fielding.

## 7. Implementation Schedule

- 7.1. Specify an implementation schedule of the activities in the pre-production phase.
- 7.2. Draw up a running programme for the project implementation period.

### 3. Financial Evaluation

The proposed pilot plant should be financially self-sustained. Bearing this in mind, detailed financial analysis should be undertaken.

- 8.1. Provide all investment cost estimates, broken down into foreign and local components, on an annual basis.
- 8.2. Estimate the amount of working capital requirement.
- 8.3. Estimate production costs and sales revenue for each year.
- 8.4. Prepare cash-flow analysis for 10 years project life.
- 8.5. Calculate internal rate of return and net present value of project at 18% hurdle rate.
- 8.6. Prepare balance sheet and income statement for 10 years.
- 8.7. Make a break-even analysis for production quantity and sales price.
- 8.8. Undertake sensitivity analysis.
- 8.9. Present suitable financial ratios.

### 9. Economic Evaluation

- 9.1. Calculate the economic internal rate of return and the net present value using 15% discount rate as the hurdle rate.
- 9.2. Impact of the pilot plant on utilization of domestic resources, R & D and other socio-economic activities.

### 10. Conclusions and Recommendations

- 10.1. Prepare a summary of conclusions and recommendations thereof.

## 4. GENERAL TIME SCHEDULE

The implementation schedule for the feasibility study compilation is as follows:

Award of contract	A
Fielding of consultants	A + 0.5 month
Completion of field work (e.g. raw material, market study, etc.)	A + 2.5 months
Completion of home office work	A + 3.5 months
Completion and submission of the draft final report	A + 4.5 months

UNIDO HQ will finalize the comments on the draft final report within 30 days after receipt of the report from the sub-contractor. The final report will be submitted within 15 days after receipt of UNIDO comments.

## 5. THE REPORT

Twenty (20) copies of the final report, compiled in English, will be submitted to UNIDO by the sub-contractor.



The required qualifications and skills of the personnel are indicated in to industrial profile for semi-synthetic Penicillins.

5. Plant location

The production of Erythromycin derivatives and Rifampicin has limited dimensions. For economic reasons, it is advisable to erect a new complex for the plant. The plant should be placed in the Chemfields factory in a new building, which should be separated from the one for Beta-lactam (Semi-synthetic Penicillins) production to avoid cross-contamination. The Chemfields plant has all the required facilities, an existing organization and a staff which has to be slightly increased to cope with the new needs. Some of the existing utilities have spare capacity, thus it will be possible to limit the investment.

INDUSTRIAL PROFILE No. 7

MULTI-PURPOSE PILOT-PLANT FOR CHEMICAL SYNTHESIS

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Investment	:	US \$ 5,265.000
Annual Output	:	63 tons
Sales Estimates	:	US \$ 2,040.000
Manpower	:	48

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∴ General consideration

The introduction and installation of a development orientated multi-purpose chemical pilot plant is viewed as the strategy in the development of the upstream integration of the pharmaceutical industry. Although production levels tend to be lower, the plant will provide a positive contribution not only to the domestic requirements and supply of pharmaceuticals but also to overhead and labour absorption in running the unit.

The most important features of the multi-purpose pilot plant are to provide the facilities to:

- 1.1 introduce and develop the experience of chemical synthesis of fine chemicals and pharmaceuticals
- 1.2 provide the range of equipment for adequate scaling up facilities and for research and development
- 1.3 provide some limited capacity in production of several pharmaceuticals or fine chemical intermediates (e.g. in semi-synthetic antibiotics)
- 1.4 provide sufficient facilities and capacity to incorporate development of additional upstream integration or introduction of new products
- 1.5 provide a training facility
- 1.6 develop the atmosphere for progressive advancement in scientific skills from innovation to accomplishment.

## 2. Plant description

A multi-purpose pilot-plant is suited for installation in developing countries when the first stage of backward integration from the pharmaceutical industry is being considered. Such plants are particularly useful in providing a secure basis for education, training and experience in chemical processing and later for the development of "in house" processes.

The installation of a multi-purpose pilot plant is coupled with the acquisition of appropriate technology which has to be determined for each unit proposed. Operation of this technology (purchase of which should include if possible prior training in the suppliers own units) gives the experience in plant operation and training of personnel. The purchase of technology also can give a lead time for development of future products.

A multi-purpose pilot-plant consists of an assembly of several reactors fabricated principally in stainless steel and glass enamel together with some smaller units in industrial glass. The sizes of the reactors will range from perhaps 50 liters through 200 liters, 500 liters and 1000 liters to a maximum in the order of 4500 liters. The reactors are fitted with the condensers and receivers mostly to furnish "general purpose" units though some may have special function such as high vacuum distillation.

Auxiliary items such as pumps, centrifuges, filters, driers, etc. complete the installation.

Such plants would normally be designed to produce a maximum of 150 tons products per annum.

3. Products and Plant Capacity

The following pharmaceuticals will be produced at the levels indicated:

	<u>Pharmaceutical</u>	<u>Tons</u>
3.1	Trimethoprim (anti-bacterial)	1
3.2	Sulfamethoxazole (anti-bacterial)	4
3.3	Ethambutol (anti-TB)	10
3.4	Ibuprofen (anti-rheumatic, anti-inflammatory, analgesic)	10
3.5	Mefenamic Acid (analgesic and antipyretic)	5
3.6	Pyrazinamide (anti-TB)	5
3.7	Furazolidone (anti-diarrhoeal)	15
3.8	Glaphenine (analgesic and antipyretic)	2
3.9	Isoniazid (anti-TB)	30
3.10	Metronidazole (anti-bacterial, anti-amoebics, anti-trichomonas)	1
3.11	<b>T o t a l</b>	<b>83</b>

4. Sales

Based on an estimated annual need in 1989, the following sales values are projected:

Pharmaceutical	Estimated Annual Need 1989 (kg)	% level production proposed	Production level sales Value US \$
4.1	2,500	40 %	22,000
4.2	8,000	50 %	60,000
4.3	25,000	40 %	290,000
4.4	17,500	60 %	200,000
4.5	15,000	33 %	55,000
4.6	10,000	50 %	215,000
4.7	35,000	42 %	135,000
4.8	4,000	50 %	130,000
4.9	65,000	45 %	180,000
4.10	2,000	50 %	15,000
<b>T o t a l</b>			<b>1,302,000<sup>(1)</sup></b>

(1) These figures were determined using latest prices of U.K. chemicals quoted in U.K. There is some difference compared with the import prices in the Philippines in 1987. Using the reported Philippine import prices in 1987, the total sales value would be US \$ 2.04 million, which is 55% higher than when using U.K. prices.

5. Investment Costs

5.1 The estimated costing in plant, equipment and building construction costs are based on:

5.1.1 plant and equipment prices in UK as of mid 1967 (F.O.B)

5.1.2 construction costs in the Philippines as of mid 1988.

5.2 The investment costs could be summarized as follows:

	US \$
5.2.1 Reaction Units, extraction	660,000
5.2.2 Centrifuges	253,000
5.2.3 Driers, filters	150,000
5.2.4 Pump, mill, sieve	97,000
5.2.5 Tanks, mobile bins	136,000
5.2.6 Column, scrubbing	56,000
5.2.7 Scales	33,000
5.2.8 Laboratory equipment	136,000
	<hr/>
	1,525,000
5.2.9 Service utilities	200,000
	<hr/>
5.2.10 Un-installed	
Equipment total	1,725,000
5.2.11 Estimated installed cost	4,312,500
Building:	
5.2.12 Production hall (1,000 m <sup>2</sup> )	400,000
5.2.13 Hydrogenation hall (50 m <sup>2</sup> )	17,500
5.2.14 Warehouse	120,000
5.2.15 Administration/Lab	165,000
5.2.16 Site Preparation	250,000
5.2.17 Estimated building cost	952,000
5.2.18 Total estimated cost	5,265,000
5.2.19 With contingencies	5,750,000
	<hr/> <hr/>

An alternative building with smaller production hall and hydrogenation hall may be considered. The total estimated cost of this building is:

Cost	:	US \$ 5,038,000
With contingency	:	US \$ 5,500,000

The price of technology, which has not been included in the figures, amounts to US \$ 100,000 to \$ 250,000.

6. Manspower

The manspower requirement and the corresponding qualifications can be summarized as follows:

	Total	PhD	S/BS	Other
General manager	1	1 (Chem. Eng)	-	
Senior managers	4	3 (Chem.) 1 (Eng.)	-	
Middle managers	5	-	5	2
Chemists	11	-	11	-
Technicians	6	-	-	6
Tradesmen	7	-	-	7
Others (administration)	7	-	-	7
Unskilled	7	-	-	7
<b>Total</b>	<b>48</b>	<b>5</b>	<b>14</b>	<b>29</b>

The lack of experience in the field of synthesis of Philippine PhD graduates pose to be a problem in the operation of the pilot-plant. Training will therefore have to be an important feature and such should be incorporated as part of any technology transfer package arrangement. Some months training at the suppliers establishment should be agreed.

It may also be necessary, and desirable to hire back to the Philippines some expatriate chemists, preferably those with experience learned abroad in the field of synthesis of pharmaceuticals or fine chemicals.

Insofar as the rest of the personnel are concerned, the majority requirement of the staff would be Bachelor's degree and no problems in staffing at this level are foreseen. The basic training of education at this level can certainly be assessed as good.

7. Location

The multi-purpose plant can be situated at Chemfields, Inc. This arrangement will have advantages such as savings in general administration and infrastructure and possible shared facilities in some instances of chemical storage or solvent recovery facilities.

Government majority equity and the United Drug shareholding in Chemfields are purely incidental and have no bearing on the recommendation.

8. Research and Development (1)

8.1 Functions

Some of the main function of the research and development department of the plant are as follows:

8.1.1 Provision of familiarisation with any transferred technologies covering not only reaction procedures but also analytical control of intermediates and products

8.1.2 Scaling up of processes

8.1.3 Supervision of, and advice on, initial production commissioning.

8.1.4 Trouble-shooting in the event of any production problems

8.1.5 Monitoring of any new or alternative supplies of critical raw materials or chemicals

8.1.6 Process improvement

8.1.7 Development of processes for alternative synthetic routes

8.1.8 Development of processes leading to new products

8.1.9 Defining of new products or intermediates the analytical control parameters and methods of determination.

8.2 Proposed areas of interest in R & D

8.2.1 Process development

8.2.2 Method development for production of pharmaceuticals newly, or shortly becoming, free of product patent coverage. As an example, between 1984 and 1996 some 96 drugs fall into this category/

Some of the products in consideration under this philosophy might be : Fraziquantel, Fenoprofen, Dilitazem, Amikacin, Carbidopa, Nadolol, Frazepam, Cimetidine, Ranitidine, Clotrimazole and Atenolol.

(1) This topic has been singled-out in view of the development orientation of the multi-purpose plant.

8.2.1 Process development

8.2.2 Method development for production of pharmaceutical newly, or shortly becoming, free of product patent coverage. As an example, between 1984 and 1996 some 96 drugs fall into this category.

Some of the products in consideration under this philosophy might be: Praziquantel, Fenoprofen, Dilitazem, Amikacin, Carbidopa, Nadolol, Prazepam, Cimetidine, Ranitidine, Clotrimazole and Atenolol.

18.2 Market, Financial and Economic Introduction to the Study

A. Background

One of the major objectives of the Philippine Pharmaceutical Industry Development Study (PPIDS) is the identification of projects leading towards the formation of an integrated pharmaceutical industry in the country, in support of the national health goals and in accordance with the National Drug Policy. The main thrust of the PPIDS has been on the selection of upstream activities for possible backward integration. In particular, from extensive consultations with experts and representatives from Government, the academe, and the industry itself, the Study has decided to focus on the manufacture of antibiotics.

The PPIDS has been guided by 15 general criteria for the identification and selection of the subsectors for upstream integration, which can be described as falling under the following categories: (a) market potential, based on present consumption levels and expected future growth, in the light of the country's health profile and world market trends; (b) availability of inputs, including raw materials, manpower, utilities, and technology; and (c) conformity with the National Development Plan and the National Drug Policy. As these aspects have been discussed extensively in the Main Report, this follow-up study on market, financial and economic aspects will concentrate on those products that have been identified in the Industrial Profiles presented at the Experts' Group Meeting in Vienna on October 27-28, 1988 (IO/R.83, UNIDO, 1988). These Industrial Profiles are: (a) the Penicillin and 6-Amino-Penicillanic Acid (6-APA) Plant; (b) the Plant for Semi-Synthesis of Ampicillin, Amoxycillin, Cloxacillin, and Cephalixin; and (c) the Erythromycin Derivatives and Rifampicin Production Plant.

A Multi-Purpose Plant for Erythromycin, Tetracyclines and Rifampicin Production (Industrial Profiles Nos. 4 and 6) has also been initially proposed, but this proposal has been withdrawn as initial indications showed poor potential. A discounted cash flow analysis of this project will nevertheless be presented to confirm its lack of viability.

APPENDIX 3-1

ANALYSIS OF LISTING OF ESSENTIAL DRUGS FOR HEALTH CARE

1. Products Common to All Lists

Acetylsalicylic Acid  
Paracetamol  
Lidocaine Hydrochloride  
Chlorpheniramine Maleate  
Atropine Sulphate  
Hydrochlorothiazide  
Isoniazid  
Mebendazole  
Piperazine Citrate  
Metronidazole  
Chloroquine  
Primaquine  
Quinine  
Sulfadoxine/Pyrimethamine  
Dicyclomine Hydrochloride  
Salbutamol Sulphate  
Terbutaline Sulphate  
Theophylline Anhydrous  
Furosemide  
Retinol (Vitamin A)

2. Products Considered of Highest Priority

Pyridoxine Hydrochloride  
Chlorpheniramine Maleate  
Metronidazole  
Cotrimoxazole (Sulfamethoxazole/Trimethoprim)  
Clofazimine  
Dapsone  
Pyrazinamide  
Quinine  
Sulfadoxine/Pyrimethamine  
Dicyclomine Hydrochloride  
Isoniazid  
Mebendazole  
Diloxanide Furoate



APPENDIX 3-1

LIST OF ESSENTIAL DRUGS FOR PUBLIC AND PRIVATE HEALTH CARE

Group	Department of Health	Philippine Medical Association
1. Analgesic	Acetylsalicylic Acid Paracetamol	Acetylsalicylic Acid Paracetamol
2. Anaesthetics	Diazepam Lidocaine HCL Propoxycaïne HCL	Diazepam Lidocaine HCL
3. Antacids	Cimetidine	
4. Anti-Allergics	Chlorpheniramine Maleate Hydrocortisone Prednisolone	Chlorpheniramine Maleate
5. Anti-Anaemic	Hydroxycobalamin	
6. Anti-Coagulants		
7. Anti-Convulsants	Carbamazepine Clonazepam Diazepam Ethosuximide	Carbamazepine Diazepam Ethosuximide
8. Anti-Diabetes	Acetohexamide Glibenolamide	
9. Antidotes	Diphenhydramine HCL Atropine Sulphate Naloxone Protamine Sulphate Pyridoxine HCL	Diphenhydramine HCL Atropine Sulphate Naloxone Protamine Sulphate Pyridoxine HCL
10. Anti-Emetics	Promethazine HCL Dicyclomine HCL	Promethazine HCL
11. Anti-Gout	Indomethacin	
12. Anti-Hypertension	Furosemide Hydrochlorthiazide Spironolactone Alprenolol Clonidine HCL Propranolol HCL Hydralazine	Furosemide Hydrochlorthiazide Hydralazine

	Group	Department of Health	Philippine Medical Association
13.	Anti-Infectives	Furazolidone Metronidazole	Furazolidone Metronidazole
	Sulphonamides	Cotrimoxazole * Sulfisoxazole Sulfaxone Sodium Triple Sulfa	Cotrimoxazole *
	Anti-Leprosy	Clofazimine Dapsone	Dapsone
	Anti-Tuberculosis	Ethambutol Isoniazid Pyrazinamide	Isoniazid Pyrazinamide
	Urinary Antiseptic	Nalidixic Acid	Nalidixic Acid
	Anti-Helminthics	Mebendazole Piperazine Citrate Praziquantel	Mebendazole Piperazine Citrate Praziquantel
	Amoebicides	Diloxamide Furoate Metronidazole	Metronidazole
	Anti-Malaria	Amodiaquine Chloroquine Primaquine Quinine Sulphate Sulfadoxine/ Pyrimethamine	Amodiaquine Chloroquine Primaquine Quinine Sulphate Sulfadoxine/ Pyrimethamine
	Anti-Schistosomes	Praziquantel	Praziquantel
	14.	Anti-Migraine	Acetylsalicylic Acid Paracetamol Propranolol HCL
Anti-Neoplastic Drugs		Megestrol Acetate Vincristine Sulphate	Vincristine Sulphate Vinblastine
16.	Anti-Parkinsons Drugs	Diphenhydramine HCL L-Dopa + Benserazide L-Dopa + Carbidopa	L-Dopa + Benserazide
17.	Anti-Pyretics	Acetylsalicylic Acid Paracetamol	

\* Sulfamethoxazole/Trimethoprim

Group	Department of Health	Philippine Medical Association
18. Anti-Rheumatics	Acetylsalicylic Acid Indomethacin	
19. Anti-Spasmodic Drugs	Atropine Sulphate Belladonna Tincture Dicyclomine HCL Hyoscine N Butyl Bromide	Atropine Sulphate Dicyclomine HCL
20. Anti-Thrombic Agents	Acetylsalicylic Acid Dipyridamole	Acetylsalicylic Acid Dipyridamole
21. Anti-Tussive	Dextromethorpan	
22. Biologicals		
23. Bronchodilators	Ephedrine Salts Salbutanol Sulphate Terbutanol Sulphate Tulabutanol Theophylline Anhyd	Salbutanol Sulphate Terbutanol Sulphate Theophylline Anhyd Beclomethasone
24. Cardiovascular Agents	Isoproterenol Alprenolol Lidocaine HCL Propanolol HCL Quinidine Sulphate Metaprolol	Lidocaine HCL Propanolol HCL Quinidine Sulphate Metaprolol
25. Carthastics & Laxatives	Glycerine Senna Extract	Glycerine
26. Cholinergic Agents		
27. Cortico-Steroids	Beclomethasone Diprop Dexamethasone Hydrocortisone Sod Succinate Prednisolone Prednisone	Dexamethasone Hydrocortisone Sod Succinate Prednisolone Prednisone
28. Dermatological Agents	Blotrimazole Betamethasone Dexamethasone Hydrocortisone Prednisolone Triamcinolone Acetonide	Blotrimazole
29. Diagnostic Agents		

Group	Department of Health	Philippine Medical Association
30. Disinfectants		
31. Diuretics	Furosemide Hydrochlorthiazide Spironolactone	Furosemide Hydrochlorthiazide Spironolactone
32. Eye, Ear, Nose & Throat Preparations	Sulfacetamide Sodium Dexamethasone Prednisolone Acetate Pilocarpine Nitrate Lidocaine HCL Ephedrine Salts Atropine Sulphate	Sulfacetamide Sodium Dexamethasone Prednisolone Acetate Pilocarpine Nitrate Lidocaine HCL Ephedrine Salts  Triamcinolone
33. Gonadal Hormones	Sodium Estrone Sulphate Testosterone Propionate	
34. Hemostatics		
35. Mucolytics		
36. Oxytocics		
37. Peripheral Vasodilators	Isoxsuprine HCL	
38. Pressor Agents	Metaraminol Bitastrate	
39. Psycho- Therapeutic Agents	Imipramine Bromazepam Chlordiazepacide Diazepam Flurazepam Lorazepam Midazolepam Chlorpromazine Estazolam	Imipramine  Diazepam  Chlorpromazine
40. Skeletal Muscle Relaxants	Diazepam	Diazepam
41. Caloric Agents		
42. Thyroid Hormones	Basbimaxole Methimazole Propranolol HCL	Methimazole  Propylthiouracil
43. Tocolytic Agents	Isoxsuprine Terbutaline Sulphate	

Group	Department of Health	Philippine Medical Association
44. Vitamins & Minerals	Vitamin A (Retinol) Vitamin B Complex Nicotinamide Pyridoxine HCL Thiamine HCL Vitamin C Vitamin D Menadione (K3) Phytonadione (K1)	Vitamin A (Retinol)  Pyridoxine HCL Thiamine HCL Vitamin C Vitamin D  Vitamin E Vitamin B2 Vitamin B5 Vitamin B6
45. Miscellaneous	Methyl Salicylate Paracetamol Powder Theophylline	

## APPENDIX 3-2

### INCIDENCE AND TREND OF MAJOR NOTIFIABLE DISEASES

#### 1. Bronchitis

Year	Number of Cases	Rate/ 100,000	Number of Deaths	Rate/ 100,000
1979	219,527	471.3	3,219	6.9
1980	206,469	427.3	2,756	5.7
1981	220,698	445.5	1,476	3.0
1982	280,431	552.2	2,250	4.4
1983	352,447	678.1	2,052	3.9
1984	606,880	1,140.9	1,764	3.3
1985	586,427	1,072.7	2,078	3.8
1986	602,851	1,076.4	1,985	3.5
1987	642,777	1,120.6	1,814	3.2
1988	759,511	1,293.4	1,438	2.4

There has been a significant increase in the number of reported cases of bronchitis since 1984, but the mortality rate has shown a slight decline. Despite the apparent effectiveness of the programme, bronchitis remains still remains an important factor in the ARI group of related illnesses.

#### 2. Diarrhoea

Year	Number of Cases	Rate/ 100,000	Number of Deaths	Rate/ 100,000
1979	217,155	466.2	16,683	35.8
1980	199,574	413.0	13,492	27.9
1981	239,117	482.7	16,196	32.7
1982	221,191	435.6	12,735	25.1
1983	275,068	529.2	15,090	29.0
1984	551,560	1,036.9	11,553	21.7
1985	522,762	956.2	11,516	21.1
1986	538,849	962.2	9,815	17.2
1987	591,858	1,031.8	9,468	16.5
1988	624,355	1,063.3	9,155	15.6

The underlying social conditions for the majority of the population have not improved, but it is probable that the morbidity rate has increased owing to better reporting. More effective treatments have significantly lowered the mortality rates, but diarrhoea will nevertheless remain a priority area for the Department of Health for the foreseeable future.

3. Influenza

Year	Number of Cases	Rate/ 100,000	Number of Deaths	Rate/ 100,000
1979	189,126	406.0	1,803	3.9
1980	202,884	419.9	1,913	4.0
1981	251,200	507.1	2,715	5.5
1982	226,237	445.5	1,297	2.6
1983	256,534	493.6	1,215	2.3
1984	453,926	853.4	1,150	2.2
1985	447,550	818.7	1,400	2.6
1986	397,715	710.2	1,221	2.2
1987	495,161	863.3	1,151	2.0
1988	576,404	981.6	791	1.3

Although treatment has become more effective over the last decade, there is no sign of any reduction in the prevalence of this disease. In fact, the converse would appear to be the case.

4. Pneumonia

Year	Number of Cases	Rate/ 100,000	Number of Deaths	Rate/ 100,000
1979	126,797	272.2	49,019	105.2
1980	117,270	242.7	45,209	93.6
1981	123,154	248.6	43,164	87.1
1982	106,563	209.8	45,373	89.3
1983	123,420	237.5	48,650	93.6
1984	193,594	363.9	45,971	86.4
1985	205,387	375.7	52,888	96.7
1986	190,208	339.6	50,621	90.4
1987	183,143	319.3	52,700	91.9
1988	201,902	343.8	47,444	80.8

Pneumonias are a major cause of death in the Philippines. Despite progress in its treatment over the last decade, it still affects more people than tuberculosis, and is likely to remain a priority area for the next decade.

5. Tuberculosis

Year	Number of Cases	Rate/ 100,000	Number of Deaths	Rate/ 100,000
1979	108,813	233.6	28,221	60.6
1980	112,307	232.4	28,798	59.6
1981	116,182	235.8	27,317	55.1
1982	104,715	206.2	28,309	55.7
1983	106,300	204.5	28,580	55.0
1984	151,867	285.5	27,320	51.4
1985	151,028	276.3	31,650	57.9
1986	153,129	273.4	30,604	54.6
1987	163,740	285.5	28,697	50.0
1988	183,113	311.8	27,020	46.0

An anti-tuberculosis programme is in operation, but better reporting from the rural areas gives the impression that little real progress is being made. This will therefore remain the top priority for several years to come.



APPENDIX 3-3

IMPORTS OF PHARMACEUTICALS BY VOLUME : 1987

1.	Paracetamol	:	348,184 kgs
2.	Ascorbic Acid	:	154,545 kgs
3.	Acetylsalicylic Acid	:	91,760 kgs
4.	Isoniazid	:	60,120 kgs
5.	Sulfamethazine	:	34,500 kgs
6.	Furazolidone	:	32,375 kgs
7.	Ethambutol	:	22,200 kgs
8.	Nicotinamide	:	17,840 kgs
9.	Ibuprofen	:	15,850 kgs
10.	Mefenamic Acid	:	14,845 kgs
11.	Pyridoxine HCL	:	10,665 kgs
12.	Phenylpropanolamine HCL	:	9,770 kgs
13.	Pyrazinamide	:	7,600 kgs
14.	Sulfamethoxazole	:	6,857 kgs
15.	Rifampicin	:	6,594 kgs
16.	Glaphenine	:	3,345 kgs
17.	Albendazole	:	2,020 kgs
18.	Trimethoprim	:	1,869 kgs
19.	Chloroquine Salts	:	1,060 kgs
20.	Metronidazole	:	1,000 kgs

Source : Philippines Pharmaceutical Development Study  
DP/PHI/87/019

**APPENDIX 3-4**

**PRIORITY DRUGS FOR GENERAL LOW COST AVAILABILITY**

	<b>Generic Name</b>	<b>Content</b>	<b>Form</b>	<b>Available</b>	<b>Use</b>
1.	Cotrimoxazole	400mg 80mg	Tablet/ Capsule	Rx Rx	Infection
2.	Amoxycillin	350mg	Capsule	Rx	Infection
3.	Rifampicin	450mg	Capsule	Rx	Tuberculosis
4.	Isoniazid	400mg	Tablet	Rx	Tuberculosis
5.	Salbutamol	2mg	Tablet	Rx	Asthma
6.	Diphenhydramine	50mg	Capsule	Rx	Allergies
7.	Nifedipine	5mg	Capsule	Rx	Hypertension
8.	Aluminium Hydroxide	225mg 200mg	Suspension	OTC	Antacid
9.	Paracetamol	5mg	Tablet	OTC	Ulcer Pain Relief
10.	Furosemide	40mg	Tablet	Rx	Diuretics

Source : Bureau of Food and Drugs

**APPENDIX 3-5**

**CLASSIFICATION OF PROVISIONAL DRUG LIST**

<b>Pharmaceutical</b>	<b>Classification</b>	<b>Use</b>
1. Ethambutol	Core Drug	Anti-Tuberculosis
2. Furazolidone	-	
3. Glahpenine	-	
4. Ibuprofen	Complementary Drug	Non-steroidal Anti-Inflammatory
5. Isoniazid	Core Drug	Anti-Tuberculosis
6. Mefenamic Acid	Complementary Drug	Non-steroidal Anti-Inflammatory
7. Metronidazole	Core Drug Core Drug	Anti-Bacterial Anti-Protozoal
8. Nifedipine	Complementary Drug Core Drug	Anti-Anginal Agent Anti-Hypertensive
9. Paracetamol	Core Drug Core Drug Core Drug	Analgesic Anti-Migraine Antipyretic
10. Pyrazinamide	Core Drug	Anti-Tuberculosis
11. Salbutamol	Core Drug Core Drug	Anti-Asthma Uterine Relaxant
12. Sulfamethoxazole/ Trimethoprim	Core Drug	Anti-Bacterial

**Source : National Drug Formulary**

**APPENDIX 3-6**

**TOTAL IMPORTS AND UNILAB MARKET SHARE : 1988 - 1990**

**1. Total Imports**

Tonnes	1988	1989	1990	Average
Ethambutol	10.4	8.7	7.3	8.8
Ibuprofen			25.2	25.2
Isoniazid	42.3	32.0	11.0	28.4
Mefenamic Acid			20.0	20.0
Metronidazole			2.0	2.0
Nifedipine			0.2	0.2
Paracetamol			192.0	192.0
Pyrazinamide			11.5	11.5
Sulfamethoxazole			12.8	12.8
Trimethoprim			3.3	3.3
Total	-	-	285.3	304.2

**2. Unilab Imports and Average Market Share**

Kgs	1988	1989	1990	Average	% Share
Ethambutol	2.3	3.2	0.9	2.1	24%
Ibuprofen			24.8	24.8	98%
Isoniazid	29.2	26.5	4.0	19.9	70%
Mefenamic Acid			4.0	4.0	20%
Metronidazole			-	-	-
Nifedipine			0.08	0.08	40%
Paracetamol			128.6	128.6	67%
Pyrazinamide			0.8	0.8	7%
Sulfamethoxazole			2.1	2.1	16%
Trimethoprim			0.4	0.4	12%
Total	-	-	166.1	182.8	60%

Source : Business Statistics Monitor

APPENDIX 3-7

DEPARTMENT OF HEALTH CENTRAL PURCHASES FOR RURAL HEALTH UNITS

	1898	1990
1. Ibuprofen	321 kgs	-
2. Isoniazid	520 kgs	5,409 kgs
3. Metronidazole	1,298 kgs	2,258 kgs
4. Nifedipine	23 kgs	-
5. Paracetamol	24,474 kgs	31,380 kgs
6. Sulfamethoxazole	522 kgs	5,905 kgs
7. Trimethoprim	104 kgs	1,181 kgs

Note : 1989 figures relate to actual awards made.  
1990 figures relate to the proposed schedule  
of purchases in that year.

Source : Department of Health records

## APPENDIX 3-8

### FORECAST FUTURE DEMAND FOR SELECTED DRUGS

#### 1. Factors Determining Future Demand

1.1 Over the 10-year period from 1980 through to 1990, the total pharmaceutical market has grown at a rate of approximately 4.75% per year in real terms. However, that period was also marked by high population growth and a relatively rapid increase in domestic consumption, and a simple extrapolation of this rate over the next decade could be misleading.

1.2 As a result, our projection of future demand for the drugs in question has been based on three principal elements :

- Population growth;
- Income elasticity of demand for drugs; and
- Relevant changes in morbidity rates.

1.3 Other elements were considered, such a price elasticity, cross-elasticity with other discretionary expenditure items and comparison with the growth rates in other countries. In each case, the information was either insufficient or there were doubts as to its validity.

#### 2. Population Growth

2.1 Population growth averaged 2.36% per year over the last decade but, with changes in the demographic pattern and the trend to urbanisation, this rate of growth is gradually slowing. New forecasts have yet to be prepared by the National Statistics Office, but the following consensus as to future growth rates was reached after discussions with several demographers in that office :

1991 - 1995	2.25% per year
1996 - 2000	2.10% per year
2001 - 2005	1.90% per year

#### 3. Income Elasticity

3.1 Although per capital GDP has declined by about 0.9% per year over the last eight years, the average family income has increased by up to 3.5% per year over the same period. In addition, expenditure on family health has gradually risen from 1.7% of income in 1965 to 2.1% in 1990. It has been calculated that the income elasticity of demand for drugs and pharmaceuticals is about 2.1 (Gabunada 1988).

- 3.2 Short-term forecasts drawn up by both the World Bank and the NSO anticipate that the economy will grow very slowly for the foreseeable future. Taking this in combination with the trend to higher expenditure on health care, demand for the commodity pharmaceuticals under review is likely to increase at an annual average rate of 1.3%.

#### 4. Morbidity Rates

- 4.1 The morbidity statistics maintained by the Department of Health show no clear trend of improvement, due primarily to the fact that the effect of improved treatment has been offset by more comprehensive reporting of the incidence of notifiable diseases in the rural areas. In particular, respiratory diseases appear to be on the increase.
- 4.2 On the basis of the DOH priorities, we would expect demand for the relevant drugs to be affected as follows :

Drug	1991-1995	1996-2000	2001-2005
Ethambutol	0.5%	0.3%	0.1%
Ibuprofen	0.2%	0.1%	0.1%
Isoniazid	0.5%	0.3%	0.1%
Mefenamic Acid	0.2%	0.1%	0.1%
Metronidazole	0.3%	0.3%	0.3%
Nifedipine	0.1%	0.3%	0.4%
Paracetamol	0.2%	0.1%	0.1%
Pyrazinamide	0.5%	0.3%	0.1%
Sulfamethoxazole	0.4%	0.4%	0.3%
Trimethoprim	0.4%	0.4%	0.3%

#### 5. Projected Annual Growth Rates per Individual Product

- 5.1 The forecast of future domestic demand for the selected drugs has been built up from the base year of 1990, using all three growth factors identified in combination :

Drug	1991-1995	1996-2000	2001-2005
Ethambutol			
Isoniazid			
Pyrazinamide			
Population Growth	2.25%	2.10%	1.90%
Income Elasticity	1.30%	1.30%	1.30%
Morbidity Rates	0.50%	0.30%	0.10%
	<hr/>	<hr/>	<hr/>
	4.05%	3.70%	3.30%

Drug	1991-1995	1996-2000	2001-2005
<b>Ibuprofen</b>			
<b>Mefenamic Acid</b>			
<b>Paracetamol</b>			
Population Growth	2.25%	2.10%	1.90%
Income Elasticity	1.30%	1.30%	1.30%
Morbidity Rates	0.20%	0.10%	0.10%
	<u>3.75%</u>	<u>3.50%</u>	<u>3.30%</u>
<b>Metronidazole</b>			
Population Growth	2.25%	2.10%	1.90%
Income Elasticity	1.30%	1.30%	1.30%
Morbidity Rates	0.30%	0.30%	0.30%
	<u>3.85%</u>	<u>3.70%</u>	<u>3.50%</u>
<b>Nifedipine</b>			
Population Growth	2.25%	2.10%	1.90%
Income Elasticity	1.30%	1.30%	1.30%
Morbidity Rates	0.10%	0.30%	0.40%
	<u>3.65%</u>	<u>3.70%</u>	<u>3.60%</u>
<b>Sulfamethoxazole</b>			
<b>Trimethoprim</b>			
Population Growth	2.25%	2.10%	1.90%
Income Elasticity	1.30%	1.30%	1.30%
Morbidity Rates	0.40%	0.40%	0.30%
	<u>3.95%</u>	<u>3.80%</u>	<u>3.50%</u>

## 5. Projected Growth in Domestic Demand

- 5.1 Applying the afore-mentioned growth rates to identified current demand, results in the following market projections from 1990 through to the year 2005 :

Tonnes	Base	1995	2000	2005
Ethambutol	8.8	10.7	12.8	15.1
Ibuprofen	25.2	30.3	36.0	42.3
Isoniazid	28.4	34.6	41.5	48.8
Mefenamic Acid	20.0	24.0	28.5	33.5
Metronidazole	2.0	2.4	2.9	3.4
Nifedipine	0.2	0.2	0.3	0.3
Paracetamol	192.0	230.8	274.1	322.4
Pyrazinamide	11.5	14.0	16.8	19.8
Sulfamethoxazole	12.8	15.5	18.7	22.2
Trimethoprim	3.3	4.0	4.8	5.7
Total	<u>302.7</u>	<u>366.5</u>	<u>436.4</u>	<u>513.5</u>



APPENDIX 3-9

PRODUCTION PROGRAMME

Assumptions

- 5 SEQUENTIAL CAMPAIGNS PER ANNUM

- SIZED TO PRODUCE ONE BATCH/DAY IN 100KG BATCHES EXCEPT PARACETAMOL 2 BATCHES/DAY of 260KG and IBUPROFEN 2 x 100KG BATCHES/DAY - 5 DAYS/WEEK BASIS

Campaigns in order:-

	<u>TOTAL TONNAGE</u> <u>1995</u>	<u>PRODUCT</u>	<u>PROCESS</u> <u>TIME/BATCH</u>	<u>SHIFTS</u>	<u>OVERALL</u> <u>ALLOWANCE</u>	<u>WEIGHT/</u> <u>BATCH</u>	<u>CAMPAIGN</u> <u>DURATION</u>	
1.	32.6	PARACETAMOL	A 4 Hrs B 4 Hrs	8 Hrs	2	2 Batches/Day	260 KG	12.5 Wks
2.	8.1	ISONIAZID	A 11 Hrs B 3 Hrs C 4 Hrs	18 Hrs	2½	1 Batch/Day	100 KG	16.2 Wks
3.	1.1	ETHAMBUTOL	A 4 Hrs B 2 Hrs C 5 + 8 Hrs	8 & 11 Hrs	2½	1 Batch/Day	100 KG	2.2 Wks
4.	2.5	MEFENAMIC ACID	A 5 Hrs B 2 Hrs C 4 Hrs	11 Hrs	1½	1 Batch/Day	100 KG	5.0 Wks
5.	11.2	IBUPROFEN	A 1 Hrs B 8 Hrs C 1 Hrs D 2 Hrs E 4 Hrs	) ) 6 Hrs) ) )	1 2 1 1 1	2 Batches/Day 2 Batches/Day 2 Batches/Day 2 Batches/Day 2 Batches/Day	100 KG 100 KG 100 KG 100 KG 100 KG	11.2 Wks
	<u>55.5</u>	<u>TONNES /ANNUM</u>				<u>TOTAL</u>		<u>47.1 WKS</u>

Note 1 - TOTAL SYNTHESIS = A + B + C + D + E

2 CHANGE ROUND TIME APPROXIMATELY 1 WEEK BETWEEN CAMPAIGNS

3 WORKING ON AVERAGE 2 SHIFTS/Day







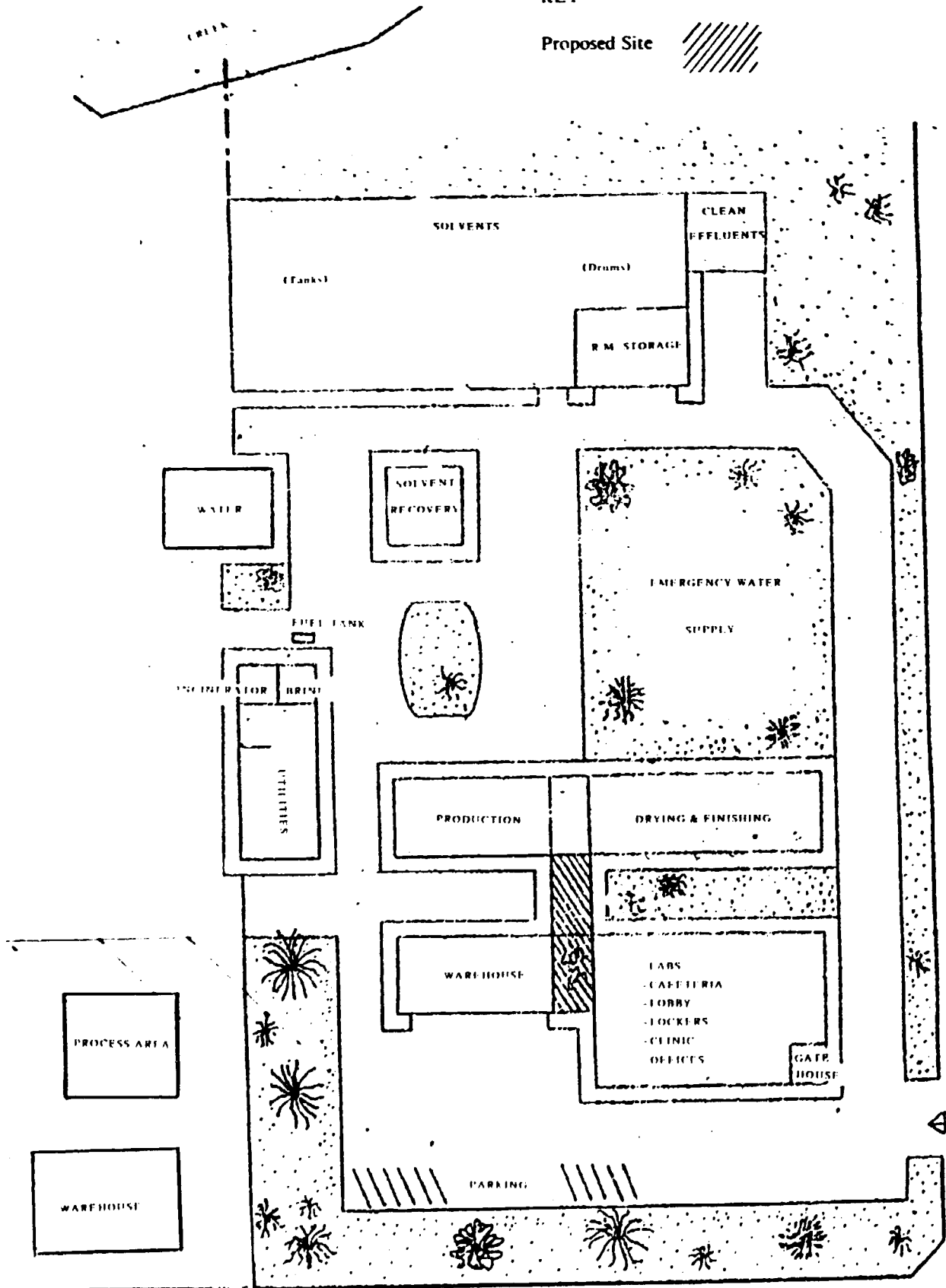


APPENDIX 5-1

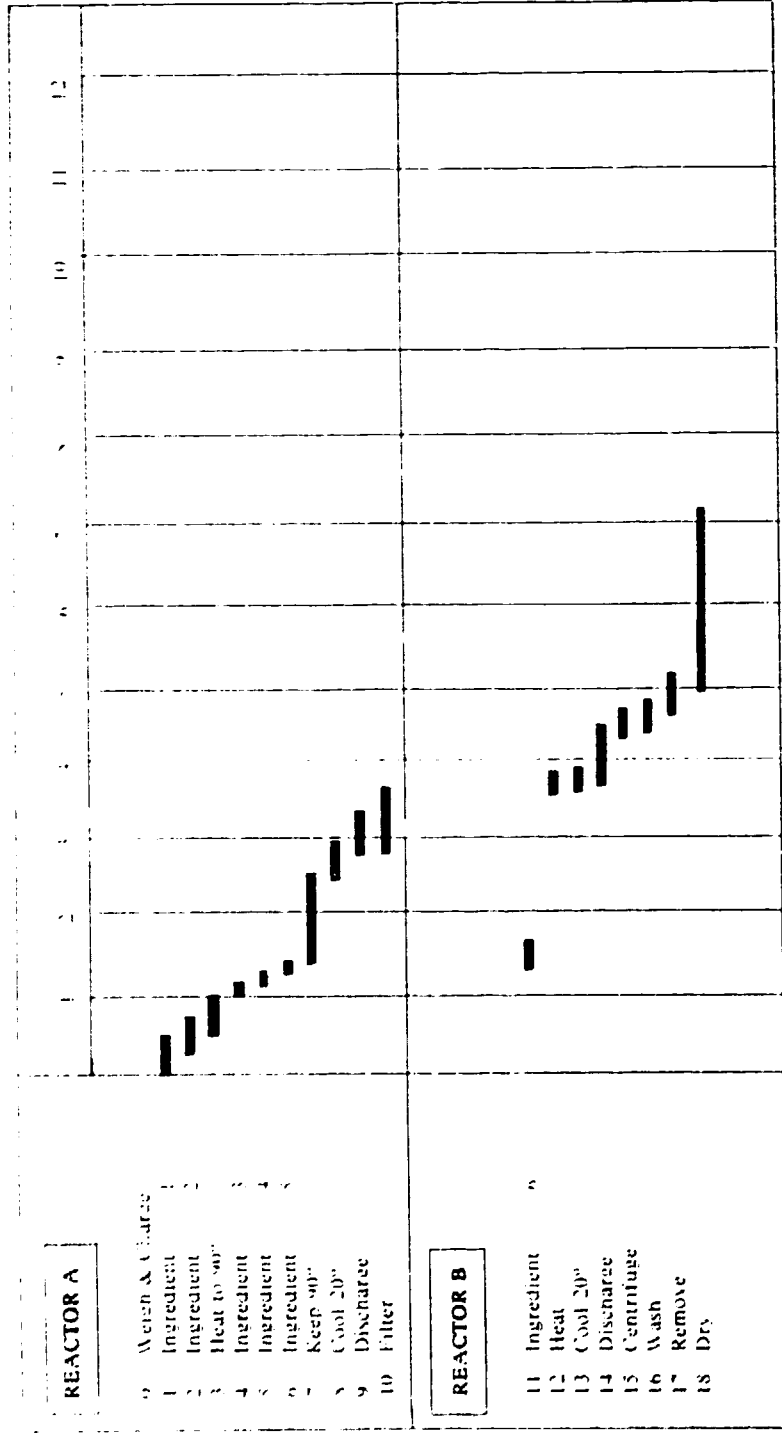
CHEMFIELDS SITE AND PROPOSED FACILITY

KEY

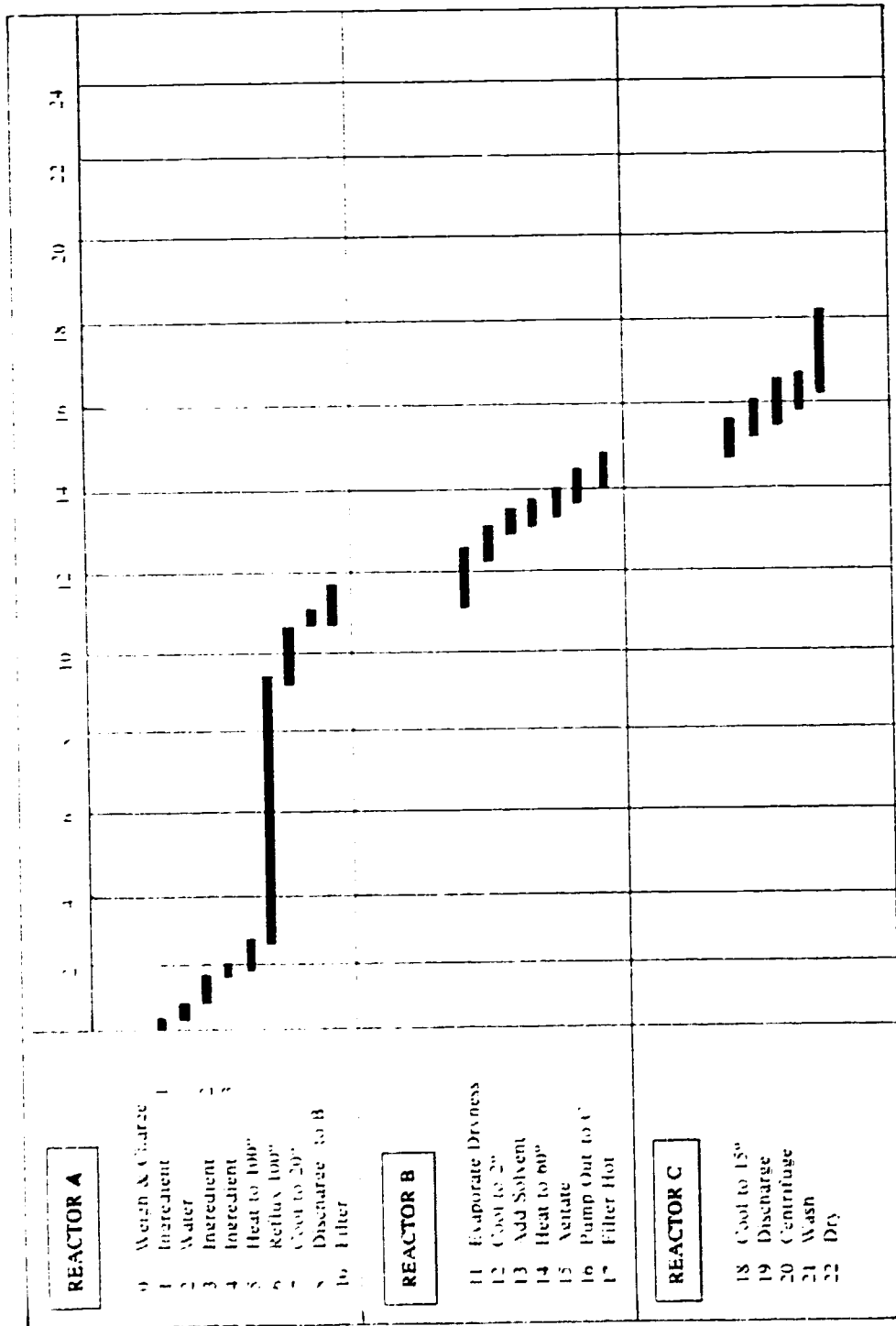
Proposed Site



PARACETAMOL  
TIME-HOURS



ISONIAZID PREPARATION  
TIME-HOURS



REACTOR A

- 0 Weigh & Charge
- 1 Inertient
- 2 Water
- 3 Inertient
- 4 Inertient
- 5 Heat to 100°
- 6 Reflux 100°
- 7 Cool to 20°
- 8 Discharge to B
- 9 Filter

REACTOR B

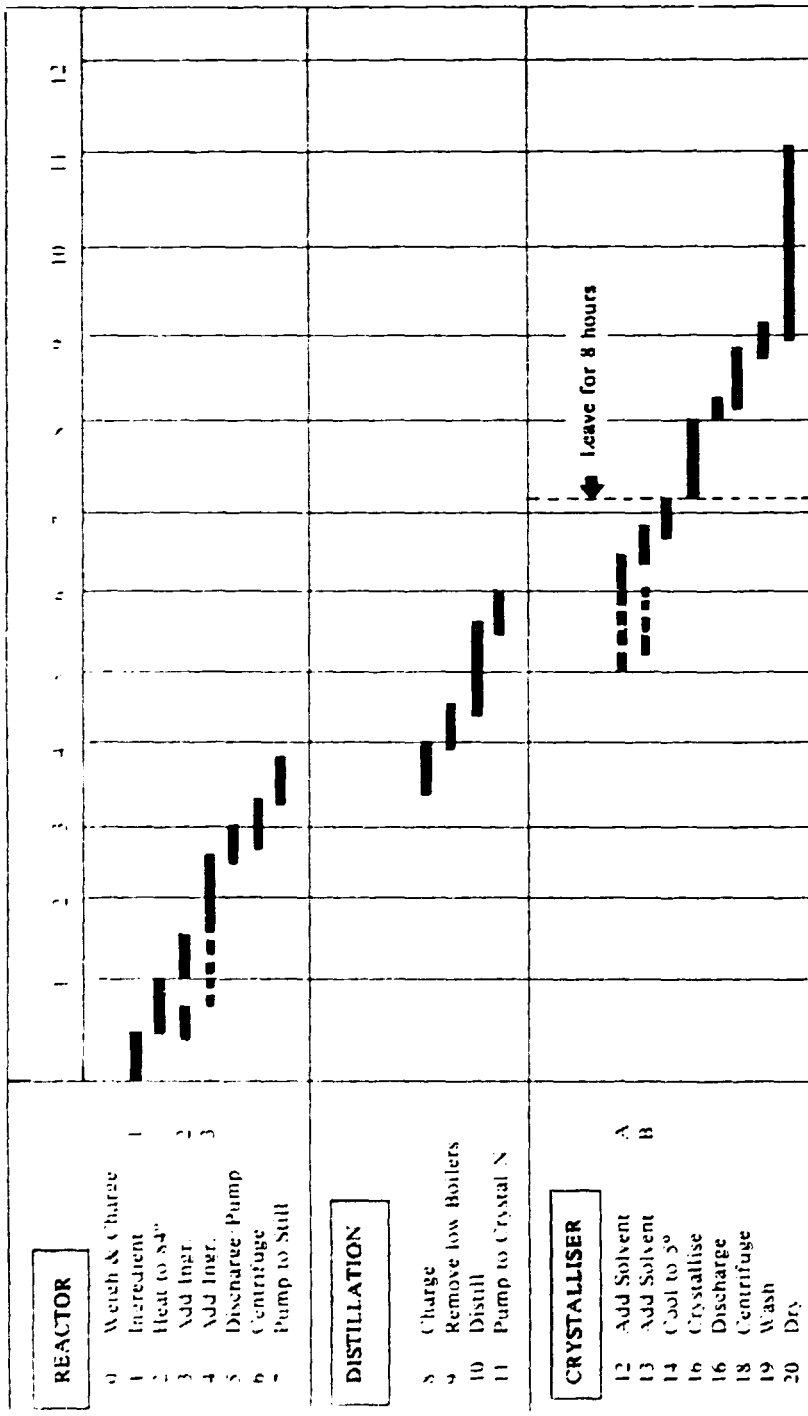
- 11 Evaporate Dryness
- 12 Cool to 20°
- 13 Add Solvent
- 14 Heat to 60°
- 15 Ventate
- 16 Pump Out to C
- 17 Filter Hot

REACTOR C

- 18 Cool to 15°
- 19 Discharge
- 20 Centrifuge
- 21 Wash
- 22 Dry



**ETHAMBUTOL HYDROCHLORIDE  
TIME-HOURS**



**REACTOR**

- 1 Wench & Charge
- 2 Incrudent
- 3 Heat to 84°
- 4 Add Ingr.
- 5 Add Ingr.
- 6 Discharge: Pump
- 7 Centrifuge  
Pump to Still

**DISTILLATION**

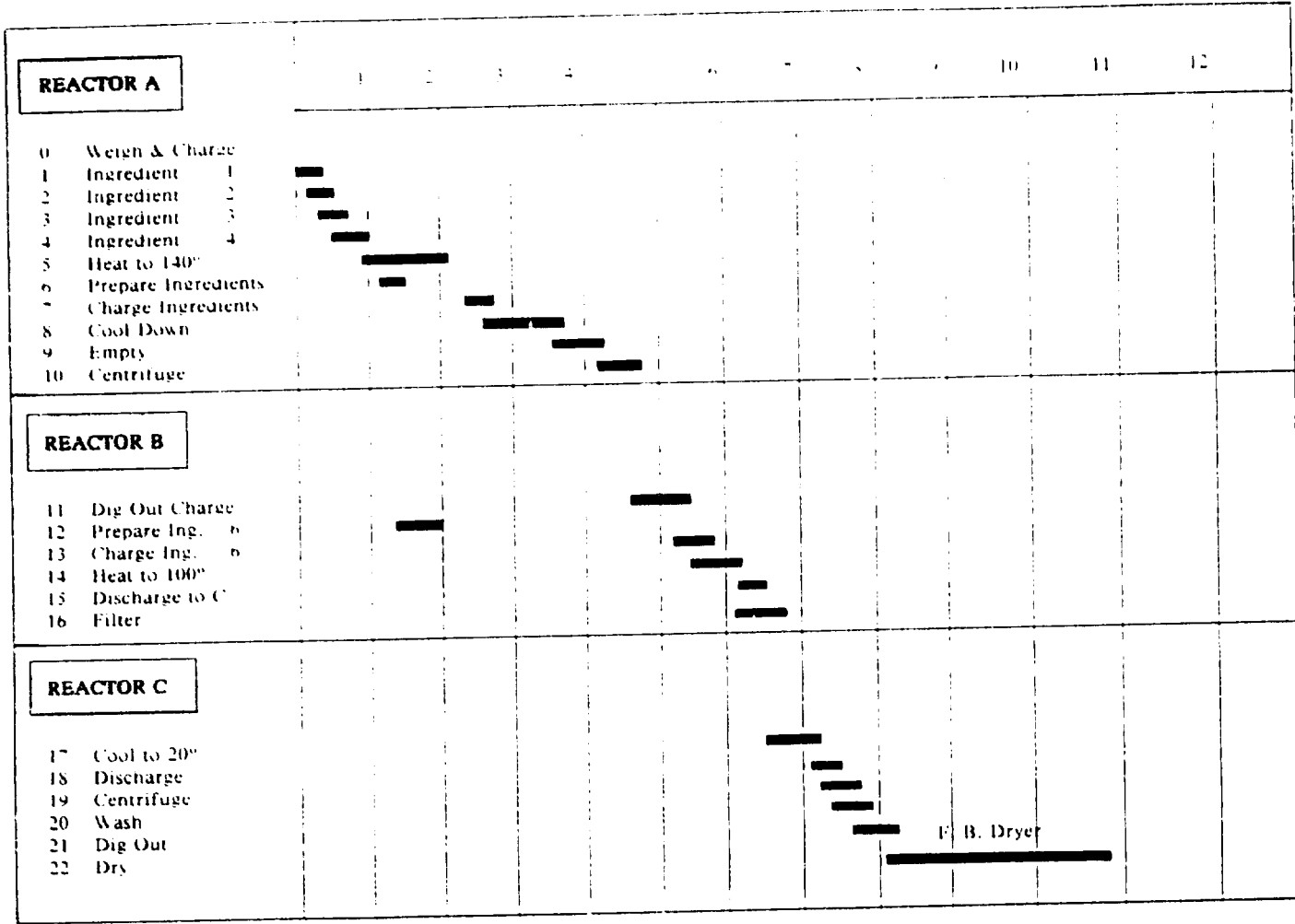
- 8 Charge
- 9 Remove low Boilers
- 10 Distill
- 11 Pump to Crstal N

**CRYSTALLISER**

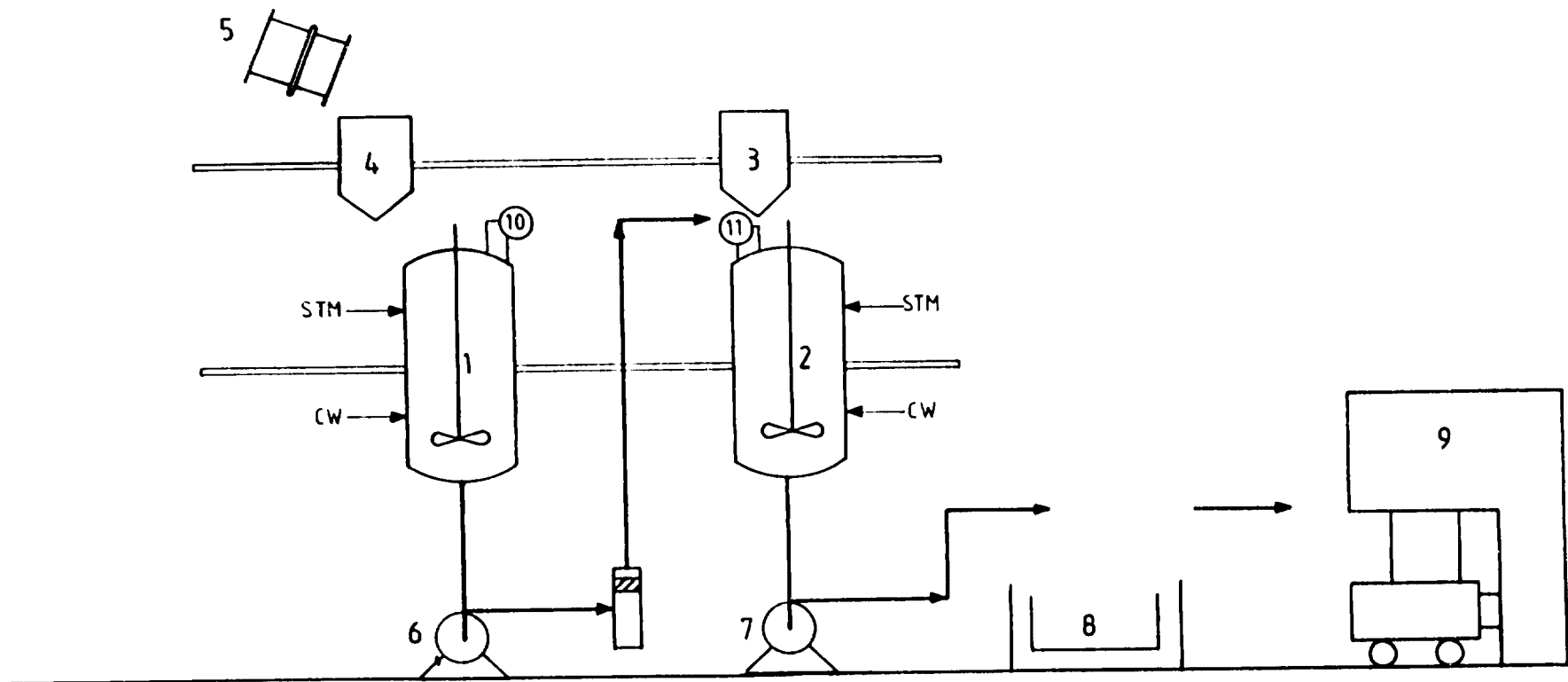
- 12 Add Solvent
- 13 Add Solvent
- 14 Cool to 5°
- 16 Crystallise
- 16 Discharge
- 18 Centrifuge
- 19 Wash
- 20 Dry

Leave for 8 hours

MEFENAMIC ACID  
TIME-HOURS







- P1 REACTOR A — 3m
- P2 REACTOR B — 3m
- P3 FEED TANK — 250 LITRE
- P4 FEED TANK — 750 LITRE
- P5 DRUM HOIST — 20kg, 8m
- P6/7 PUMPS — 5m<sup>3</sup>/h 3 BARGE
- P8 BASKET CENTRIFUGE - 500 LITRE
- P9 DRYER — 500 LITRE
- P10/11 CONDENSER - 1m<sup>2</sup>

**LEGEND**  
 STM=STEAM  
 CW =COOLING WATER

**NOTES**

1. MATERIAL OF CONSTRUCTION: ALL WETTED PARTS TO 316 STAINLESS STEEL.
2. REACTORS: PRESSURE VESSELS VACUUM-3 BAR G PRESSURE 5kw EXPLOSION PROOF TURBINE AGITATORS 4 BAFFLES MILD STEEL JACKETS WITH FLANGED CONNECTIONS TO STEAM & WATER PRESSURE RATING 3 BAR'G
3. ALL MOTORS AND ELECTRICAL INSTALLATIONS TO BE MADE EXPLOSION PROOF

1	1.10.92	UNIDO COMMENTS INCORPORATED	PL
REV	DATE	DESCRIPTION	CHK'D

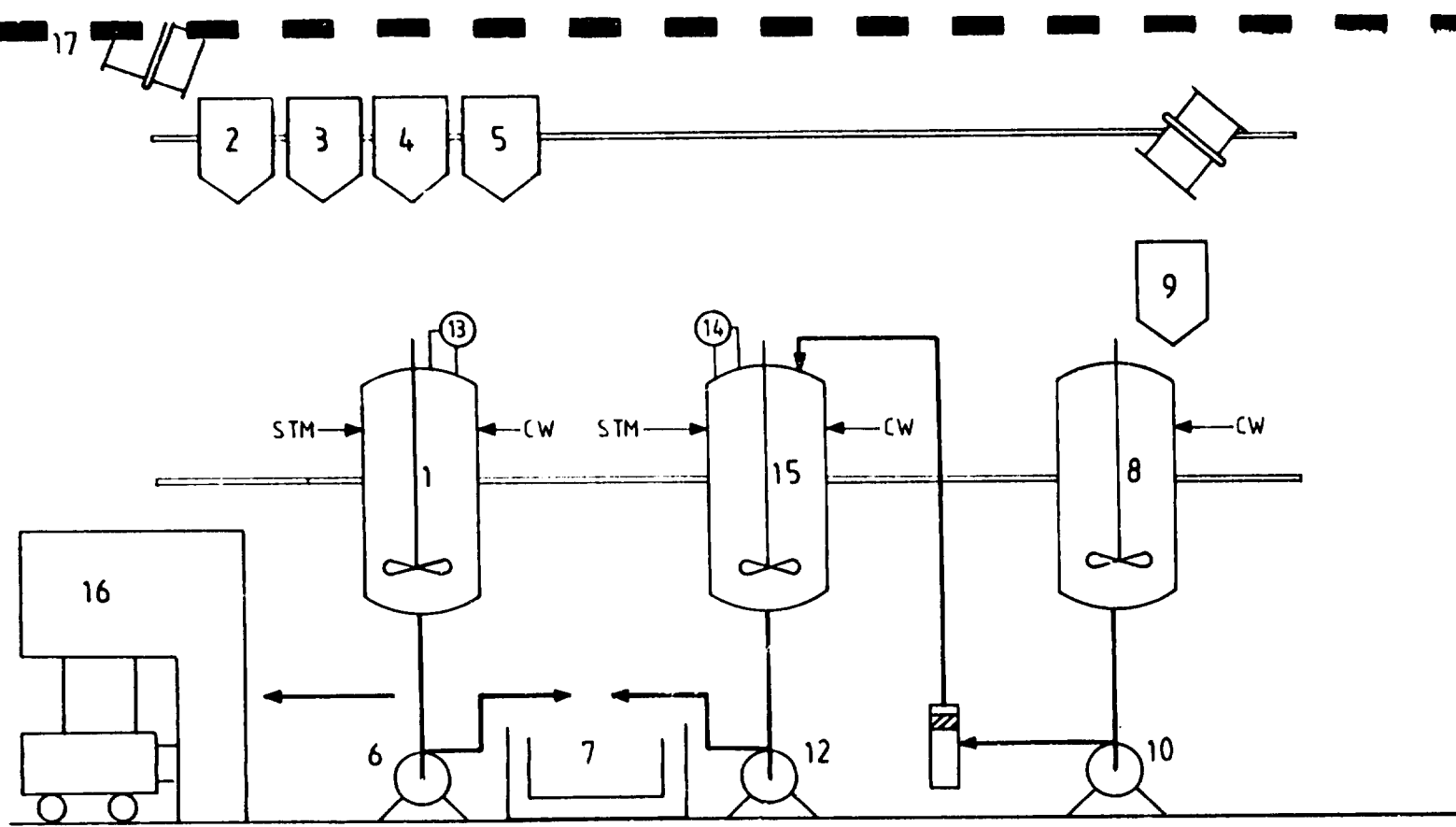
**THE MANDERSTAM GROUP**  
 CONSULTING ENGINEERS  
 2/10 HARBOUR YARD, CHELSEA HARBOUR, LONDON SW10

TITLE PARACETAMOL FLOW DIAGRAM No 1

APPENDIX 6-2

JOB No.	DATE	SCALE	REV 1
DRAWN C.S.H.	6/3/92		
CHK'D R.C.S.	6/3/92		
APPR'D P.	6/3/92		

DRG. No.



- M1 REACTOR A 2m<sup>3</sup>
- M2/3/4/5 FEED TANKS 500LITRE
- M6 DISCHARGE PUMP 3m<sup>3</sup>/h 2bar
- M7 CENTRIFUGE 500LITRE
- M8 REACTOR B 2m<sup>3</sup>
- M9 FEED TANK 500LITRE
- M10 DISCHARGE PUMP 3m<sup>3</sup>/h, 2 bar
- M11 IN-LINE FILTER 0.5m<sup>2</sup>
- M12 SLURRY PUMP 3m<sup>3</sup>/h 2bar
- M13/14 CONDENSER 1m<sup>2</sup>
- M15 CRYSTALLISER 2m<sup>3</sup>
- M16 DRYER 500 LITRE

**LEGEND**  
 STM=STEAM  
 CW =COOLINGWATER

**NOTES**  
 1 ALL WETTED PARTS 316 STAINLESS STEEL  
 2 REACTORS WITH MILD STEEL JACKETS TO 3 BAR G VESSELS FOR VACUUM & 3 BAR G PRESSURE, TURBINE AGITATORS 4 BAFFLES

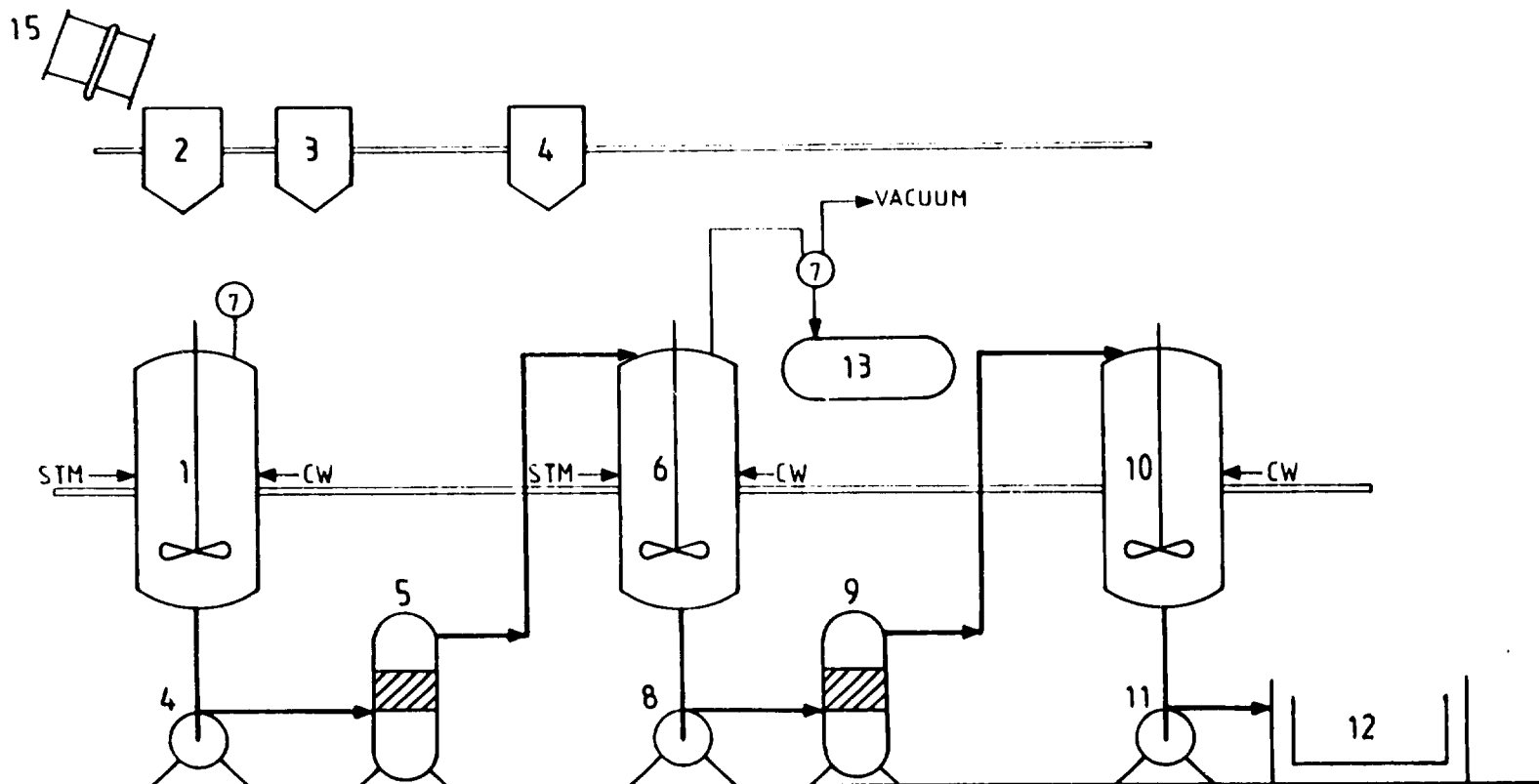
REV	DATE	DESCRIPTION	CHK'D
1	1.10.92	(UNDO COMMENTS INCORPORATED)	PL

**THE MANDERSTAM GROUP**  
 CONSULTING ENGINEERS  
 2/10 HARBOUR YARD, CHELSEA HARBOUR, LONDON SW10

TITLE  
**MEFENAMIC ACID FLOW DIAGRAM No**

JOB No.	DATE	SCALE	REV 1
DRAWN <i>CSH</i>	<i>5/3/91</i>		
CHK'D <i>RLS</i>	<i>5/3/91</i>		
APPRD <i>PL</i>	<i>5/3/91</i>		

DRG. No.  
 APPENDIX 6-2



- I1 REACTORA ————— 1 m<sup>3</sup>
- I2/3/4 FEEDTANKS ————— 250 LITRE
- I3 CONDENSER ————— GLASS
- I4 DISCHARGE PUMP
- I5 FILTER ————— 0.5 m<sup>2</sup>
- I6 MIXER-EVAPORATOR — 1 m<sup>3</sup>
- I7 CONDENSER
- I8 DISCHARGE PUMP
- I9 FILTER ————— 0.5 m<sup>2</sup>
- I10 CRYSTALLISER ————— 1 m<sup>3</sup>
- I11 SLURRY PUMP ————— 3 BAR G, 3 m<sup>3</sup>/h
- I12 CENTRIFUGE ————— 500 LITRE
- I13 RECEIVER ————— 500 LITRE
- I14 DRYER (NOT SHOWN)

**LEGEND**  
 STM = STEAM  
 CW = COOLING WATER

**NOTES**

1. ALL MATERIALS OF CONSTRUCTION TYPE 316 STAINLESS STEEL EXCEPT WHERE STATED
2. ALL REACTORS JACKETED (MILD STEEL TO 3 BAR G) VESSELS TO 3 BAR G AND FULL VACUUM, AGITATORS TURBINE.

REV	DATE	DESCRIPTION	CHK'D
1	1.10.92	UNIDO COMMENTS INCORPORATED	PI.

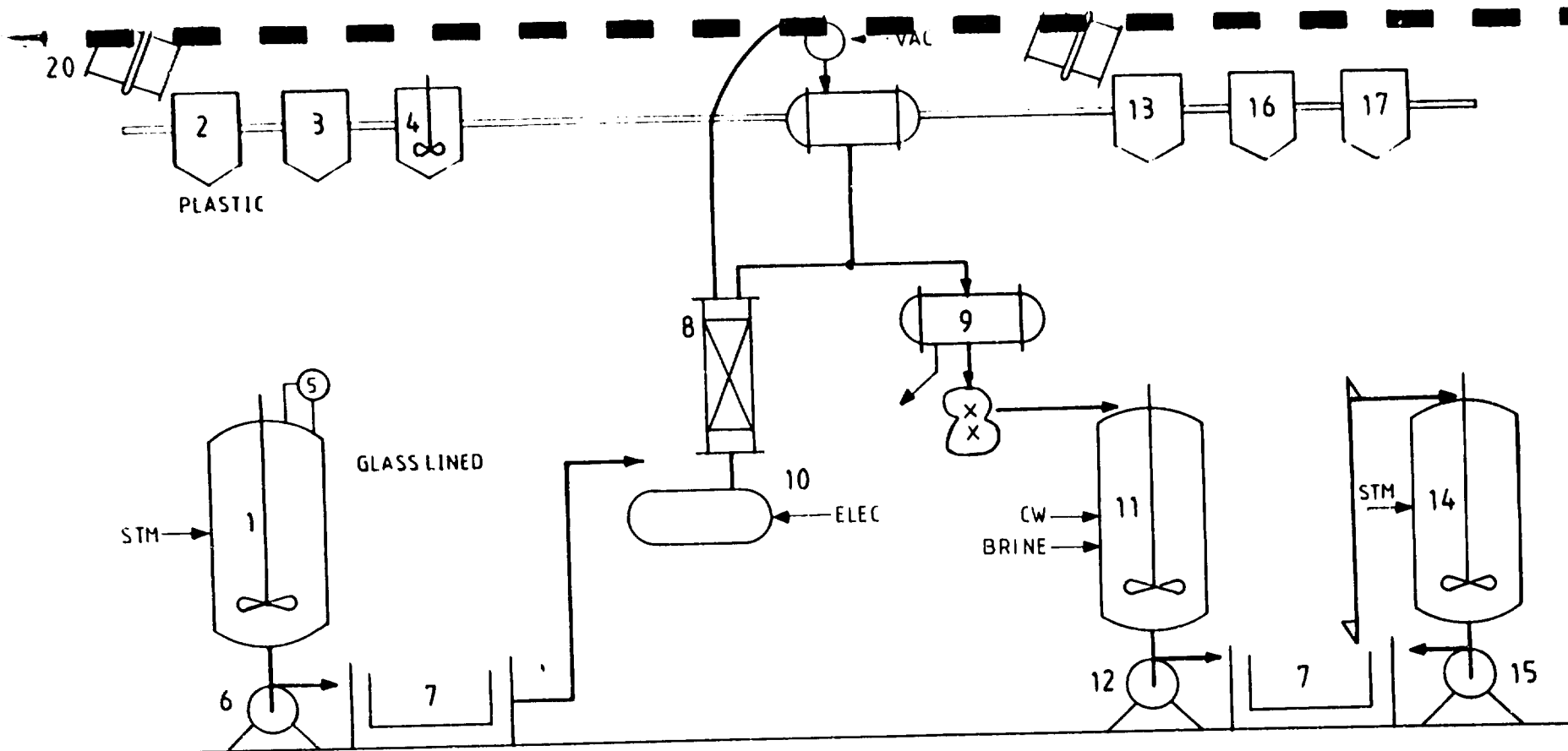
**THE MANDERSTAM GROUP**  
 CONSULTING ENGINEERS  
 2/10 HARBOUR YARD, CHELSEA HARBOUR, LONDON SW10

TITLE **ISONIAZID DIAGRAM. No 3**

APPENDIX 6-2

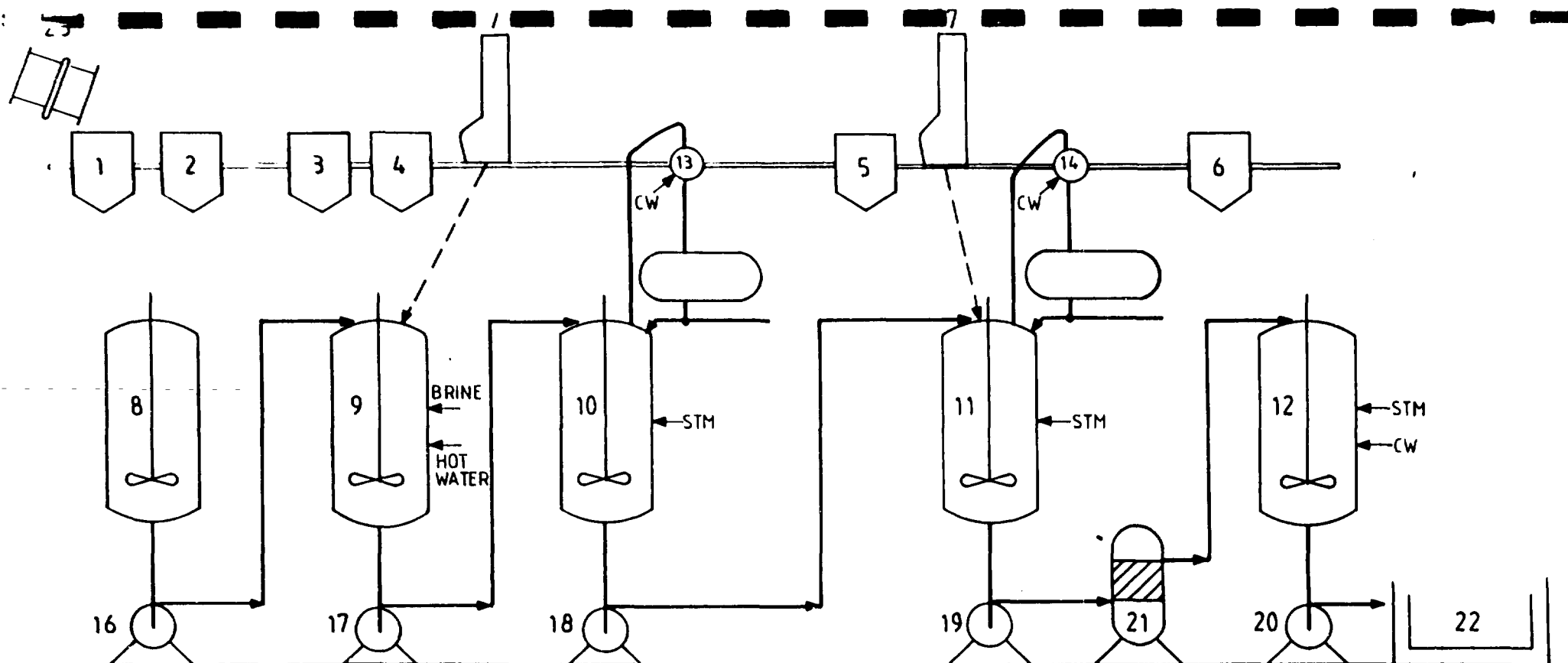
JOB No.	DATE	SCALE	REV 1
DRAWN C 311	6/3/92		
CHK'D RLS	6/3/92		
APPRD ic	6/3/92		

DRG. No.



- E1 REACTOR — 2m<sup>3</sup>G/L
  - E2/3/4 FEED TANKS-500LITRE
  - E5 CONDENSER — 1m<sup>3</sup>
  - E6 DISCHARGE PUMP-5m<sup>3</sup>/h
  - E7 CENTRIFUGE — 500LITRE
  - E8 BATCH STILL — 1m<sup>3</sup>
  - E9 RECEIVER — 0.5m<sup>3</sup>
  - E10 PUMP — 5m<sup>3</sup>/h
  - E11 CRYSTALLISER — 2m<sup>3</sup>
  - E12 PUMP — 5m<sup>3</sup>/h
  - E13 FEED TANK — 500LITRE
  - E14 RECRYSTALLISER-2m<sup>3</sup>
  - E15 SLURRY PUMP — 5m<sup>3</sup>
  - E16/17 FEED TANKS — 500LITRE
  - E19 DRYER (NOT SHOWN)-500LITRE
  - E20 DRUM HOIST — 8m, 250kg
3. REACTORS: JACKETED.  
TURBINE AGITATORS.  
VACUUM & PRESSURE TO 3 BAR G
- LEGEND  
STM = STEAM  
CW = COOLING WATER  
VAC = VACUUM
- NOTE  
1. ONLY ONE CENTRIFUGE  
IN ACTUAL USE E7  
2. ALL EQUIPMENT 316  
STAINLESS STEEL EXCEPT  
WHERE NOTED.

1	1.10.92	UNDO COMMENTS INCORPORATED	PL
REV	DATE	DESCRIPTION	CHK'D
<b>THE MANDERSTAM GROUP</b> CONSULTING ENGINEERS 2/10 HARBOUR YARD, CHELSEA HARBOUR, LONDON SW10 C			
TITLE <b>ETHAMBUTOL DIAGRAM No 4</b> APPENDIX 6-2			
JOB No.	DATE	SCALE	REV 1
DRAWN	6/5/92		
CHK'D	6/5/92		
APPR'D	6/5/92		
DRG. No.			



- I 1-6 FEED VESSELS 316
- I 7 BAG SLITTER PLASTIC COATED
- I 8 REACTOR A 500LITRE
- I 9 REACTOR B 1m<sup>3</sup>
- I 10 REACTOR C 500 LITRE 316
- I 11 REACTOR D 1m<sup>3</sup>
- I 12 REACTOR E 316 500 LITRE
- I 13/14 CONDENSERS GLASS
- I 15 RECEIVERS (NOT SHOWN) 316, 1m<sup>3</sup>
- I 16- 20 DISCHARGE PUMPS PLASTIC
- I 21 FILTER 316
- I 22 CENTRIFUGE 316
- I 23 DRUM HOIST STANDARD, 300kg, 8m

**LEGEND**  
 STM STEAM  
 CW COOLING WATER

**NOTES**

1. ALL EQUIPMENT WETTED PARTS GLASS LINED STEEL EXCEPT WHERE STATED
2. REACTORS: ALL WITH MILD STEEL JACKETS TO 3 BAR G PRESSURE, VESSELS TO VACUUM AND 3 BAR G PRESSURE, ALL WITH TURBINE AGITATORS
3. PUMPS 3m<sup>3</sup>/h TO 2 BAR G PRESS.

REV	DATE	DESCRIPTION	CHK'D
1	1.10.92	UNDO COMMENTS INCORPORATED	PL

THE MANDERSTAM GROUP  
 CONSULTING ENGINEERS  
 21/10 HARBOUR YARD, CHELSEA HARBOUR, LONDON SW10 C

TITLE **BUPROFEN PREPARATION**  
**DIAGRAM No 5**

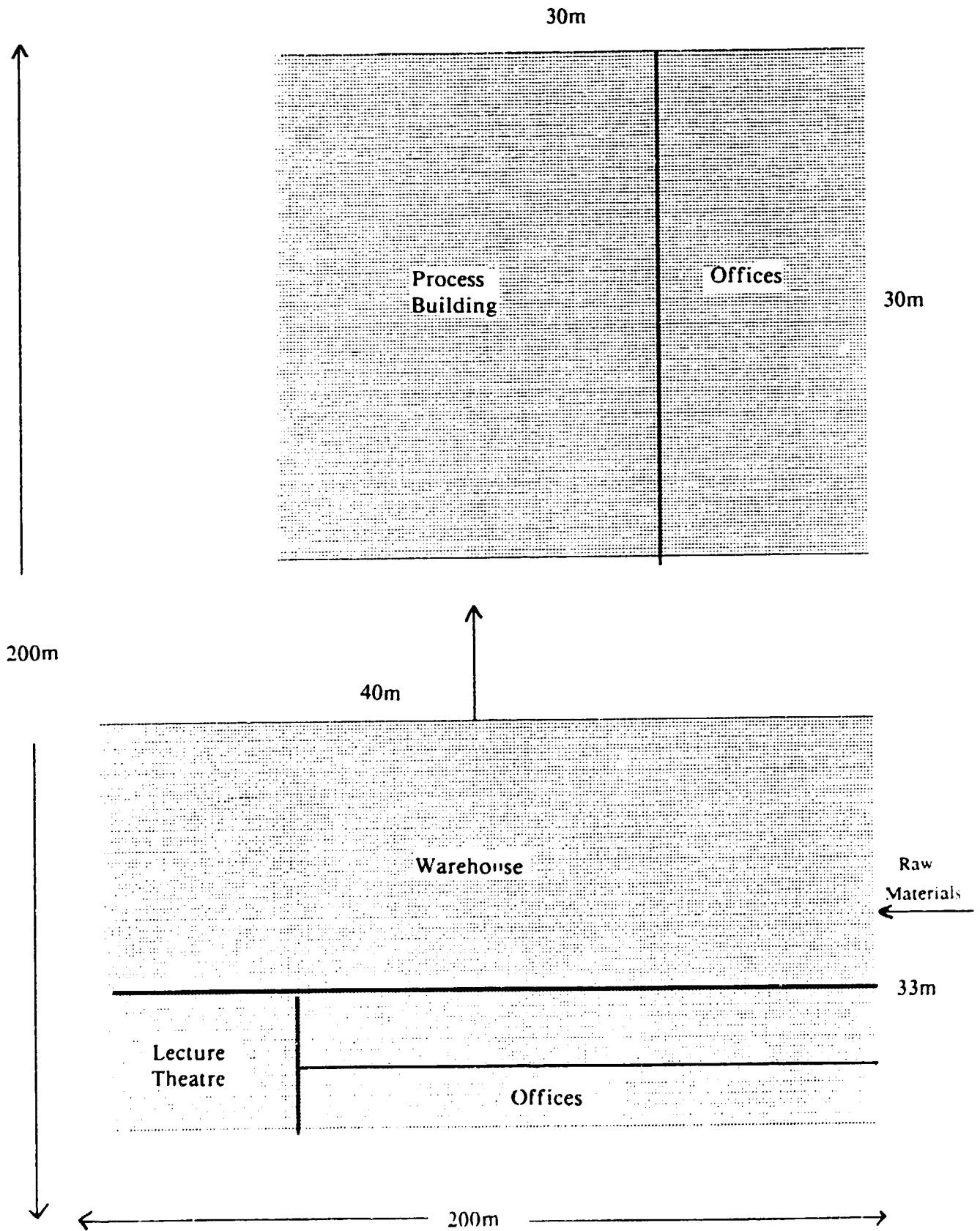
JOB No.	DATE	SCALE	REV 1
DRAWN	CSH	6/3/92	DRG. No.
CHK'D	RES	8/5/92	
APPR'D	PL	6/3/92	APPENDIX 6-2



## EQUIPMENT LIST

TYPE	DESCRIPTION	SIZE/CAPACITY	NO
<b>REACTORS</b> Explosion proof motors with carbon steel jacket to 3 barge with flanged connection for steam and water. All with turbine agitators and 4 buffers Pressure rating vessel vacuum - 3 barge	316 5kW agitator	3m <sup>3</sup>	2
	316 3kW agitator	2m <sup>3</sup>	3
	316 1.5kW agitator	1m <sup>3</sup>	3
	GL steel 5kW agitator	1m <sup>3</sup>	2
	316 3kW agitator	0.5m <sup>3</sup>	1
	GL steel 10kW agitator	0.5m <sup>3</sup>	1
<b>PROCESS VESSELS</b> Not pressure vessels. All vertical cylindrical aspect ratio 1.5:1 with lid. All agitators turbine or propellor. All flanged connections. All explosion proof motors.	316 3kW agitator	1m <sup>3</sup>	3
	316 3kW agitator	1m <sup>3</sup>	2
	plastic 3kW agitator	1m <sup>3</sup>	3
	plastic 3kW agitator	1m <sup>3</sup>	2
	316 3kW agitator	0.5m <sup>3</sup>	5
	316 3 kW agitator	0.5m <sup>3</sup>	5
<b>STORAGE VESSELS (PRESSURE)</b> Vessels to 5 barge. Vertical, cylindrical. Flanged connections.	plastic 3kW agitator	0.5m <sup>3</sup>	5
	plastic 3kW agitator	0.5m <sup>3</sup>	5
	316	2m <sup>3</sup>	2
	ditto	1.5m <sup>3</sup>	2
	ditto	1m <sup>3</sup>	1
<b>STORAGE VESSELS (ATMOSPHERIC)</b> Vertical, cylindrical, flanged connection. Lids.	ditto	0.5m <sup>3</sup>	1
	316	5m <sup>3</sup>	2
	ditto	3m <sup>3</sup>	2
<b>PUMPS</b> Flanged connections, explosion proof motors	ditto	1m <sup>3</sup>	2
	316 centrifugal, 3 barge pressure	5m <sup>3</sup> /h	8
	plastic centrifugal, 3 barge pressure	5m <sup>3</sup> /h	8
	316 vacuum	15 tor	2
<b>STILL</b>	316 drum emptying	5m <sup>3</sup> /h	5
	316 distillation column; 1m <sup>3</sup> capacity electric heater to 250°C; vac t. 2 bar; condenser and reflux at 1500 l/h boil up rate. Explosion proof motors	see previous column	1
<b>CHILLER</b>	water to 0°C	50kW	1
<b>MISCELLANEOUS</b>	sack tip unit	100kg	2
	drum tip hoists	8m, 250kg	2
	316 fluid bed dryer	0.5m <sup>3</sup>	1
	316 centrifuge (bowl type)	0.5m <sup>3</sup>	2
	weigh scale	50kg	1
	weigh scale	250Kg	1
	316 condenser	1m <sup>2</sup>	3
	316 filter	5m <sup>3</sup> /h	3

**APPENDIX 6-4**  
**DETAILED SITE LAYOUT**



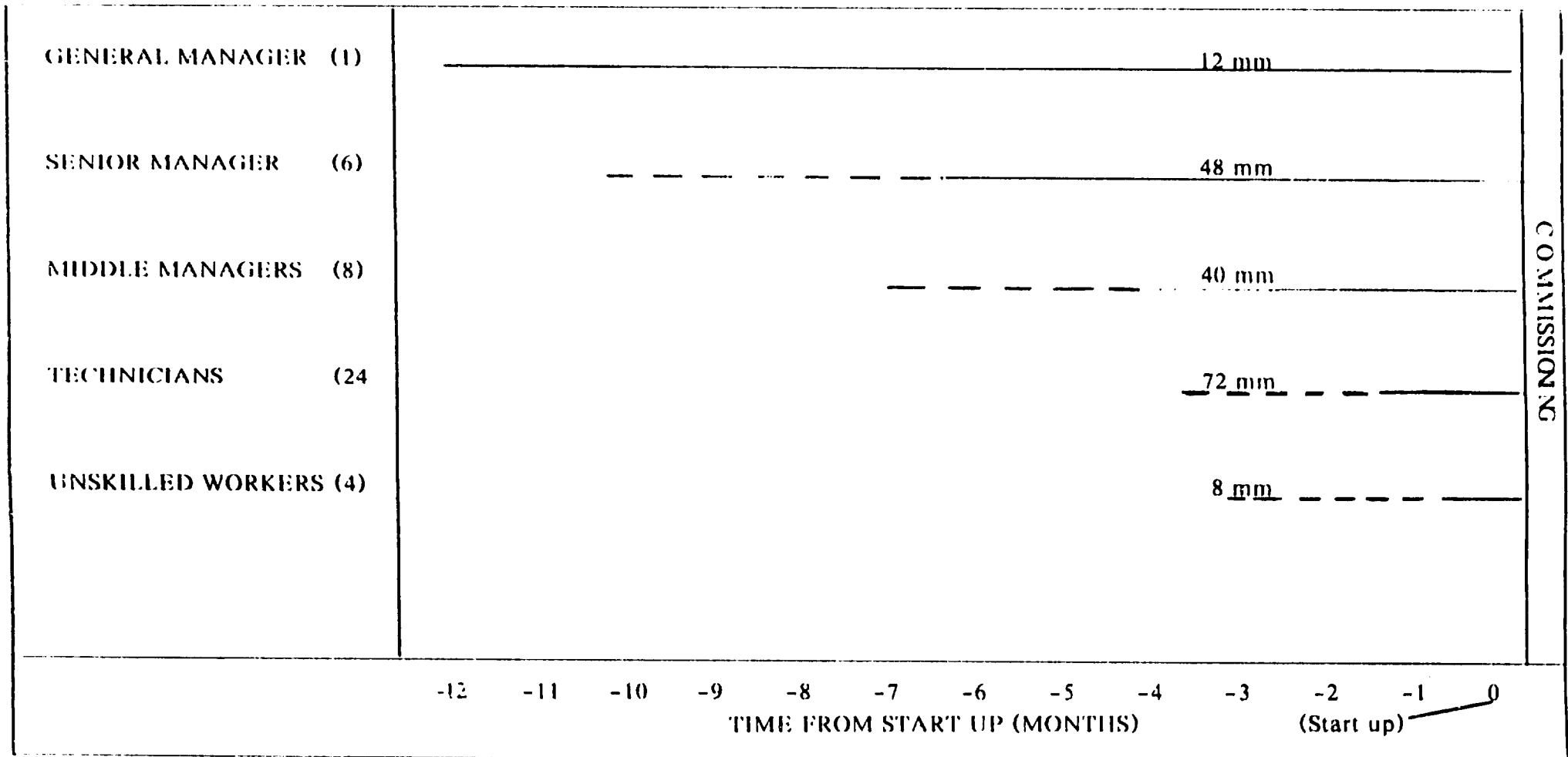
APPENDIX 7-1

		Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
<b>FACTORY COSTS</b>		Factor :	1.0									
<b>Direct Production Staff</b>		Salary	24	2,840								
-----												
Process Superintendents	180,000	3	540	Annual								
Technicians/Operators	120,000	6	720	Cost								
Unskilled Labour	40,000	2	80									
<b>Laboratory &amp; Engineering Staff</b>												
-----												
Maintenance Foreman	180,000	1	180	Annual								
Warehouse Foreman	120,000	2	240	Cost								
Chemists	120,000	6	720									
Maintenance Technicians	80,000	3	240									
<b>Factory Overheads</b>												
-----												
Replacement Spare Parts	62,571	2	1,251	1,314	1,380	1,449	1,521	1,597	1,677	1,761	1,849	1,941
Repairs & Maintenance		2	498	603	663	663	663	663	663	663	663	663
Protective Clothing, etc			200	per annum								
<b>OVERHEAD COSTS</b>		Factor :	1.0									
<b>Management</b>		Salary	17	2,560								
-----												
General Manager	500,000	1	500	Annual								
Chemical Engineers	250,000	2	500	Cost								
Chemists	250,000	2	500									
Administration/Training	250,000	2	500									
<b>Administration/Other Personnel</b>												
-----												
Accounts Officer	120,000	1	120	Annual								
Storekeepers	60,000	3	180	Cost								
Secretary	60,000	1	60									
Clerical Staff	40,000	4	160									
Drivers	40,000	1	40									
<b>Administrative Overheads</b>												
-----												
Insurance	182,228	1	1,822	Annual								
Office Supplies			195	Cost								
Communications			195									
Land/Property Charges			65									
Licences & Fees			65									
Travel & Transport			360									
Sundries			263									

			1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
<b>SALES COSTS</b>												
Factor :	1.0											
<b>Manpower</b>												
Salary	2		200									
-----												
Liaison Officer	180,000	1	180 Annual									
Driver	40,000	1	40 Cost									
<b>Other Sales-Distribution Costs</b>												
-----												
Product Promotion - Field			300 Annual									
Travel & Transport			180 Cost									
<b>FINANCIAL COSTS</b>												
<b>Initial loans</b>												
-----												
Foreign Currency Loans	45,542		45,542	36,434	27,326	18,218	9,110	0	0	0	0	0
Repayments	9,108	5.0	0	9,108	9,108	9,108	9,108	9,110				
Interest		8.0	3,643	3,279	2,550	1,822	1,093	364	0	0	0	0
Local Currency Loans	70,411		70,411	46,941	23,471	0	0	0	0	0	0	0
Repayments	23,470	3.0		23,470	23,470	23,471						
Interest		25.0	17,603	11,735	8,802	2,934	0	0	0	0	0	0
<b>DEPRECIATION</b>			19,781	19,781	19,781	19,781	19,780	12,751	12,751	12,751	12,751	12,752
<b>Initial Investment</b>												
-----												
Buildings and Civil Works	116,247	5	5,812	5,812	5,812	5,812	5,812	5,812	5,812	5,812	5,812	5,812
Production Equipment	30,006	10	3,001	3,001	3,001	3,001	3,001	3,001	3,001	3,001	3,001	2,997
Ancillary Prod. Equipment	22,032	10	2,203	2,203	2,203	2,203	2,203	2,203	2,203	2,203	2,203	2,205
Auxiliary Equipment	10,533	10	1,053	1,053	1,053	1,053	1,053	1,053	1,053	1,053	1,053	1,056
Vehicles	3,410	20	682	682	682	682	682	0	0	0	0	0
Pre-Production Expenditure	35,149	20	7,030	7,030	7,030	7,030	7,029	0	0	0	0	0
<b>Replacement Investment</b>												
-----												
Vehicles - Year 2000	3,410	20	0	0	0	0	0	682	682	682	682	682

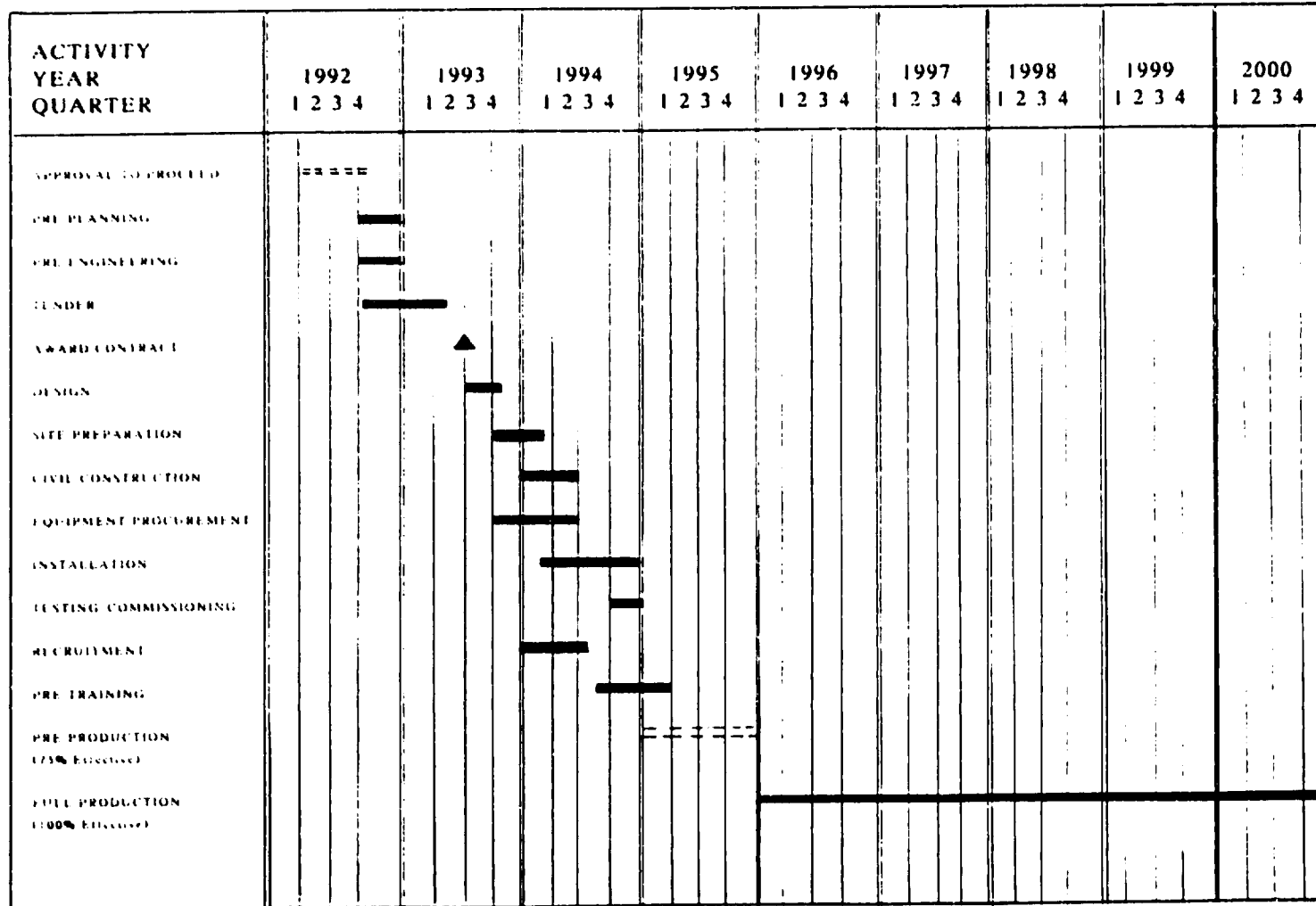
APPENDIX 8-1

SCHEDULE OF RECRUITMENT AND TRAINING ACTIVITIES PRIOR TO START UP



PROJECT IMPLEMENTATION SCHEDULE

APPENDIX 9-1



## APPENDIX 9-2

### PROJECT COST ESTIMATES

#### 1.0 INTRODUCTION

This is a cost estimate for a multi purpose pilot plant to be constructed in the Philippines.

All cost estimates include:

Major Equipment Procurement Costs,  
Bulk Material, Procurement Costs,  
Freight,  
Construction, Labour & Indirect Costs,  
Construction Sub-contracts,  
Process Licenses,  
Consultants & Studies,  
Design Contractor Costs,  
Construction Supervision Costs &  
Commissioning Team Costs

The cost estimates have been prepared based on the preliminary engineering design, and flowsheets.

The overall accuracy of the estimate is  $\pm 15\%$ .

#### 2.0 GENERAL

All costs contained herein are based in IQ92. No forward escalation beyond this datum is included.

#### 3.0 BASE DATA

The following referenced technical data forms the basis of the estimate.

- |    |                         |                |
|----|-------------------------|----------------|
| a) | Process sequence charts | (Appendix 6-1) |
| b) | Flow sheets 1 to 5      | (Appendix 6-2) |
| c) | Equipment lists         | (Appendix 6-3) |

#### 4.0 COST ESTIMATE SUMMARIES

The following lists the cost estimate summary.

	<u>FILIPINO BUILD MILL US\$</u>
Equipment Procure	1.28
Bulk Material Procure	0.64
Construction	0.64
Sub-contracts	0.33
Minor Support Contracts	0.64
Major Support Contracts	0.704
Civil Engineering	2.974
Tie-ins	<u>0.111</u>
	6.750
Capitalised Spares	0.059

#### 5.0 BASIS OF COSTS ESTIMATES

Where item costs for equipment are not provided, costs are based on a) factored from those provided, or, b) based on in house data, or c) estimated.

##### **Bulk Material Procurement Costs.**

Covered here are piping, electrical, instrumentation & commissioning spares. Instrumentation is assumed to include telecommunications.

As the majority of equipment is designated as stainless steel, then consequently, all piping is assumed to be of similar high grade material.

Also, as this is a pharmaceutical plant & purity is of the utmost importance it is assumed that instrumentation & controls will suitably be to very high specifications.

No special electrical requirements are assumed.

Commissioning spares are included to allow for consumables during the initial pre & system commissioning phases. No allowances are included for insurance or operating spares.

Cost estimates are based on in house data factors specifically relating to a pharmaceutical plant, under construction in the UK.

##### **Construction and Sub-contracts**

Covered here are direct construction labour costs for equipment, piping, electrical, instrumentation and steelwork erection. Steel work is assumed a supply and erect contract.



Sub-contracts are included for insulation, painting, fire & gas, control system, scaffolding & pre-commissioning.

All the above are based on in-house data factors.

An allowance is included for crane hire over & above the requirements which will form part of the installation contractors statutory contractual obligations.

Costs are included for site establishment, general civils & piling sub-contracts. These cannot be accurately or sensibly forecast until such a time that actual site conditions & locations are established.

#### **Minor Support Contracts**

Allowances are included here to cover for vendor representatives during construction, process licenses (if required), engineering support during construction, consultants & studies. Most projects attract these costs in one form or another, the exact scope must be established before these can be accurately forecast.

#### **Major Support Contracts**

Costs are included here for conceptual design, detail design contractor, construction supervision, commissioning team & commissioning trades to assist the commissioning team.

Manhours are first estimated to which a contract rate is applied to realise total costs. Manhours are based on in house data from projects of similar nature. These may vary when all contractual philosophies are established.

For instance, if all design is to be awarded to a single design contractor without competitive bidding, conceptual engineering may be greatly reduced or eliminated due to the combining of work scopes & non requirement of familiarisation.

60 EXCLUSIONS

The following must be considered excluded from all cost estimates contained herein.

LAND AND RIGHTS OF WAY  
PLANNING APPLICATION COSTS  
SEISMIC & SITE SURVEYS (including bore holes and soil sampling)  
ESCALATION  
CONTINGENCIES (although an indicative % is shown in Section 7.0)  
ALL CLIENT COSTS & EXPENSES  
OPERATOR TRAINING & MANUALS  
POWER GENERATION  
INSURANCES, BONDS & WARRANTIES  
LOCAL AGENTS FEES & DISPURSEMENTS  
BONDED STORES and/or WAREHOUSING  
PRESERVATION DURING STORAGE  
TAXES, DUTIES & DUES  
CONSTRUCTION CAMP COSTS  
ANY EXTENSION TO LOCAL INFRASTRUCTURE (if reqd)  
MANAGEMENT CONTRACTOR COSTS  
LOCAL OFFICE ESTABLISHMENT  
RIOTS AND WARS  
STRIKES AND MAJOR DISRUPTIONS

7.0 COST ESTIMATE DETAILS

The proceeding pages show the detail estimate sheets for all study options.

As an indication, it is recommended to add a 10% contingency to the figures shown.

MANDERSTAM CONSULTING SERVICES

PILOT PLANT - UNIDO - PHILIPPINES

DATE Mar 82  
SHEET 1 of 2  
PRIME CASE 10. PHILIPINO RUBBER

COMPOSITE PLANT - REV 3

DESCRIPTION	UNIT	BASE QTY	DESIGN GROWTH ALL'CE	CUT & WASTE ALL'CE	PURCH QTY	PURCH US\$ UNIT RATE	PURCH COST US\$ x 1000	INST'D QTY	INST'N MHR UNIT RATE	MHRS	LAB RATE US\$ PER MHR	SUB-CONTRACT US\$ UNIT RATE	LAB COST US\$ x 1000	SUB-CONTRACT US\$ x 1000	TOTAL COSTS US\$ x 1000	REMARKS
<b>EQUIPMENT PROCUREMENT</b>																
REACTORS																
1 m3 GLASS LINED (JACKETED)	EA	20	00	00	20	10,000	200	20		0			00	00	200	
AGITATOR FOR ABOVE	EA	20	00	00	20	7,000	140	20		0			00	00	140	
0.5 m3 GLASS LINED (JACKETED)	EA	10	00	00	10	8,000	80	10		0			00	00	80	
AGITATOR FOR ABOVE	EA	10	00	00	10	8,000	80	10		0			00	00	80	
3 m3 316 SS (JACKETED)	EA	20	00	00	20	14,000	280	20		0			00	00	280	
AGITATOR FOR ABOVE	EA	20	00	00	20	7,000	140	20		0			00	00	140	
2 m3 316 SS (JACKETED)	EA	30	00	00	30	12,500	375	30		0			00	00	375	
AGITATOR FOR ABOVE	EA	30	00	00	30	5,000	150	30		0			00	00	150	
1 m3 316 SS (JACKETED)	EA	30	00	00	30	10,000	300	30		0			00	00	300	
AGITATOR FOR ABOVE	EA	30	00	00	30	3,500	105	30		0			00	00	105	
0.5 m3 316 SS (JACKETED)	EA	10	00	00	10	9,500	95	10		0			00	00	95	INC AGITATOR
VESSELS																
1 m3 FEED VESSEL 316 SS	EA	50	00	00	50	7,500	375	50		0			00	00	375	
AGITATOR FOR ABOVE	EA	30	00	00	30	3,500	105	30		0			00	00	105	
1 m3 STORAGE VESSEL 316 SS	EA	20	00	00	20	12,000	240	20		0			00	00	240	
3 m3 STORAGE VESSEL 316 SS	EA	20	00	00	20	27,500	550	20		0			00	00	550	
500 L FEED VESSEL 316 SS	EA	100	00	00	100	6,000	600	100		0			00	00	600	
AGITATOR FOR ABOVE	EA	50	00	00	50	2,750	138	50		0			00	00	138	
5 m3 STORAGE VESSEL 316 SS	EA	20	00	00	20	30,000	600	20		0			00	00	600	
2 m3 PRESSURE VESSEL 316 SS	EA	20	00	00	20	30,000	600	20		0			00	00	600	
1.5 m3 PRESSURE VESSEL 316 SS	EA	20	00	00	20	25,000	500	20		0			00	00	500	INC AGITATOR
0.5 m3 FEED VESSEL PLASTIC	EA	100	00	00	100	3,000	300	100		0			00	00	300	
AGITATOR FOR ABOVE	EA	50	00	00	50	2,750	138	50		0			00	00	138	
1 m3 FEED VESSEL PLASTIC	EA	50	00	00	50	5,000	250	50		0			00	00	250	
AGITATOR FOR ABOVE	EA	30	00	00	30	3,500	105	30		0			00	00	105	
1 m3 PRESSURE VESSEL 316 SS	EA	10	00	00	10	20,000	200	10		0			00	00	200	
500 L PRESSURE VESSEL 316 SS	EA	10	00	00	10	15,000	150	10		0			00	00	150	
1500 L FEED VESSEL 316 SS	EA	00	00	00	00	10,000	00	00		0			00	00	00	
2000 L FEED VESSEL 316 SS	EA	00	00	00	00	12,000	00	00		0			00	00	00	
3 m3 STORAGE VESSEL 316 SS	EA	00	00	00	00	27,500	00	00		0			00	00	00	
PUMPS																
CENTRIF 5 m3/hr 316 SS	EA	80	00	00	80	5,000	400	80		0			00	00	400	
CENTRIF 5 m3/hr PLASTIC	EA	80	00	00	80	2,500	200	80		0			00	00	200	
DRUM EMPTYING PLASTIC	EA	50	00	00	50	170	09	50		0			00	00	09	
VACUUM LIO RING	EA	20	00	00	20	2,500	50	20		0			00	00	50	
MISC																
SACK TIP M/C	EA	20	00	00	20	1,700	34	20		0			00	00	34	
DRUM TIP M/C	EA	20	00	00	20	4,250	85	20		0			00	00	85	
FLUID BED DRYER	EA	10	00	00	10	59,500	595	10		0			00	00	595	
CENTRIFUGE (BOWL TYPE)	EA	20	00	00	20	20,000	400	20		0			00	00	400	
WEIGH SCALES	EA	20	00	00	20	1,500	30	20		0			00	00	30	
CONDENSER	EA	30	00	00	30	10,000	300	30		0			00	00	300	
STILL	EA	10	00	00	10	20,000	200	10		0			00	00	200	
INLINE FILTER	EA	30	00	00	30	1,500	45	30		0			00	00	45	
SUB TOTAL EQUIPMENT PROCUREMENT							912.3			0			00	00	912.3	
ALLOW							228.1			0			00	00	228.1	
MISC UTILITIES							45.6			0			00	00	45.6	
LAB EQUIP							59.3			0			00	00	59.3	
CIF/SHIPPING	5%									0			00	00		
CHILLER	EA	10	00	00	10	35,000	350	10		0			00	00	350	
TOTAL EQUIPMENT PROCUREMENT							1,280.2			0			00	00	1,280.2	



MINIG MULTI-PURPOSE PILOT PLANT

Appendix 10-1

INITIAL FIXED INVESTMENT COSTS

in Pesos '000

	Foreign Currency	Local Currency	Total Cost
2.1 Buildings & Civil Works			
Filling	0	5,834	5,834
Construction	0	16,640	16,640
Buildings	0	29,250	29,250
Warehouse, Offices, etc	0	42,250	42,250
Steel Supplies, Instrumentation, etc	1,359	127	1,359
Miscellaneous Sub-contracts	0	8,959	8,959
Connections to Existing Plant	0	1,950	1,950
10% Contingency Allowance	127	10,441	10,568
	1,359	114,651	116,017
2.2 Production Machinery & Equipment			
Reactors	5,005	501	5,506
Vessels	12,813	1,251	13,874
Pumps	1,711	171	1,892
Miscellaneous Items	4,331	439	4,830
Packing, Insurance & Shipping	1,185	0	1,185
10% Contingency Allowance	2,491	237	2,728
	27,397	2,603	30,006
2.3 Auxiliary Production Equipment			
Electrical, Instrumentation, etc	16,662	1,668	18,350
Capitalised Spares	1,528	153	1,679
10% Contingency Allowance	1,821	192	2,003
	19,991	2,003	22,032
2.4 Auxiliary & Service Equipment			
Miscellaneous Utilities	5,331	533	6,524
Laboratory Equipment	1,166	119	1,305
Chiller	310	31	1,001
Office Equipment & Furniture	0	390	390
Packing, Insurance & Shipping	356	0	356
10% Contingency Allowance	838	119	957
	9,291	1,312	10,533
2.5 Vehicles			
Company Cars	0	1,200	1,200
Lorry, Pick-up Truck, Fork-lift	0	1,900	1,900
10% Contingency Allowance	0	310	310
	0	3,410	3,410
<b>Total</b>	<b>58,043</b>	<b>124,185</b>	<b>182,228</b>

APPENDIX 10-1

INITIAL FIXED INVESTMENT COSTS

1. Buildings and Civil Works

- 1.1 The prices quoted are in accordance with the detailed cost estimates presented at Appendix 9-2, converted into Pesos.
- 1.2 Further provision has been made for payment of 10% customs duties on all imported items (steel supply, electrics and instrumentation installation), and for an overall 10% contingency allowance.

2. Production/Auxiliary Machinery and Equipment

- 2.1 The prices quoted are in accordance with the detailed cost estimates presented at Appendix 9-2, converted into Pesos.
- 2.2 Further provision has been made for payment of 10% customs duties on all imported items, and for an overall contingency allowance of 10%.

3. Vehicles

- 3.1 It has been assumed that the project would require the following vehicles, all of which could be purchased from local suppliers :

3 x Company Cars  
1 x 3-tonne Lorry  
1 x Pick-up Truck or Van  
1 x Fork-lift Truck

- 3.2 The prices quoted have been based on information obtained in the Philippines. Separate provision has been made for a contingency allowance of 10%, calculated by reference to the total cost estimate.

WICO MULTI-PURPOSE FIRST PLANT

Appendix 19-2

INITIAL FIXED INVESTMENT COST SCHEDULE

in Pesos (000)

Year	1993	1994	1995
1. Structures & Civil works			
- Foreign Currency	173	1,117	0
- Local Currency	10,151	21,581	0
- Total	10,324	22,698	0
2. Plant, Machinery & Equipment			
- Foreign Currency	3,404	45,243	0
- Local Currency	353	2,481	0
- Total	3,757	47,724	0
3. Total Initial Investment costs			
- Foreign Currency	3,577	46,360	0
- Local Currency	10,704	24,062	0
Total	14,281	70,422	0

APPENDIX 10-2

INITIAL FIXED INVESTMENT COST SCHEDULE

1. Buildings and Civil Works

- 1.1 It has been assumed that 20% of the cost of the structures and civil works would be incurred in 1993, and the balance of 80% upon completion of this work in 1994.

2. Production Machinery and Equipment

- 2.1 It has been assumed that the suppliers of the production machinery and equipment would require a 20% downpayment in 1993, and that the balance of the total purchase price would be payable in 1994.

3. Ancillary and Auxiliary Equipment

- 3.1 It has been assumed that the suppliers of the ancillary production equipment and of the auxiliary equipment would also require a 10% downpayment in 1993, and that the balance of the total purchase price would be payable in 1994.

4. Vehicles

- 4.1 It has been assumed that the entire cost of purchasing the vehicles required would be incurred in the final phase of project implementation in 1994, prior to the start-up of operations.



INCO MULTI-PURPOSE PILOT PLANT

Appendix 10-3

PRE-PRODUCTION EXPENDITURE SCHEDULE

in Pesos '000

Year	1993	1994	1995	1996
1. Pre-Investment Studies				
- Foreign Currency	503	0	0	0
2. Preparatory Engineering Studies				
- Foreign Currency	1,127	0	0	0
3. Management of Project Implementation				
- Foreign Currency	277	207	0	0
- Detailed Engineering Rendering				
- Foreign Currency	7,071	4,314	0	0
4. Supervision, Testing and Commissioning				
- Foreign Currency	334	3,573	0	0
- Local Currency	139	437	0	0
- Total	11,333	4,315	0	0
5. Recruitment and Staff Training				
- Foreign Currency	0	3,120	3,120	1,560
- Local Currency	0	2,947	0	0
- Total	0	6,067	3,120	1,560
6. Arrangements for Supplies				
- Local Currency	0	135	0	0
7. Arrangements for Marketing				
- Local Currency	0	65	0	0
8. Build-up of Connections				
- Local Currency	104	156	0	0
9. Capital Issue Expenditure				
- Local Currency	156	624	0	0
10. 10% Contingency Allowance				
- Foreign Currency	1,026	1,232	312	156
- Local Currency	37	432	0	0
- Total	1,063	1,664	312	156
11. Total Pre-Production Expenditure				
- Foreign Currency	11,239	13,551	3,432	1,716
- Local Currency	406	4,756	0	0
Total	11,634	18,307	3,432	1,716

## APPENDIX 10-3

### PRE-PRODUCTION EXPENDITURE SCHEDULE

#### 1. Pre-Investment and Preparatory Engineering Studies

- 1.1 It has been assumed that the entire cost of pre-investment and preliminary engineering studies would be incurred in the earliest phase of project implementation in 1993.

#### 2. Project Implementation, Supervision and Commissioning

- 2.1 It has been assumed that 20% of the cost of the management team in charge of project implementation would be incurred during 1993, and the balance of 80% during 1994. The same timing has been assumed in respect of the total combined cost of supervising the buildings and civil works, and testing and commissioning the plant and equipment.

#### 3. Detailed Engineering and Tendering

- 3.1 It has been assumed that 60% of the cost of the detailed engineering work to be undertaken would be incurred during 1993, and the balance of 40% during 1984.

#### 4. Recruitment and Staff Training

- 4.1 It has been assumed that the cost of recruiting staff and sending them for advance training overseas, as well as that of project familiarisation, would be incurred during 1994.
- 4.2 However, further provision has been made for an expatriate training expert, specialised in chemical plant operation, safety and health, to be employed for an 18-month period thereafter, and for the cost of this to be capitalised.

#### 5. Other Pre-Production Expenditure

- 5.1 It has been assumed that all preliminary expenditure in respect of arrangements for supplies and marketing would be incurred in 1994, prior to the start-up of operations.
- 5.2 It has been assumed that 40% of the cost of project and other approvals and 20% of the cost of legal and other fees related to the registration and financing of the project would be incurred in 1993, with the respective balances of 60% and 80% falling due in 1994.

UNIDU: MULTI-PURPOSE PILOT PLANT

Appendix 10-4

WORKING CAPITAL REQUIREMENTS

in Pesos mil

	Minimum Coverage Coefficient	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1. Current assets												
a) Accounts Receivable	30	1,071	1,203	1,208	1,214	1,220	1,227	1,232	1,239	1,248	1,255	
b) Inventory												
- Reported Materials	120	3,753	4,990	4,990	4,990	4,990	4,990	4,990	4,990	4,990	4,990	4,990
- Spare Parts	130	626	657	690	725	761	799	839	881	925	971	
- Work-in-Progress	30	1,351	1,684	1,690	1,695	1,701	1,708	1,714	1,721	1,729	1,736	
- Finished Products	30	5,435	6,434	5,450	6,466	6,486	6,505	6,525	6,546	6,568	6,591	
c) Cash in hand	15	1,344	1,064	944	672	553	495	484	487	491	495	
<b>Total Current assets</b>		<b>14,579</b>	<b>17,062</b>	<b>16,972</b>	<b>16,764</b>	<b>16,861</b>	<b>16,724</b>	<b>16,785</b>	<b>16,865</b>	<b>16,951</b>	<b>17,038</b>	
2. Current Liabilities												
a) Accounts Payable	30	532	1,266	1,266	1,266	1,266	1,266	1,266	1,266	1,266	1,266	
3. Working Capital												
a) Net Working Capital		13,427	15,796	15,706	15,498	15,415	15,458	15,519	15,599	15,685	15,772	
b) Increase in Working Capital		13,427	2,369	(90)	(208)	(83)	43	61	80	86	87	
4. Total Production Costs		63,468	61,230	57,624	51,107	47,515	39,833	39,549	39,633	39,721	39,814	
less: Raw Materials		11,258	14,969	14,969	14,969	14,969	14,969	14,969	14,969	14,969	14,969	
Utilities		169	224	224	224	224	224	224	224	224	224	
Depreciation		19,781	19,781	19,781	19,781	19,780	12,751	12,751	12,751	12,751	12,752	
		32,260	26,256	22,660	16,133	12,542	11,889	11,605	11,689	11,777	11,869	
5. Required Cash Balance	15	1,344	1,094	944	672	523	495	484	487	491	495	

Accounts Receivable : 30 days x operating costs (production costs minus depreciation and interests)

Work-in-Progress : 30 days x factory costs

Finished Products : 90 days x factory costs plus administrative overheads

Cash in Hand : 15 days x production costs (less raw materials, utilities and depreciation)

Accounts Payable : 30 days x raw materials and utilities

WICO MULTI-PURPOSE PLANT

Appendix 10-4

CALCULATION OF WORKING CAPITAL

in Pesos 000

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Raw Materials	11,256	14,969	14,969	14,969	14,969	14,969	14,969	14,969	14,969	14,969
Direct Labour	1,340	1,340	1,340	1,340	1,340	1,340	1,340	1,340	1,340	1,340
Utilities	169	224	224	224	224	224	224	224	224	224
Replacement Spare Parts	1,251	1,314	1,380	1,449	1,521	1,597	1,677	1,761	1,849	1,941
Repairs & Maintenance	458	663	663	663	663	663	663	663	663	663
Factory Overhead Costs	1,700	1,700	1,700	1,700	1,700	1,700	1,700	1,700	1,700	1,700
1. Total Factory Costs	16,216	20,210	20,276	20,345	20,417	20,493	20,573	20,657	20,745	20,837
Administrative Overheads	5,525	5,525	5,525	5,525	5,525	5,525	5,525	5,525	5,525	5,525
Sales & Distribution Costs	700	700	700	700	700	700	700	700	700	700
2. Operating Costs	22,441	26,435	26,501	26,570	26,642	26,718	26,798	26,882	26,970	27,062
Financial Costs	21,246	15,014	11,352	4,756	1,093	364	0	0	0	0
Depreciation	19,781	19,781	19,781	19,781	19,780	12,751	12,751	12,751	12,751	12,752
3. Total Production Costs	63,468	61,230	57,634	51,107	47,515	39,833	39,549	39,633	39,721	39,814

APPENDIX 10-4

CALCULATION OF WORKING CAPITAL

1. Calculation of Working Capital Requirement

1.1 The provisions made in respect of total current assets and current liabilities have been calculated by reference to the following minimum requirements :

Accounts Receivable : 30 days x operating costs

Inventory

- Imported Materials : 120 days x cost of materials  
- Spare Parts : 180 days x cost of spare parts  
- Work-in-Progress : 30 days x factory costs  
- Finished Products : 90 days x factory costs plus  
administrative overheads

Cash in Hand : 15 days x production costs less  
raw materials, utilities  
and depreciation

Accounts Payable : 30 days x cost of raw materials  
plus utilities

1.2 The difference between total current assets and current liabilities represents the net working capital requirement in each year.

1.3 The total initial investment costs of the project include provision for the net working capital requirement in 1996, given that the plant would then be operating at its maximum of 100% capacity utilisation.

2. Total Production Costs

2.1 The figures quoted in respect of total factory costs, administrative overheads, sales and distribution costs, financial costs and depreciation have been taken directly from the detailed production cost schedule presented at Appendix 10-8b.

UNICOM MULTIPURPOSE PROJECT PLAN

Appendix 10-5

TOTAL INVESTMENT COST SCHEDULE : 1993 - 2004

in Pesos '000

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1. Initial Investment Costs												
- Foreign Currency	8,683	49,260	"	0	0	0	0	0	0	"	0	0
- Local Currency	23,823	100,362	0	0	0	0	0	0	0	0	0	0
- Total	32,506	149,722	0	0	0	0	0	0	0	0	0	0
Replacement Investment												
- Foreign Currency	0	0	0	0	0	0	0	0	0	0	0	0
- Local Currency	0	0	0	0	0	0	0	3,410	0	0	0	0
- Total	0	0	0	0	0	0	0	3,410	0	0	0	0
2. Preproduction Expenditure												
- Foreign Currency	11,288	13,551	3,432	1,716	0	0	0	0	0	0	0	0
- Local Currency	406	4,756	0	0	0	0	0	0	0	0	0	0
- Total	11,694	18,307	3,432	1,716	0	0	0	0	0	0	0	0
3. Working Capital Increase	0	0	13,427	2,369	(90)	(208)	(83)	43	61	80	86	87
Total Investment Costs	44,200	168,029	16,859	4,085	(90)	(208)	(83)	43	61	80	86	87

APPENDIX 10-5

TOTAL INVESTMENT COST SCHEDULE

1. Initial and Replacement Investment Costs

1.1 The figures quoted in respect of initial investment costs have been taken directly from the cost schedule presented at Appendix 10-2.

1.2 It has been assumed that there would be no replacement investment in plant, machinery or equipment during the period to 2004, but that all the project vehicles would be replaced after five years.

2. Pre-Production Expenditure

2.1 The figures quoted in respect of pre-production capital expenditure have been taken directly from the expenditure schedule presented at Appendix 10-3.

3. Working Capital Increase

3.1 The figures quoted in respect of the increase in the net working capital requirement in each year have been taken directly from the working capital schedule presented at Appendix 10-4.

UNIDO MULTI-PURPOSE FLOOD PLANT

Appendix 10-b

TOTAL ASSETS SCHEDULE : 1992 - 2004

in Pesos '000

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1. Initial Investment Costs												
- Foreign Currency	6,603	49,200	0	0	0	0	0	0	0	0	0	0
- Local Currency	20,821	100,361	0	0	0	0	0	0	0	0	0	0
- Total	27,424	149,561	0	0	0	0	0	0	0	0	0	0
Replacement Investment												
- Foreign Currency	0	0	0	0	0	0	0	0	0	0	0	0
- Local Currency	0	0	0	0	0	0	0	3,410	0	0	0	0
- Total	0	0	0	0	0	0	0	3,410	0	0	0	0
2. Reproduction Expenditure												
- Foreign Currency	11,238	13,551	3,432	1,716	0	0	0	0	0	0	0	0
- Local Currency	496	4,756	0	0	0	0	0	0	0	0	0	0
- Total	11,734	18,307	3,432	1,716	0	0	0	0	0	0	0	0
3. Current Assets Increase	0	0	14,379	2,683	(90)	(208)	(83)	43	61	80	86	87
Total Assets	44,200	168,029	17,811	4,399	(90)	(208)	(83)	3,453	61	80	86	87



APPENDIX 10-6

TOTAL ASSETS SCHEDULE

1. Initial and Replacement Investment Costs

1.1 The figures quoted in respect of initial investment costs have been taken directly from the cost schedule presented at Appendix 10-2.

1.2 It has been assumed that there would be no replacement investment in plant, machinery or equipment during the period to 2004, but that all the project vehicles would be replaced after five years.

2. Pre-Production Expenditure

2.1 The figures quoted in respect of pre-production capital expenditure have been taken directly from the expenditure schedule presented at Appendix 10-3.

3. Current Assets Increase

3.1 The figures quoted in respect of the increase in current assets in each year have been calculated by reference to the working capital schedule detailed in Appendix 10-4.

3.2 The total initial assets of the project include provision for the total current assets figure in 1996, given that the plant would then be operating at 100% capacity utilisation.



APPENDIX 10-7

INITIAL FINANCING PLAN

1. Equity Subscription

1.1 It has been assumed that both the local promoters and those financial institutions invited to participate in the project would subscribe for their shares in full during 1993, and would therefore take up their respective shareholdings of 60% and 40% at the outset.

1.2 It may be noted that this would ensure that the project had sufficient funds in hand to cover anticipated expenditure on all investment items, both local and imported, during the first half of the implementation phase.

2. Foreign Currency Loans

2.1 It has been assumed that the foreign currency loans would be drawdown in two tranches as follows :

1994	:	P 35,994,000	=	79.0%
1995	:	P 9,548,000	=	21.0%
		<hr/>		
		P 45,542,000		
		<hr/>		

3. Local Currency Loans

3.1 It has been assumed that the local currency loans would be drawdown in two tranches as follows :

1994	:	P 59,015,000	=	83.8%
1995	:	P 11,396,000	=	16.2%
		<hr/>		
		P 70,411,000		
		<hr/>		

4. Current Liabilities

4.1 The figures quoted in respect of the increase in current liabilities in each year have been calculated by reference to the working capital schedule detailed in Appendix 10-4.

UNION MULTI-PURPOSE COAST FISH

Appendix I-100a

PRODUCTION COST SCHEDULE

in Pesos 000

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1. Direct Materials & Inputs	11,427	15,197	15,193	15,193	15,197	15,197	15,193	15,197	15,193	15,193
2. Direct Manpower	1,340	1,340	1,340	1,340	1,340	1,340	1,340	1,340	1,340	1,340
3. Factory Overheads	2,449	3,671	3,743	3,812	3,684	3,960	4,040	4,124	4,212	4,304
<b>Factory Costs</b>	<b>15,216</b>	<b>20,210</b>	<b>20,276</b>	<b>20,345</b>	<b>20,417</b>	<b>20,497</b>	<b>20,573</b>	<b>20,657</b>	<b>20,745</b>	<b>20,837</b>
4. Administrative Overheads	5,525	5,525	5,525	5,525	5,525	5,525	5,525	5,525	5,525	5,525
5. Sales & Distribution Costs	700	700	700	700	700	700	700	700	700	700
<b>Operating Costs</b>	<b>21,441</b>	<b>26,435</b>	<b>26,501</b>	<b>26,570</b>	<b>26,642</b>	<b>26,718</b>	<b>26,798</b>	<b>26,882</b>	<b>26,970</b>	<b>27,062</b>
6. Financial Costs	21,248	15,014	11,352	4,750	1,093	364	"	0	0	0
7. Depreciation	19,781	19,781	19,781	19,781	19,780	12,751	12,751	12,751	12,751	12,752
<b>Total Production Cost</b>	<b>63,468</b>	<b>61,230</b>	<b>57,634</b>	<b>51,107</b>	<b>47,515</b>	<b>39,833</b>	<b>39,549</b>	<b>39,633</b>	<b>39,721</b>	<b>39,814</b>



DETAILED PRODUCTION COST SCHEDULE (continued)

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
5. Sales & Distribution Costs										
Manpower	220	220	220	220	220	220	220	220	220	220
Product Promotion	300	300	300	300	300	300	300	300	300	300
Travel	180	180	180	180	180	180	180	180	180	180
	700	700	700	700	700	700	700	700	700	700
6. Financial Costs										
Foreign Currency Loans	3,643	3,279	2,550	1,822	1,093	364	0	0	0	0
Local Currency Loans	17,693	11,735	8,802	2,934	0	0	0	0	0	0
	21,336	15,014	11,352	4,756	1,093	364	0	0	0	0
7. Depreciation										
Buildings	5,812	5,812	5,812	5,812	5,812	5,812	5,812	5,812	5,812	5,812
Plant, Machinery & Equipment	6,257	6,257	6,257	6,257	6,257	6,257	6,257	6,257	6,257	6,258
Vehicles	682	682	682	682	682	682	682	682	682	682
Intangibles	7,030	7,030	7,030	7,030	7,029	0	0	0	0	0
	19,781	19,781	19,781	19,781	19,780	12,751	12,751	12,751	12,751	12,752
Total Production Cost	63,468	61,230	57,634	51,107	47,515	39,833	39,549	39,633	39,721	39,814

APPENDIX 10-8

PRODUCTION COST SCHEDULE

1. Direct Materials and Inputs

1.1 Expenditure on raw material inputs has been calculated by reference to the detailed production schedule presented at Appendix 3-10, and the following usage and cost figures :

Ethanbutol Hydrochloride

	kg/batch *	cost/tonne
Production Materials		
- 2 Amino 1 Butanol	77	\$ 2,304
- Dichloroethane	285	\$ 430
- Methanol	850	\$ 133
- Caustic Soda - 50% solution	470	\$ 420
- Ethanol	650	\$ 511
- Petroleum Ether	400	\$ 337

\* production per batch = 100 kg (net)

Ibuprofen

	kg/batch *	cost/tonne
Production Materials		
- i Butyl Benzene	89	\$ 4,560
- Aluminium Chloride	87	\$ 538
- Carbon Disulphide	20	\$ 504
- Acetic Acid	42	\$ 888
- Sulphuric Acid - concentrate	200	\$ 102
- Propylene Oxide	77	\$ 1,546
- Sodium Dichlorate	212	\$ 2,957

\* production per batch = 100 kg (net)

Isoniazid

	kg/batch *	cost/tonne
Production Materials		
- 4 Cyanopyridine	125	\$ 6,828
- Hydrazine Hydrate	125	\$ 3,360
- Sodium Hydroxide	2.5	\$ 420

\* production per batch = 100 kg (net)

Mefenamic Acid

	kg/batch *	cost/tonne
Production Materials		
- Potassium o Bromo Benzoate	178	\$ 5,016
- Bis 2 Methoxyethylether	335	\$ 2,280
- N-Methyl Morpholine	80	\$ 4,008
- Dimethylaniline	84	\$ 2,640
- Cupric Acetate	6.7	\$ 7,714
- Hydrochloric Acid - concentrate	58	\$ 114

\* production per batch = 100 kg (net)

Paracetamol

	kg/batch *	cost/tonne
<b>Production Materials</b>		
- Sodium Sulphite	1.2	\$ 662
- P Aminophenol	257	\$ 6,300
- Acetic Acid	150	\$ 888
- Acetic Anhydride	270	\$ 1,277
- Sodium Thiosulphate	1.2	\$ 1,222

\* production per batch = 260 kg (net)

1.2 It may be noted that all raw material costs are quoted per tonne of active ingredient, delivered to the factory site, and include provision for payment of 3% customs duties.

1.3 Expenditure on utilities has been calculated by reference to the detailed production schedule presented at Appendix 3-10, and the following usage and cost figures :

Ethambutol

	per batch	cost/unit
<b>Utilities</b>		
- Steam	0.12 tonnes	P 600
- Power	110 Kwh	P 2.22
- Water	6.40 cu.metres	P 3.17

Cost per 100 kg batch : P 336

Ibuprofen

	per batch	cost/unit
<b>Utilities</b>		
- Steam	0.12 tonnes	P 600
- Power	125 Kwh	P 2.22
- Water	6.40 cu.metres	P 3.17

Cost per 100 kg batch : P 1,036

Isoniazid

	per batch	cost/unit
<b>Utilities</b>		
- Steam	0.16 tonnes	P 600
- Power	270 Kwh	P 2.22
- Water	2.60 cu.metres	P 3.17

Cost per 100 kg batch : P 704

Mefenamic Acid

	per batch	cost/unit
<b>Utilities</b>		
- Steam	0.04 tonnes	P 600
- Power	165 Kwh	P 2.22
- Water	2.10 cu.metres	P 3.17

Cost per 100 kg batch : P 397



**Paracetamol**

	per batch	cost/unit
Utilities		
- Steam	0.08 tonnes	P 600
- Power	105 Kwh	P 2.22
- Water	3.80 cu.metres	P 3.17

Cost per 260 kg batch : P 293

2. **Direct Manpower**

2.1 The wage and salary cost of the production staff employed in the factory has been estimated at a total of P 1.34 million per annum. This figure may be broken down as follows :

	Number	Salary	Annual Cost
Direct Production Staff			
- Process Superintendents	3	180,000	540,000
- Technicians/Operators	6	120,000	720,000
- Unskilled Labour	2	40,000	80,000
	—		—
Total	11		1,340,000
	—		—

3. **Factory Overheads**

3.1 The wage and salary cost of the laboratory and engineering staff employed in the factory has been estimated at a total of P 1.5 million per annum. This figure may be broken down as follows :

	Number	Salary	Annual Cost
Laboratory/Engineering Staff			
- Maintenance Foreman	1	180,000	180,000
- Warehouse Foremen	3	120,000	360,000
- Chemists	6	120,000	720,000
- Maintenance Technicians	3	80,000	240,000
	—		—
Total	13		1,500,000
	—		—

3.2 The provision made for the importation of replacement spare parts has been calculated at 2% of the initial value of the production and auxiliary machinery and equipment to be installed in the factory. However, this figure has then been projected to rise at a compound growth rate of 5% per annum to cover the expected increase in servicing needs over time.

3.3 The provision made for repairs and maintenance has been calculated at the rate of 3% by reference to projected sales revenues in each year.

3.4 Additional provision has been made for annual expenditures totalling P 200,000 on protective clothing and sundry other consumables such as cleaning materials, lubricants and loose tools used within the factory complex.

4. Administrative Overheads

4.1 The wage and salary cost of the senior management team and the administration and other personnel employed has been estimated at a total of P 2.56 million per annum. This figure may be broken down as follows :

	Number	Salary	Annual Cost
<b>Senior Management</b>			
- General Manager	1	500,000	500,000
- Chemical Engineers	2	250,000	500,000
- Chemists	2	250,000	500,000
- Administration/Training	2	250,000	500,000
<b>Administration/Other Personnel</b>			
- Accounts Officer	1	120,000	120,000
- Storekeepers	3	60,000	180,000
- Secretary	1	60,000	60,000
- Clerical Staff	4	40,000	160,000
- Driver	1	40,000	40,000
Total	17		2,560,000

4.2 The cost of insuring the factory and other buildings, plus all the plant, machinery and equipment installed therein and the project vehicles, against fire, theft and accidental damage has been estimated at 1% of the initial value of the assets. The figure quoted of approximately P 1.8 million should also include the cost of providing accident cover for the workforce.

4.3 Various provisions totalling just under P 0.9 million have been specified to cover annual expenditures on office supplies, communications, land/property charges, licences, fees and travel/transport.

4.4 Finally, provision has been made for what is, in effect, a contingency allowance, calculated at 5% of total overhead costs, to cover those items which have not been separately specified (such as donations, entertainment, staff medical and canteen expenses and the like).

5. Sales and Distribution Costs

5.1 The wage and salary cost of those directly involved in marketing has been estimated at a total of P 220,000 per annum, broken down as follows :

	Number	Salary	Annual Cost
- Sales Liaison Officer	1	180,000	180,000
- Driver	1	40,000	40,000
			<hr/>
			220,000
			<hr/>

5.2 The figures quoted in respect of product promotion, travel and transport have been taken directly from Section 3.7.2.

6. Financial Costs

6.1 It has been assumed that the foreign currency loans would be made available on the basis of the following terms and conditions :

Loan Amount : P 45,542,000, equivalent to just over \$ 1.75 million.  
Loan Term : 6 years, inclusive of a grace period of one year.  
Loan Drawdown : final tranche drawn by mid-1995.  
Interest Rate : 8% per annum, payable on the balance outstanding.  
Repayment : in five equal annual instalments, commencing one year after final drawdown (that is, by mid-1996).

6.2 It has been assumed that the local currency loans would be made available on the basis of the following terms and conditions :

Loan Amount : P 70,411,000, equivalent to just over \$ 2.7 million.  
Loan Term : 4 years, inclusive of a grace period of one year.  
Loan Drawdown : final tranche drawn by mid-1995.  
Interest Rate : 25% per annum, payable on the balance outstanding.  
Repayment : in three equal annual instalments, commencing one year after drawdown (that is, by mid-1996).

7. Depreciation

7.1 Depreciation in respect of the proposed investment has been calculated on a straight line basis in accordance with the following rates :

Buildings and Civil Works	:	5%
Production Equipment	:	10%
Ancillary Production Equipment	:	10%
Auxiliary Equipment	:	10%
Vehicles	:	20%
Intangibles *	:	20%

\* pre-production capital expenditure

## UNIDO MULTI-PURPOSE FLEET FUND

Appendix 10-9

## NET INCOME STATEMENT

in Pesos 000

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1. Sales Revenues	16,595	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114
2. Operating Costs	22,441	26,435	26,501	26,570	26,642	26,718	26,798	26,882	26,970	27,062
3. Operating Profit/(Loss)	(5,846)	(4,321)	(4,387)	(4,456)	(4,528)	(4,604)	(4,684)	(4,766)	(4,856)	(4,948)
4. Financial Costs	21,246	15,014	11,352	4,756	1,093	364	0	0	0	0
5. Depreciation	19,781	19,781	19,781	19,781	19,780	12,751	12,751	12,751	12,751	12,752
6. Gross Profit/(Loss) before Tax	(46,873)	(39,116)	(35,520)	(28,993)	(25,401)	(17,719)	(17,435)	(17,519)	(17,607)	(17,700)
7. Corporate Taxation	0	0	0	0	0	0	0	0	0	0
8. Net Profit/(Loss)	(46,873)	(39,116)	(35,520)	(28,993)	(25,401)	(17,719)	(17,435)	(17,519)	(17,607)	(17,700)
9. Dividends	0	0	0	0	0	0	0	0	0	0
10. Retained Profits	(46,873)	(39,116)	(35,520)	(28,993)	(25,401)	(17,719)	(17,435)	(17,519)	(17,607)	(17,700)
11. Revenue Reserves	(46,873)	(85,989)	(121,509)	(156,502)	(175,903)	(193,622)	(211,057)	(228,576)	(246,183)	(263,883)
Gross Profit : Sales	-282.5%	-176.9%	-160.6%	-131.1%	-114.9%	-80.1%	-78.6%	-79.2%	-79.6%	-80.0%
Net Profit : Equity	-40.0%	-33.4%	-30.3%	-24.7%	-21.7%	-15.1%	-14.9%	-14.9%	-15.0%	-15.1%

APPENDIX 10-9

NET INCOME STATEMENT

1. Sales Revenues

1.1 The figures quoted in respect of sales revenues have been calculated by reference to forecast sales and the prices assumed for individual products, as detailed in Sections 3.4.4.10 and 3.6.2.2 respectively.

1.2 Provision has been made for all sales to be limited to 75% in 1995 only, in order to take account of any shortfall in production during the first year of operation.

2. Operating Costs, Financial Costs and Depreciation

2.1 The figures quoted in respect of operating costs, financial costs and depreciation have all been taken directly from the production cost schedule presented at Appendix 10-8a.

3. Taxation

3.1 It has been assumed that the project would be successful in negotiating an initial tax holiday of six years from the commencement of commercial operations.

3.2 However, the extent of the losses anticipated over this period is such that, in effect, this tax exemption becomes immaterial.

4. Dividends

4.1 Given the magnitude of the losses anticipated, the project would not be in a position to declare dividends throughout the period under review.

5. Revenue Reserves

5.1 The revenue reserves reflect the accumulated loss position of the project, and the changes thereto, as reflected in the income statement and final loss figure for each year.

## UNICO MULTI-PURPOSE PILOT PLANT

Appendix 10-10

## CASH FLOW TABLE FOR FINANCIAL PLANNING

in Pesos '000

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
<b>CASH INFLOW</b>	117,220	95,009	28,491	22,428	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114
1. Financial Resources	117,220	95,009	21,896	714	0	0	0	0	0	0	0	0
2. Sales Revenues	0	0	16,595	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114
<b>CASH OUTFLOW</b>	(44,200)	(168,029)	(61,498)	(70,426)	(70,341)	(63,697)	(36,760)	(39,645)	(26,859)	(26,962)	(27,056)	(27,149)
1. Total Assets Schedule	(44,200)	(168,029)	(17,811)	(4,399)	90	208	83	(3,453)	(61)	(80)	(86)	(87)
2. Operating Costs	0	0	(22,441)	(26,435)	(26,501)	(26,570)	(26,642)	(26,718)	(26,798)	(26,882)	(26,970)	(27,062)
3. Debt Service: Interest												
- Foreign Currency Loans	0	0	(3,643)	(3,279)	(2,550)	(1,822)	(1,093)	(344)	0	0	0	0
- Local Currency Loans	0	0	(17,603)	(11,735)	(8,802)	(2,934)	0	0	0	0	0	0
Debt Service: Repayments												
- Foreign Loan	0	0	0	(9,108)	(9,108)	(9,108)	(9,108)	(9,110)	0	0	0	0
- Local Loan	0	0	0	(23,470)	(23,470)	(23,471)	0	0	0	0	0	0
4. Corporate Tax	0	0	0	0	0	0	0	0	0	0	0	0
5. Dividends	0	0	0	0	0	0	0	0	0	0	0	0
<b>SURPLUS/(DEFICIT)</b>	73,020	(73,020)	(23,007)	(55,998)	(48,227)	(41,583)	(14,646)	(17,531)	(4,745)	(4,848)	(4,942)	(5,035)
<b>CUMULATIVE CASH SHORTFALL</b>	73,020	0	(23,007)	(79,005)	(127,232)	(168,815)	(183,461)	(200,992)	(205,737)	(210,585)	(215,527)	(220,562)

**APPENDIX 10-10**

**CASH FLOW TABLE FOR FINANCIAL PLANNING**

**1. Cash Inflow**

- 1.1 The figures quoted in respect of financial resources have been taken directly from the initial financing plan detailed in Appendix 10-7, and reflect the sum of the subscription for equity in the project, the foreign and local currency loans drawdown and the increase in current liabilities in each year.
- 1.2 The figures quoted in respect of sales revenues have been taken directly from the net income statement presented at Appendix 10-9.

**2. Cash Outflow**

- 2.1 The figures quoted in respect of total assets have been taken directly from the total assets schedule detailed in Appendix 10-6, and reflect the sum of the initial investment costs, pre-production capital expenditures and the increase in current assets in each year.
- 2.2 The figures quoted in respect of operating costs have been taken directly from the net income statement presented at Appendix 10-9.
- 2.3 The figures quoted in respect of debt service have been calculated on the basis of the terms and conditions assumed for the foreign and local currency loans, as respectively detailed in sections 6.1 and 6.2 of Appendix 10-9 :

**Foreign Currency Loans**

Interest Rate : 8% per annum, payable on the balance outstanding.

Repayment : in five equal annual instalments, commencing one year after final drawdown (that is, by mid-1996).

**Local Currency Loans**

Interest Rate : 25% per annum, payable on the balance outstanding.

Repayment : in three equal annual instalments, commencing one year after drawdown (that is, by mid-1996).

- 2.4 Neither taxation nor dividends would be payable throughout the period under review.



## UNIGO MULTI-PURPOSE FLEET FLEET

Appendix 10-11

## PROJECTED BALANCE SHEET

in Pesos 000

Year	1992	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
<b>ASSETS</b>	117,220	212,229	210,259	194,877	175,006	155,017	135,154	125,856	113,166	100,495	87,830	75,165
1. Fixed Assets												
- Buildings	23,249	110,247	110,435	104,023	99,811	92,499	87,187	81,275	75,563	69,751	63,929	58,127
- Plant & Machinery	9,257	65,571	56,314	50,057	43,800	37,543	31,286	25,019	18,772	12,515	6,258	0
- Vehicles	0	3,410	2,728	2,046	1,364	682	0	0	0	0	0	0
- Intangibles	11,294	20,001	26,463	21,089	14,059	7,029	0	0	0	0	0	0
	44,200	212,229	195,000	177,015	158,034	138,151	118,473	109,172	96,361	83,630	70,879	58,127
2. Current Assets												
- Accounts Receivable	0	0	1,879	2,203	2,298	2,214	2,220	2,227	2,233	2,240	2,248	2,255
- Inventory	0	0	11,165	12,765	13,820	13,878	13,938	14,002	14,068	14,138	14,212	14,288
- Cash on Hand	0	0	1,344	1,094	944	672	523	495	484	467	491	495
- Cash Balance	73,020	0	0	0	0	0	0	0	0	0	0	0
	73,020	0	14,379	17,062	16,972	16,784	16,681	16,724	16,785	16,665	16,951	17,038
<b>LIABILITIES</b>	117,220	212,229	210,259	194,877	175,006	155,017	135,154	125,856	113,166	100,495	87,830	75,165
1. Equity Capital	117,220	117,220	117,220	117,220	117,220	117,220	117,220	117,220	117,220	117,220	117,220	117,220
2. Revenue Reserves	0	0	(46,873)	(85,989)	(121,509)	(150,502)	(175,903)	(193,622)	(211,057)	(228,576)	(246,183)	(263,883)
3. Term Borrowings												
- Foreign Currency Loan	0	35,994	45,542	36,434	27,326	18,218	9,110	0	0	0	0	0
- Local Currency Loan	0	59,015	70,411	46,941	23,471	0	0	0	0	0	0	0
	0	95,009	115,953	83,375	50,797	18,218	9,110	0	0	0	0	0
4. Current Liabilities												
- Accounts Payable	0	0	952	1,266	1,266	1,266	1,266	1,266	1,266	1,266	1,266	1,266
- Cash Shortfall	0	0	23,007	79,005	127,232	168,815	183,461	200,992	205,737	210,385	215,527	220,562
	0	0	23,959	80,271	128,498	170,081	184,727	202,258	207,003	211,651	216,793	221,828

## APPENDIX 10-11

### PROJECTED BALANCE SHEET

#### 1. Assets

- 1.1 The figures quoted in respect of fixed assets reflect the value of the project investment by individual category, net of depreciation calculated at the rates specified in section 7.1 of Appendix 10-9.
- 1.2 The figures quoted in respect of accounts receivable, total inventory and cash in hand have been taken directly from the schedule detailing the working capital requirement in each year presented at Appendix 10-4.
- 1.3 For the purpose of the financial projections, it has been assumed that all cash surpluses reflected in the cash flow table at Appendix 10-10 would be retained as cash balances.

#### 2. Liabilities

- 2.1 It has been assumed that there would be no change in the shareholding structure and, more specifically, no further increase in the issued and paid-up share capital to that detailed in the initial financing plan.
- 2.2 The figures quoted in respect of revenue reserves have been taken directly from the net income statement presented at Appendix 10-9, and reflect the accumulated loss position of the project.
- 2.3 Provision has been made for the foreign and local currency loans to be drawdown as per the initial financing plan detailed in Appendix 10-7, and to be repaid as specified in the cash flow table at Appendix 10-10.
- 2.4 The figures quoted in respect of accounts payable have been taken directly from the schedule detailing the working capital requirement in each year set out in Appendix 10-4.
- 2.5 The figures quoted in respect of the cash shortfall have been taken directly from the cash flow table presented at Appendix 10-10, and reflect the accumulated cash deficits of the project.

UNION MULTI-PURPOSE FLOOD PLANT

Appendix 10-12

CASH FLOW TABLE : TOTAL INVESTMENT

in Pesos '000

Year	1	2	3	4	5	6	7	8	9	10	
<b>CASH INFLOWS</b>											
1. Sales Revenues	0	16,595	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114
<b>CASH OUTFLOWS</b>											
1. Total Investment Outlay	(212,229)	(16,859)	(4,665)	0	268	83	(43)	(61)	(80)	(86)	(87)
2. Residual Value of Assets	0	0	0	0	0	0	0	0	0	0	58,127
3. Operating Costs	0	(22,441)	(26,455)	(26,501)	(26,570)	(26,642)	(26,718)	(26,798)	(26,862)	(26,970)	(27,062)
4. Corporate Tax	0	0	0	0	0	0	0	0	0	0	0
<b>NET CASH FLOW</b>	<b>(212,229)</b>	<b>(22,705)</b>	<b>(8,406)</b>	<b>(4,297)</b>	<b>(4,248)</b>	<b>(4,445)</b>	<b>(4,647)</b>	<b>(4,745)</b>	<b>(4,848)</b>	<b>(4,942)</b>	<b>53,092</b>
Internal Rate of Return	-17.5%										
Net Present Value @ 18%	(203,159)										
Net Present Value @ 15%	(208,219)										
Cumulative Net Cash Flow	(212,229)	(234,934)	(243,340)	(247,637)	(251,885)	(256,330)	(260,977)	(265,722)	(270,570)	(275,512)	(222,420)
Pay-Back Period											

UNIDO MULTI-PURPOSE PILOT PLANT

Appendix 10-12

CASH FLOW STATEMENT: EQUITY CAPITAL

in Pesos 000

Year	0	1	2	3	4	5	6	7	8	9	10
<b>CASH INFLOWS</b>											
1. Sales Revenues	0	16,545	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114	22,114
<b>CASH OUTFLOWS</b>											
1. Equity Subscription	(117,220)	0	0	0	0	0	0	0	0	0	0
2. Replacement Investment	0	0	0	0	0	0	(3,410)	0	0	0	0
3. Residual Value of Assets	0	0	0	0	0	0	0	0	0	0	58,127
4. Debt Service: Repayments	0	0	(9,108)	(9,108)	(9,108)	(9,108)	(9,110)	0	0	0	0
- Forex Loan	0	0	(9,108)	(9,108)	(9,108)	(9,108)	(9,110)	0	0	0	0
- Local Loan	0	0	(23,470)	(23,470)	(23,471)	0	0	0	0	0	0
5. Debt Service: Interest	0	0	0	0	0	0	0	0	0	0	0
- Forex Loan	0	(3,643)	(3,279)	(2,550)	(1,822)	(1,093)	(364)	0	0	0	0
- Local Loan	0	(17,603)	(11,735)	(8,802)	(2,934)	0	0	0	0	0	0
6. Operating Costs	0	(22,441)	(26,435)	(26,501)	(26,570)	(26,642)	(26,718)	(26,798)	(26,882)	(26,970)	(27,062)
7. Corporate Tax	0	0	0	0	0	0	0	0	0	0	0
<b>NET CASH FLOW</b>	<b>(117,220)</b>	<b>(27,092)</b>	<b>(51,913)</b>	<b>(48,317)</b>	<b>(41,791)</b>	<b>(14,729)</b>	<b>(17,488)</b>	<b>(4,684)</b>	<b>(4,768)</b>	<b>(4,856)</b>	<b>53,179</b>
Internal Rate of Return	-22.9%										
Net Present Value @ 18%	(199,165)										
Net Present Value @ 15%	(210,551)										

## APPENDIX 10-12

### CASH FLOW TABLES

#### 1. Total Investment

- 1.1 The figures quoted in respect of sales revenues, operating costs and corporate taxation have been taken directly from the net income statement presented at Appendix 10-9.
- 1.2 The figures quoted in respect of the total investment outlay have been taken directly from the schedule presented at Appendix 10-5, and reflect the sum of the initial investment costs, pre-production capital expenditures and the increase in working capital requirements in each year. For the purpose of these calculations, the investment outlay in the project implementation phase has been combined as one total.
- 1.3 The residual value of the assets reflects the total book value of the fixed assets of the project in 2004, as per the projected balance sheet presented at Appendix 10-11.

#### 2. Equity Capital

- 2.1 The figures quoted in respect of sales revenues, operating costs and corporate taxation have been taken directly from the net income statement presented at Appendix 10-9.
- 2.2 The figures quoted in respect of equity subscription have been taken directly from the initial financing plan set out in Appendix 10-7.
- 2.3 It has been assumed that there would be no replacement investment in plant, machinery or equipment during the the period under review, but that all the project vehicles would be replaced in the year 2000.
- 2.4 The residual value of the assets reflects the total book value of the fixed assets of the project in 1999, as per the projected balance sheet presented at Appendix 10-11.
- 2.5 The figures quoted in respect of debt service (repayments and interest) have all been taken directly from the cash flow table for financial planning which is presented at Appendix 10-10.

SENSITIVITY ANALYSIS III

UNIGLO MULTI-PURPOSE FILM COMPANY

NET INCOME STATEMENT

in Pesos 000

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1. Sales Revenues	33,000	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761
2. Operating Costs	21,355	25,312	25,312	25,478	25,526	25,599	25,665	25,735	25,808	
3. Operating Profit (Loss)	11,645	19,449	19,449	19,283	19,235	19,162	19,096	19,026	18,953	
4. Financial Costs	21,158	14,972	11,296	4,232	1,091	384	"	"	0	0
5. Depreciation	19,719	19,719	19,719	19,719	12,751	12,751	12,751	12,751	12,751	12,752
6. Gross Profit (Loss) before Tax	(28,555)	(15,202)	(11,612)	(5,110)	(1,525)	6,110	6,411	6,345	6,275	6,201
7. Corporate Taxation	0	0	0	0	0	0	2,244	2,221	2,196	2,176
8. Net Profit (Loss)	(28,555)	(15,202)	(11,612)	(5,110)	(1,525)	6,110	4,167	4,124	4,079	4,025
9. Dividends	0	0	0	0	0	0	0	0	0	0
10. Retained Profits	(28,555)	(15,202)	(11,612)	(5,110)	(1,525)	6,110	4,167	4,124	4,079	4,025
11. Revenue Reserves	(28,555)	(43,756)	(55,368)	(60,477)	(62,003)	(55,892)	(51,725)	(47,601)	(43,521)	(39,490)

Gross Profit : Sales	-84.8%	-34.0%	-25.9%	-11.4%	-3.4%	13.7%	14.3%	14.2%	14.0%	13.9%
Net Profit : Sales	-84.8%	-34.0%	-25.9%	-11.4%	-3.4%	13.7%	9.3%	9.2%	9.1%	9.0%
Net Profit : Equit.	-24.5%	-13.0%	-10.0%	-4.4%	-1.3%	5.3%	3.6%	3.5%	3.5%	3.5%

UNITED MULTI-PURPOSE FLOUT PLAN

SENSITIVITY ANALYSIS III

Appendix 10-13

CASH FLOW TABLE FOR FINANCIAL PLANNING

in Pesos 000

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
CASH INFLOW	110,021	45,200	54,706	45,001	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761
1. Financial Resources	110,021	45,200	21,021	300	0	0	0	0	0	0	0	0
2. Sales Revenues	0	0	33,685	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761
CASH OUTFLOW	(44,200)	(167,721)	(59,543)	(76,953)	(63,962)	(62,382)	(35,560)	(36,425)	(27,889)	(27,949)	(27,999)	(28,047)
1. Total assets Schedule	(44,200)	(167,721)	(17,022)	(4,299)	102	221	97	(3,437)	(46)	(63)	(68)	(69)
2. Operating Costs	0	0	(21,395)	(25,312)	(25,364)	(25,419)	(25,476)	(25,530)	(25,599)	(25,665)	(25,735)	(25,808)
3. Debt Service : Interest	0	0	13,636	(3,272)	(2,545)	(1,818)	(1,091)	(264)	0	0	0	0
- Foreign Currency Loans	0	0	(17,490)	(11,660)	(8,745)	(2,915)	0	0	0	0	0	0
- Local Currency Loans	0	0	0	0	0	0	0	0	0	0	0	0
Debt Service : Repayments	0	0	0	0	0	0	0	0	0	0	0	0
- Forex Loan	0	0	0	(9,090)	(9,090)	(9,090)	(9,090)	(9,088)	0	0	0	0
- Local Loan	0	0	0	(23,320)	(23,320)	(23,321)	0	0	0	0	0	0
4. Corporate Tax	0	0	0	0	0	0	0	(2,244)	(2,221)	(2,196)	(2,170)	0
5. Dividends	0	0	0	0	0	0	0	0	0	0	0	0
SURPLUS/(DEFICIT)	72,421	(72,421)	(4,836)	(31,892)	(24,201)	(17,581)	9,201	6,336	16,872	16,812	16,762	16,714
CUMULATIVE CASH SHORTFALL	72,421	0	(4,836)	(36,728)	(60,929)	(78,509)	(69,308)	(62,971)	(46,099)	(29,287)	(12,524)	4,190





UNIGO MULTI-PURPOSE FLEET PLANT

SENSITIVITY ANALYSIS III

Appendix 10-13

CASH FLOW TABLE: TOTAL INVESTMENT

in Pesos '000

Year	1	2	3	4	5	6	7	8	9	10	
<b>CASH INFLOWS</b>											
1. Sales Revenues	33,685	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761	44,761	
<b>CASH OUTFLOWS</b>											
1. Total Investment Outlay	(211,921)	(16,110)	(3,999)	162	221	93	(27)	(46)	(63)	(68)	
2. Residual Value of Assets	0	0	0	0	0	0	0	0	0	58,127	
3. Operating Costs	(21,395)	(25,312)	(25,364)	(25,419)	(25,476)	(25,536)	(25,599)	(25,665)	(25,735)	(25,808)	
4. Corporate Tax	0	0	0	0	0	0	(2,244)	(2,221)	(2,196)	(2,170)	
<b>NET CASH FLOW</b>	<b>(211,921)</b>	<b>(3,826)</b>	<b>15,450</b>	<b>19,499</b>	<b>19,563</b>	<b>19,382</b>	<b>19,198</b>	<b>16,872</b>	<b>16,812</b>	<b>16,762</b>	<b>74,841</b>
Internal Rate of Return	0.2%										
Net Present Value @ 10%	(117,518)										
Net Present Value @ 15%	(110,011)										
Cumulative Net Cash Flow	(211,921)	(215,740)	(200,290)	(180,791)	(161,227)	(141,845)	(122,646)	(105,774)	(88,962)	(72,199)	2,642
Pay-Back Period	9.5 years										

JUNCO MULTIPURPOSE FLEET FUND

CASH FLOW TABLE - EQUITY CAPITAL

SENSITIVITY ANALYSIS III

appendix 10-13

16 Pesos mil

Year	1	2	3	4	5	6	7	8	9	10
<b>CASH INFLOWS</b>										
1. Sales Revenues	0	33,885	44,011	44,761	44,761	44,011	44,761	44,761	44,761	44,761
<b>CASH OUTFLOWS</b>										
1. Equity subscription	(116,621)	(142,521)	(2,654)	(9,064)	(21,165)	(36,398)	(27,843)	(27,866)	(27,931)	30,149
2. Replacement Investment	0	0	0	0	0	(3,410)	0	0	0	0
3. residual Value of assets	0	0	0	0	0	0	0	0	0	58,127
4. Debt Service - Repayments	0	(9,090)	(9,090)	(9,090)	(9,090)	(9,088)	0	0	0	0
- Foreign Loan	0	(23,320)	(23,320)	(23,321)	0	0	0	0	0	0
- Local Loan	0	0	0	0	0	0	0	0	0	0
5. Debt Service : Interest	0	(3,636)	(3,272)	(2,545)	(1,818)	(1,091)	(364)	0	0	0
- Foreign Loan	0	(17,490)	(11,666)	(8,745)	(2,915)	0	0	0	0	0
- Local Loan	0	0	0	0	0	0	0	0	0	0
6. Operating Costs	0	(21,355)	(25,312)	(25,344)	(25,419)	(25,476)	(25,536)	(25,594)	(25,665)	(25,735)
7. Corporate Tax	0	0	0	0	0	0	(2,344)	(2,221)	(2,196)	(2,170)
<b>NET CASH FLOW</b>										
	(116,621)	(8,836)	(27,692)	(24,303)	(17,862)	9,104	6,363	16,918	16,875	16,810
<b>Internal Rate of Return</b>	-6.12									
<b>Net Present Value @ 18%</b>	(113,449)									
<b>Net Present Value @ 15%</b>	(112,258)									

in Pesos 000

	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954
1. Sales Revenues	27,876	26,503	26,467	26,827	26,933	26,993	26,993	26,993	26,993	26,993
2. Operating Costs	24,100	23,811	23,600	23,430	23,618	23,674	23,674	23,674	23,674	23,674
3. Operating Profit (Loss)	3,776	2,692	2,867	3,397	3,315	3,319	3,319	3,319	3,319	3,319
4. Financial Costs	14,000	10,500	10,000	10,000	10,000	10,000	10,000	10,000	10,000	10,000
5. Extraordinary	1,458	1,458	1,458	1,458	1,458	1,458	1,458	1,458	1,458	1,458
6. Total Profit (Loss) Before Tax	11,326	10,342	10,317	11,407	11,315	11,319	11,319	11,319	11,319	11,319
7. Corporate Income Tax	2,622	2,622	2,622	2,622	2,622	2,622	2,622	2,622	2,622	2,622
8. Net Profit (Loss)	8,704	7,720	7,695	8,785	8,693	8,697	8,697	8,697	8,697	8,697
9. Dividends	0	0	0	0	0	0	0	0	0	0
10. Retained Profits	8,704	7,720	7,695	8,785	8,693	8,697	8,697	8,697	8,697	8,697
11. Revenue Reserves	0	0	0	0	0	0	0	0	0	0
Gross Profit - Sales	3,776	2,692	2,867	3,397	3,315	3,319	3,319	3,319	3,319	3,319
Net Profit - Sales	8,704	7,720	7,695	8,785	8,693	8,697	8,697	8,697	8,697	8,697
Net Profit - Equity	8,704	7,720	7,695	8,785	8,693	8,697	8,697	8,697	8,697	8,697

UNITED STATES AIR FORCE

FINANCIAL STATEMENTS

FOR THE YEAR ENDING

1964

	1964	1963	1962	1961	1960	1959	1958	1957	1956	1955	1954	1953
Cash	1,200	1,100	1,000	900	800	700	600	500	400	300	200	100
Accounts receivable	5,000	4,500	4,000	3,500	3,000	2,500	2,000	1,500	1,000	500	0	0
Inventory	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
Prepaid expenses	500	500	500	500	500	500	500	500	500	500	500	500
Operating assets	10,000	9,500	9,000	8,500	8,000	7,500	7,000	6,500	6,000	5,500	5,000	4,500
Operating liabilities	5,000	4,500	4,000	3,500	3,000	2,500	2,000	1,500	1,000	500	0	0
Operating surplus	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000
Investments	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
Other assets	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
Other liabilities	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
Total	18,000	17,500	17,000	16,500	16,000	15,500	15,000	14,500	14,000	13,500	13,000	12,500

UNITED STATES AIR FORCE

FINANCIAL STATEMENTS

FOR THE YEAR ENDING

1964

IN PAGES 1000

in pesos

	1997	1998	1999	2000	2001	2002	2003	2004
<b>ASSETS</b>								
1. <b>Current assets</b>								
Accounts receivable	15,024	59,272	99,083	33,944	15,395	16,134	16,626	41,040
Plant & Machinery	3,225	3,224	3,643	43,800	11,133	11,230	5,029	16,772
Vehicles	2,410	2,249	1,046	1,284	1,770	2,646	1,354	882
Intangibles	11,644	23,403	14,099	14,099	0	0	0	0
Total	32,303	99,148	128,271	93,226	32,336	35,010	27,695	65,692
2. <b>Long-term assets</b>								
Cash	15,800	15,800	15,800	15,800	15,800	15,800	15,800	15,800
Total	15,800	15,800	15,800	15,800	15,800	15,800	15,800	15,800
<b>LIABILITIES</b>								
1. <b>Equity Capital</b>	95,000	95,000	95,000	95,000	95,000	95,000	95,000	95,000
2. <b>Foreign Interests</b>								
Foreign borrowings	41,850	55,152	46,122	23,092	27,082	11,032	0	0
Local Currency Loan	35,812	38,379	25,506	12,793	0	0	0	0
Total	77,662	93,531	71,628	35,884	27,114	11,032	0	0
3. <b>Current liabilities</b>								
Accounts Payable	1,534	1,534	1,534	1,534	1,534	1,534	1,534	1,534
Cash Shortfalls	16,604	16,604	16,604	16,604	16,604	16,604	16,604	16,604
Total	18,138	18,138	18,138	18,138	18,138	18,138	18,138	18,138
<b>Total</b>	165,547	167,516	167,516	167,516	167,516	167,516	167,516	167,516

11

in tens of 100

NET ASSETS UNDER FUTURE PLAN

NET ASSETS UNDER FUTURE INVESTMENT

RESERVE FOR DEPRECIATION

19

NET ASSETS

1. sales revenues 36,993 36,993 36,993 36,993 36,993 36,993

2. depreciation 15,750 15,750 15,750 15,750 15,750 15,750

3. total in account with 21,243 21,243 21,243 21,243 21,243 21,243

4. present value of assets 24,000 24,000 24,000 24,000 24,000 24,000

5. operating costs 3,993 3,993 3,993 3,993 3,993 3,993

6. corporate tax 1,250 1,250 1,250 1,250 1,250 1,250

NET ASSET VALUE 10,993 10,993 10,993 10,993 10,993 10,993

Interest rate on future 10.0%

Net present value @ 10% 10,993

Net present value @ 15% 9,750

Operating net cash flow 10,993



SENSITIVITY ANALYSIS

NIDO MULTIPURPOSE FIELDS (Cont)  
NET INCOME STATEMENT

Year	1985	1986	1987	1988	1989	1990	2001	2002	2003	2004
1. Sales Revenues	42,177	56,251	56,251	56,251	56,251	56,251	56,251	56,251	56,251	56,251
2. Operating Costs	21,152	18,276	18,276	18,425	18,437	18,573	18,653	18,727	18,823	18,917
3. Operating Profit/(Loss)	19,985	17,961	17,975	17,826	17,814	17,678	17,598	17,524	17,428	17,334
4. Financial Costs	14,503	13,171	13,142	13,267	13,241	14,277	0	0	0	0
5. Depreciation	17,458	17,458	17,458	17,457	17,457	17,458	17,428	17,428	17,428	17,428
6. Gross Profit/(Loss) before tax	(2,976)	(10,298)	(2,730)	(2,898)	(2,904)	(4,053)	7,170	7,096	6,998	6,905
Corporate Taxation	0	0	0	0	0	0	1,510	1,400	1,409	1,417
7. Net Profit/(Loss)	20,976	(10,298)	(2,730)	(2,898)	(2,904)	(4,053)	4,660	4,696	4,589	4,488
8. Dividends	0	0	0	0	0	0	0	0	0	0
9. Retained Profits	(20,976)	(10,298)	(2,730)	(2,898)	(2,904)	(4,053)	4,660	4,696	4,589	4,488
10. Revenue Reserves	(20,976)	(31,185)	(28,893)	(14,435)	(43,476)	(56,873)	(32,013)	(27,407)	(22,958)	(18,370)
Gross Profit : Sales	49.7%	31.9%	31.9%	31.9%	31.9%	31.9%	31.9%	31.9%	31.9%	31.9%
Net Profit : Sales	49.7%	18.1%	13.7%	13.7%	13.7%	13.7%	8.3%	8.3%	8.2%	8.0%
Net Profit : Equity	23.4%	10.4%	7.8%	7.8%	7.8%	7.8%	4.7%	4.7%	4.6%	4.5%





## UNIDO MULTI-PURPOSE PILOT PLANT

## SENSITIVITY ANALYSIS v

Appendix 10-15

## PROJECTED BALANCE SHEET

in Pesos 000

Year	1992	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
<b>ASSETS</b>	<b>90,217</b>	<b>165,754</b>	<b>174,906</b>	<b>161,517</b>	<b>144,014</b>	<b>126,446</b>	<b>108,951</b>	<b>101,968</b>	<b>91,599</b>	<b>81,251</b>	<b>77,568</b>	<b>82,056</b>
1. Fixed Assets												
- Buildings	13,754	69,772	66,283	62,794	59,205	55,816	52,327	48,838	45,349	41,860	38,371	34,882
- Plant & Machinery	9,257	62,571	56,314	50,057	43,800	37,543	31,286	25,029	18,772	12,515	6,258	0
- Vehicles	0	3,410	2,708	2,046	1,384	622	0	1,728	2,046	1,364	682	0
- Intangibles	11,694	29,001	26,403	21,689	14,659	7,019	0	0	0	0	0	0
	<b>34,905</b>	<b>165,754</b>	<b>151,708</b>	<b>135,986</b>	<b>118,358</b>	<b>101,070</b>	<b>83,613</b>	<b>76,595</b>	<b>66,167</b>	<b>55,739</b>	<b>45,311</b>	<b>34,882</b>
2. Current Assets												
- Accounts Receivable	0	0	2,399	3,191	3,196	3,202	3,208	3,214	3,221	3,228	3,235	3,243
- Inventory	0	0	16,852	21,403	21,457	21,515	21,575	21,638	21,705	21,775	21,848	21,925
- Cash in Hand	0	0	1,075	937	673	439	555	521	506	509	513	517
- Cash Balance	63,312	0	2,452	0	0	0	0	0	0	0	6,661	21,489
	<b>63,312</b>	<b>0</b>	<b>22,178</b>	<b>25,531</b>	<b>25,486</b>	<b>25,376</b>	<b>25,338</b>	<b>25,373</b>	<b>25,432</b>	<b>25,512</b>	<b>32,257</b>	<b>47,174</b>
<b>LIABILITIES</b>	<b>90,217</b>	<b>165,754</b>	<b>174,906</b>	<b>161,517</b>	<b>144,014</b>	<b>126,446</b>	<b>108,951</b>	<b>101,968</b>	<b>91,599</b>	<b>81,251</b>	<b>77,568</b>	<b>82,056</b>
1. Equity Capital	90,217	90,217	90,217	90,217	90,217	90,217	90,217	90,217	90,217	90,217	90,217	90,217
2. Revenue Reserves	0	0	(20,976)	(31,165)	(36,893)	(42,432)	(41,476)	(36,673)	(32,613)	(27,407)	(22,858)	(18,370)
3. Term Borrowings	0	43,595	55,876	44,701	33,526	22,351	11,176	0	0	0	0	0
- Foreign Currency Loan	0	23,942	46,131	26,754	13,377	0	0	0	0	0	0	0
- Local Currency Loan	0	19,653	9,745	17,947	20,149	22,351	11,176	0	0	0	0	0
4. Current Liabilities	0	0	1,658	2,209	2,209	2,209	2,209	2,209	2,209	2,209	2,209	2,209
- Accounts Payable	0	0	0	20,821	25,578	46,101	40,825	38,215	33,186	28,232	0	0
- Cash Shortfall	0	0	1,658	23,030	37,787	48,310	43,036	40,424	25,395	10,441	2,209	2,209

ALDO MULTI-PURPOSE FLEET PLAN

SENSITIVITY ANALYSIS

Appendix 10-15

CASH FLOW TABLE - TOTAL INVESTMENT

in Pesos 000

	0	1	2	3	4	5	6	7	8	9	10
<b>CASH INFLOWS</b>											
1. Sales Forecasts	0	41,177	56,251	56,251	56,251	56,251	56,251	56,251	56,251	56,251	56,251
<b>CASH OUTFLOWS</b>											
2. Total Investment Outlay	(152,250)	(22,200)	(4,100)	45	10	26	25	50	80	50	(80)
3. Residual Value of Assets	0	0	0	0	0	0	0	0	0	0	14,882
4. Operating Costs	0	(11,150)	(38,200)	(38,250)	(38,425)	(38,625)	(38,850)	(39,125)	(39,450)	(39,825)	(40,250)
5. Corporate Tax	0	0	0	0	0	0	0	5,510	(3,480)	(2,446)	(2,417)
<b>NET CASH FLOW</b>	(152,250)	(11,273)	11,951	17,956	17,826	17,326	17,403	15,029	16,956	14,893	46,710
Internal Rate of Return	0.11										
Net Present Value @ 10%	+51,937										
Net Present Value @ 15%	+87,968										
<b>Cumulative Net Cash Flow</b>	(152,250)	(127,977)	(116,026)	(98,070)	(75,244)	(47,918)	(15,515)	13,506	30,462	45,355	92,065

Appendix 10-15

3065117211, 0001, 5515, 7

in Pesos 000

ALBANY MULTIPURPOSE FUND FUND

CASH FLOW STATEMENT - EQUITY CAPITAL

year 0 1 2 3 4 5 6 7 8 9 10

CASH (MILLIONS)

1. Sales Receipts 42,177 56,251 56,251 56,251 56,251 56,251 56,251 56,251 56,251 56,251 56,251

CASH OUTFLOWS

2. Equity subscription 15,055 15,055 15,055 15,055 15,055 15,055 15,055 15,055 15,055 15,055 15,055

3. Replacement Investment 3,416 3,416 3,416 3,416 3,416 3,416 3,416 3,416 3,416 3,416 3,416

4. Debt Service - Payments 11,175 11,175 11,175 11,175 11,175 11,175 11,175 11,175 11,175 11,175 11,175

5. Debt Service - Interest 4,473 4,473 4,473 4,473 4,473 4,473 4,473 4,473 4,473 4,473 4,473

6. Operating Costs 31,182 31,182 31,182 31,182 31,182 31,182 31,182 31,182 31,182 31,182 31,182

7. Corporate Tax 0 0 0 0 0 0 0 0 0 0 0

NET CASH FLOW 10,717 17,203 17,203 17,203 17,203 17,203 17,203 17,203 17,203 17,203 17,203

Internal Rate of Return 10.22%

Net Present Value @ 10% 10,717

Net Present Value @ 15% 8,221