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ESTABLISHMENT OF A MULTI-PURPOSE PILOT PLANT

UC/CUB/78/093

CUBA

Technical report: Transfer of technology*

Prepared for the Government of Cuba
by the United Nations Industrial Development Organization

Backstopping officer: C. Chari, Chemical Industries Branch

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ANNEXURES

1. INTRODUCTION

The technology involved in the production of pharmaceuticals in dosage form is relatively simple and is well diffused in several developing countries specially in the Asian and Latin American regions. This type of industry is also characterized by licencing arrangements, foreign subsidiaries and joint ventures. However, the technology in the case of manufacture of pharmaceutical chemicals or bulk drugs is rather sophisticated and is held by a limited number of technology holders. This is one of the reasons why only a few developing countries have been able to make some head way in this area.

The consultation meeting on transfer of technology and technical know-how between developing countries in the field of pharmaceutical industries organized by UNIDO and held at Lucknow, India during 1976 recommended cooperation amongst developing countries as one of the ways in which transfer of technology could take place. Pursuant to this, UNIDO organized the visit of an Indian technical team to Brazil, Cuba, Mexico and Peru in 1977. The team recommended the establishment of a multipurpose plant for the production of pharmaceutical chemicals in Cuba.

The availability, pricing and transfer of technology for the bulk drugs formed one of the major issues of both the UNIDO consultations on the Pharmaceutical Industry held in 1980 and 1983 respectively 1. The first consultation recommended that mutually acceptable transfer of technology should be facilitated through UNIDO providing reference information relevant to the transfer of technology, including technical aspects, such as level of production, magnitude of investments, inputs, infrastructure, etc..., which could be significant aid to individual developing countries in bilateral negotiations for transfer of technology.

The second consultation recommended that in respect of offers of technology for the production of bulk drugs and intermediates, UNIDO should in cooperation with technology holders prepare feasibility studies at the request by interested countries.

In the above context, the project entitled "Establishment of a Multi-purpose Pilot Plant in Cuba" is a very interesting example of transfer of technology in the area of manufacture of pharmaceutical chemicals based on

1. First consultation on the Pharmaceutical Industry, UNIDO/ID/259, 1980; Second consultation, UNIDO/ID/311, 1983

chemical systhesis and constitutes an important milestone in the development of Pharmaceutical Industry in Cuba and has significance for other developing countries in this field.

The pharmaceutical industry in Cuba, like in many other developing countries is confined mostly to the production of pharmaceuticals in dosage form based on imported active ingredients or pharmaceutical chemicals. Dependence on imports has been limiting the growth and development of the indigenous pharmaceutical industry. The Government is, therefore, keen to achieve self reliance to the extent feasible in this sector through taking up of local manufacture of pharmaceutical chemicals using available indigenous raw materials and skills. To achieve this, Cuba should have access to technology for the manufacture of pharmaceutical chemicals. As mentioned above, such technology is rather sophisticated and is held by few sources. The mere acquisition of such technology is not enough. This has to be adapted to the local conditions and raw materials.

Concept of Multipurpose Pilot Plant

The quantities of different pharmaceutical chemicals required by the Cuban pharmaceutical industry are rather small. In view of this, establishing single lines of production for each pharmaceutical chemical is not economically viable. Hence, the concept of multipurpose plant was applied in this case. What this really means is that several pharmaceutical chemicals in varying quantities can be produced in the same plant either sequentially or sometimes simultaneously. The plant can thus be kept busy round the year which renders it economically more viable than establishing single lines of production for each pharmaceutical chemical with large under utilized capacities.

UNIDO entered into a contract with Sarabhai Research Centre (SRC) of India in 1978 for the supply of technical know-how and major equipment; training of Cuban personnel in India as well as supervision over installation, testing and commisioning the multipurpose pilot plant. The financial inputs for the project are from the Government of Cuba, UNIDO, UNDP and the Government of India in that order and the Project thus represents a joint cooperation between them.

Sarabhai supplied equipment for process, utilities and laboratory. They

prepared basic engineering design based on which the Cuban counterpart worked out the detailed engineering design. Two batches of Cuban technical personnel were trained at Sarabhai facilities in India in the field of production, quality control, maintenance and engineering design. The technological process for the production of 15 pharmaceutical chemicals was demonstrated to them with stipulated efficiencies and quality during the course of their training. Installation materials were procured from other sources in India. Equipment such as storage tanks were fabricated in Cuba. Civil works and the installation of equipment were carried out by Cuban counterpart based on the design approved by Sarabhai. Final installation, testing and commissioning were done under the supervision of Sarabhai team. Trial batches in the multi-purpose pilot plant were completed in 1986.

2. OBJECTIVES AND LOGIC OF PROJECT

Development Objective

The development objective of the project is the transfer of technology for the production of active ingredients/pharmaceutical chemicals and the build up of technological capability through which necessary infrastructure and manpower could be developed. This will lead to the production in the country of some essential pharmaceutical chemicals required for social health programmes in a more rational and economic manner.

Immediate Objectives

a) Establishment of a multipurpose pilot plant for process development, adaptation and back integration of technology.

b) Transfer of technology for the production of 15 pharmaceutical chemicals from raw materials, intermediates through chemical synthesis.

c) Technical skill and manpower development.

3. MAIN CHARACTERISTICS OF THE MULTIPURPOSE PILOT PLANT

The multipurpose pilot plant constitutes a sophisticated industrial installation within the Pharmaceutical Industry in Cuba. The following are the main features of the pilot plant:

a) Civil Works

The project area measures 23.000 m^2. Out of this, an area of 7.155 m^2 is constructed and 3.882 m^2 is covered. The areas of important buildings are indicated below:

- Storage area for raw materials and finished products 2.376 m^2
- Production building 1.080 m^2
- Storage area for solvents 825 m^2
- Building for general services 216 m^2

b) Production Level of Pharmaceutical Chemicals

Pharmaceutical Chemical	Pharmacopoeal Standard	Annual Capacity (tons)
1. Acetyl Salicylicacid (Aspirin)	U.S.P.	190
2. Chlorodiazepoxide	N.F.	1
3. Clofibrate	U.S.P.	1
4. Diazepam	U.S.P.	1
5. Diphenyl hydantoin	U.S.P.	2
6. Indomethacin	B.P.	1
7. Lignocaine hydrochloride	I.P.	0.3
8. Methyl Salicylate	U.S.P.	8
9. Metronidazole	U.S.P.	4
10. Nalidixic Acid	N.F.	3
11. Nicotinamide	U.S.P.	15
12. Nikethamide	B.P.	1
13. Paracetamol	B.P.	1
14. Phenylbutazone	B.P.	4
15. Procaine hydrochloride	B.P.	10
		242.3

c) Budget

The total budget for the project amounts to US$ 4.472.288 out of which the equipment component amounts to US$ 2.210.553 and the cost of buildings is US$ 1 [illegible].111. UNIDO contribution was in the form of US$, Indian Rupees and Cuban Pesos. UNDP contribution was in US$ while that of the Government of India was in Indian Rupees. The Cuban Government contribution was in Cuban Pesos and in kind.

e) Value of Production

Based on 1981 prices the value of annual production amounts to about US$ 2.8 million.

4. ACTIVITIES CARRIED OUT AND OUTPUTS PRODUCED

The dockets containing technology and the technical specifications of raw materials and finished products were sent to CUBA in October/November 1979. The Cuban technical personnel underwent training both in the laboratory and in the pilot plant from 29.1.1981 to 20.2.1981 and from 20.1.1984 to 8.2.1984. The first team of technical personnel came on 29.1.1981. The members were

Mrs. Mayra Sanchez,
Mr. Arango Ramon,
Mrs. Perez Maria Elena,
Miss Grau Silvia
Miss Alba Susana and
Mr. Hernandez Angel

The second team came on 20th January 1984 consisting of the following members:

Mrs. Mayra Sanchez,
Mr. Oscar Gonzalez,
Mr. Ramon Arango,
Mr. Angel Hernandez,
Ms. Maria Perez,
Ms. Susana Alba,
Ms. Tania Delgado and
Mr. Josquin Orrve.

The equipment supply was completed in May 1984. The list of equipment is given in Annexure A.

In Annexure B : information supplied to the Cuban team both on operations and quality control as well as drawings (Civil and Mechanical) of all the equipment supplied is mentioned.

The Engineering group visited SRC along with the other members both for finalizing plan and for training in maintenance from 20.1.1984 to 8.2.1984. After the completion of the construction of pilot plant and installation of

the equipment, SRC engineer, Mr. S.D. Maharaj, was in Cuba between 1 August 1985 and 13 January 1986. During his stay, he had ensured leak-proof satisfactory performance of service equipment and suitability of the equipment for taking initial batches. Some details are given in Annexure C.

Between 23 November 1985 and 11 May 1986 a group of four chemists (Mr. D. M. Desai, Mr. J.C. Soni, Mr. N.V. Upadhyaya and Mr. J. J. Panchal) worked for the establishment of technology in the laboratory in Cuba with the raw materials that had been procured by the Cuban Government. The actual demonstrations of the technology on the pilot plant were carried out between 1 April 1986 and 11 May 1986. During the last phase of demonstration the team leader from SRC and the analyst from SRC were present to ensure the satisfactory completion of the job. During this period, all the technologies were demonstrated in the laboratory and in the pilot plant to the complete satisfaction of the Cuban team. The batch sizes were in conformity with SRC proposal; the yeilds and the quality of the products were also in accordance with the guaranteed yields from the technology (See Annexure C). In Annexure C the experimental batches taken in Cuba both in the laboratory and in the pilot plant are summarized. Details of a few batches are also incorporated to give an idea of the thoroughness of transfer of technology. The project was handed over to UNDP Resident Representative, Havana, Cuba with a request to communicate to UNIDO about the completion of the project and to take necessary steps to formally hand over the project to Cuba.

The main objectives of the training programme for the Cuban technical personnel were :

a) To familiarize the people with technology for the pharmaceuticals under consideration.
b) To high-light the importance of strictly adhering to the details given in the dockets.
c) To explain the technical implications of the procedural details.
d) To explain the advantages of the technology given.
e) To explain the problems that might arise unwittingly due to failure of services, inferior raw materials and process modifications adopted for considerations of ease of operations.

f) To explain theoretical considerations that have been taken into account while preparing the technical mannuals.

g) Some details regarding manufacture of Aspirin, Paracetamol, Nalidixic acid, Metronidazole, Indomethacin, etc. are given in Annexure C.

5. ACHIEVEMENT OF IMMEDIATE OBJECTIVES

a) The transfer of technology for the manufacture of 15 basic pharmaceuticals from available intermediates, along with the suppply of plant equipment and laboratory equipment has been achieved.

b) The training of Cuban technical personnel in the laboratory, pilot plant and quality control laboratory has been achieved.

c) The multipurpose pilot plant has been commissioned in Cuba (May 1986).

d) The operating personnel have been trained.

e) Maintenance personnel have been trained.

f) Trial batches have been taken on the multipurpose pilot plant and the products have been analyzed. The yields of the products are found to be in conformity with yields claimed for the technologies, and the quality of the products are found to be in conformity with pharmacoepial requirements.

6. UTILIZATION OF PROJECT RESULTS

The technologies for 15 bulk pharmaceuticals have been demonstrated on the multipurpose pilot plant put up in Cuba on the UNIDO project No. UC/CUB/78/093. Products are now being produced on the pilot plant regularly. The absorption of the above technologies and regular production of bulk pharmaceuticals would contribute to Cuban self-sufficiency in bulk pharmaceuticals.

7. REASONS FOR THE DELAY IN IMPLEMENTING THE PROJECT

A variety of reasons can contribute to delay in the implementation of a project of this type.

a) Definition of responsibilities of the contractor and the host country should be clear and unambiguous. Details of the responsibilities should be written up in an unambiguous manner after discussion with both parties. A workable time frame should be fixed so that discharge of responsibilities can be monitored.

b) Correspondence delays could be reduced not only by sending telexes but by sending follow-up letters clearly pointing out deviations from norms during the implementation of a project.

c) Brief meetings between the parties should be arranged once in 6 months after the commencement of the project to review progress, to analyse unavoidable delays and to clear up misunderstandings.

d) When a project takes more than two years for implementation, factors such as inflation may have to be taken into account. If the delay is not attributable to the contractor, a suitable provison on reasonable basis may have to be made in the contract for the delays of the host country.

In the course of the implementation of this project, some delays were encountered in transport of equipment because of limited shipping facilities between the two countries.

This project has suffered some unavoidable delays also under a) and b) above.

During the implementation of the project, it was felt many times that more preplanned meetings between the host country and the contractor might have cut down the delays to some extent.

8. HIGHLIGHTS OF THE PROJECT

a) Transfer of Technology

The multipurpose pilot plant constitutes a significant step in the acquisition and adaptation of sophisticated technology for the basic manufacture of essential drugs and to this extent the country becomes self sufficient.

b) Economic Importance

So far Cuba has been importing most of the active ingredients to feed its pharmaceutical industry expending foreign currency. This plant will facilitate the local production of 15 essential drugs and this will save valuable foreign exchange.

c) TCDC

The project involves technical cooperation between Cuba and India - South - South cooperation. After commissioning the pilot plant, Cuba can provide technical cooperation to other developing countries in the sub-region by transfer of technology, demonstration and training.

d) Export Possibilities

After satisfying domestic requirements, Cuba will be in a position to export some active ingredients to the neighbouring countries to feed their pharmaceutical industry.

e) Growth and Development of the Pharmaceutical Industry

The pilot plant will facilitate the development and introduction of new technological processes and production techniques, which will promote the growth and development of indigenous pharmaceutical industry. In case the technology so developed leads to economically viable production and if the demand for a specific drug justifies, a single line production can be established.

f) Technical Skill Development

The pilot plant led to the development of indigenous technical skills, which will facilitate the designing, establishment and operation of plants for the manufacture of active ingredients through chemical synthesis.

9. CONCLUSION

a) The multipurpose pilot plant with an annual production capacity of 240-250 tons, covering a range of 15 bulk pharmaceuticals, has been commissioned and regular production operations have commenced.

b) The project is an important milestone in Cuban self-sufficiency for bulk pharmaceuticals. It is the first effort in Cuba for the production of synthetic pharmaceuticals. Cuban chemists and engineers have acquired the know-how through training and are in a position to utilize acquired technologies for regular production of bulk pharmaceuticals. This achievement has been possible because of financial help and monitoring provided by UNIDO/UNDP, Governments of Cuba and India.

c) The successful completion of the project demonstrates that developing countries can transfer technology and implement projects in less-developed countries. Acquisition of technology from developing countries would be advantageous to less-developed countries as assimilation would be easier.

d) The completion of the project has given a lot of self-confidence to chemists and engineers of Cuba which has several qualified and competent engineers and technicians.

e) The success of the project also illustrates the capability of Indian chemists and engineers to put up pharmaceutical plants for manufacture of bulk drugs.

f) The success of the project is also due to a large extent to the keen interest and hardwork of the Cuban team of engineers, scientists and technicians.

g) The success is also due to the ability and cooperation extended by Sarabhai Research Centre.

10. RECOMMENDATIONS

There is an immense scope for technical training, transfer of technology and tehnical cooperation among the developing countries. In the first place, the scope of each phase of activity has to be adequately defined.

For instance, technical training can be in the laboratory, pilot plant or plant. It can be for one or more products. The more advanced developing countries might only look for technologies for specific products or for specific intermediates as they would be having enough experience and expertise to adapt the acquired technologies themselves.

Acquisition of technologies for selected products and intermediates may not be very expensive, and some institutions or companies might be willing to cooperate in such an activity as it does not involve much expenditure of time

and man-power on their part. Technical training for specific products would not be difficult to arrange for provided the country seeking such help has the necessary infrastructure to benefit by it.

As mentioned earlier, UNIDO can assist in identifying specific products for each developing country and facilitating the acquisition of technology by each country. This would help a developing country to deploy the minimum number of technical persons with the specific task of implementing a project where one or two products only are manufactured. This will enable a country to acquire expertise in narrow areas, which, later on, can be expanded to other products.

Countries which have a nucleus for the manufacture of basic drugs and formulations can be encouraged to acquire newer technologies gradually. Here, again, UNIDO, can help a given country by identying technology for a product or two, assisting the country by identifying a source for the technology and in some cases acquiring the technology on behalf of the country.

When each country looks for fewer technologies, it would be easier to select the best technology available for the product.

The modular approach to a multipurpose plant will be less expensive and more easy to implement, expansions taking place as and when desired.

Collaborations between developing countries in technological fields should be encouraged. Countries which can part with technology can be identified. Charges for technology transfer can be assessed on the basis of terms of transfer of technology, like demonstration, training. etc.

Countries which have already collaborated could be encouraged to interact further for mutual benefit, by arranging for further acquisition of technology, for further training of technical personnel or for arranging for visits of technical experts, depending on the needs of developing countries.

ANNEXURE : A

LIST OF EQUIPMENT

SR.NO.	ITEM - PROCESS EQUIPMENT	CAPACITY	NO.
1.	Jacketted glass-lined reactor with agitator	1000 l.	2
2.	G. L. Condenser	4 sq. m.	2
3.	G. L. Receiver	600 l.	1
4.	Jacketted S.S. Reactor with agitator	1000 l.	4
5.	S. S. Condenser	4 sq. m.	4
6.	S. S. Receiver	600 l.	2
7.	Jacketted S. S. Reactor with agitator	600 l.	4
8.	S. S. Condenser	3 sq. m.	4
9.	S. S. Receiver	500 l.	2
10.	Jacketted S.S. flat top reactor with agitator	600 l.	1
11.	M.S.R.L. flat top reactor with agitator	600 l.	2
12.	Jacketted S.S. Concentration pan with agitator	400 l.	1
13.	Jacketted S.S. Vacuum still pot with agitator	200 l.	1
14.	S. S. Condenser	1.5 sq.m.	1
15.	Jacketted S. S. Receiver	200 l.	1

G.L. : Glasslined

S.S. : Stainless steel

M.S.R.L. : Mild Steel Rubberlined.

(ANNEXURE : A ..... Contd. ....)

SR.NO.	ITEM - PROCESS EQUIPMENT	CAPACITY	NO.
16.	12000 S. S. Basket centrifuge		2
17.	10000 S. S. Basket centrifuge		1
18.	M. S. R. L. Filter box	600 l.	2
19.	S. S. Filter box	600 l.	1
20.	S. S. Sparkler filter		1
21.	S. S. Pressure leaf filter		1
22.	Forced draft dryer	94 trays	3
23.	Forced draft dryer	40 trays	1
24.	Forced draft dryer	30 trays	1
25.	Forced draft dryer	10 trays	1
26.	Vacuum shelf dryer with condenser		1
27.	Water ring vacuum pumps	7 h.p.	4
28.	High vacuum pump	2 h.p.	1
29.	S. S. Centrifugal pump	50 lbm at 25 m.	4
30.	M. S. R. L. Pump	50 lbm at 25 m.	2
31.	All glass reactor	100 l.	2
32.	S. S. Pulveriser		1
33.	S. S. Mechanical sieve		1
34.	S. S. Resin column	0.6 mo 1.5 m high	2
35.	S. S. Blender		1
36.	S. S. Vent. Condenser	1.5 sq.m.	5
37.	Dial type balance	To weigh 50 kg.	2
38.	Miscellaneous equipment		

(ANNEXURE : A ..... Contd. .....)

SR.NO.	ITEM - PROCESS EQUIPMENT	CAPACITY	NO.
TANK FARM EQUIPMENT			
1.	Tank for storing hydrochloric acid, high density polythene	10000 l.	1
2.	M. S. Storage tank for sulfuric acid	10000 l.	1
3.	M. S. Storage tank for caustic soda	10000 l.	1
4.	M. S. Storage tank for benzene	10000 l.	1
5.	M. S. Storage tank for toluene	10000 l.	1
6.	M. S. Storage tank for acetone	10000 l.	1
7.	M. S. Storage tank for ethanol	10000 l.	1
8.	M. S. Storage tank for methanol	10000 l.	1
9.	M. S. Storage tank for diesel Oil	10000 l.	2
10.	C. I. Submersible pump for solvent		5
11.	C. I. Pump for sulfuric acid		1
12.	C. I. Pump for caustic soda		1
13.	Polypropylene pump for hydrochloric acid		1
14.	M. S. Vent condensers	1 sq.m.	5
15.	C. I. Pump for diesel oil		1
SERVICE EQUIPMENT			
1.	Steam generator to generate steam at 10 atm.	500 kg/hr.	2
2.	Demineralized water unit	3 m^3/hr.	1
3.	Sbft water unit, dealkalizer	3 m^3/hr.	1

C.I. : Cast Iron

(ANNEXURE : A ..... Contd. .....)

SR.NO.	ITEM - PROCESS EQUIPMENT	CAPACITY	NO.
4.	H.D.P. Storage tank for D.M. Water	10000 l.	2
5.	H.D.P. Storage tank for soft water	10000 l.	2
6.	S. S. Pump for D. M. Water	25 lpm at 25 m.	1
7.	C. I. Pump for soft water	25 lpm at 25 m.	1
8.	Refrigeration unit for chilled water at SC	30 tr	2
9.	Refrigeration unit for chilled brine	10 tr	1
10.	Cooling tower	150 tr	1
11.	C. I. Cooling water pump	1500 lpm at 25 m.	2
12.	C. I. Chilled water pump	500 lpm at 25 m.	2
13.	C. I. Chilled brine pump	100 lpm at 25 m.	2
14.	Hot oil circulation unit	70000 K. cal/hr.	1
15.	Air compressor		2
16.	Electric substation 50 KVA		1
17.	Diesel generator 50 KVA		1
18.	Incinerator		1
19.	Battery operated fork lift truck		1

H.P.D.: High Density Polyethylene

D.M.: Demineralized.

(ANNEXURE : A ..... Contd. .....)

EQUIPMENT FOR ANALYTICAL LABORATORY

		No.
1.	a) Metler semimicro balance	1
	b) Single pan Indian balance	1
	c) Rough balance (Avery. type)	1
2.	Melting point apparatus	1
3.	Laboratory drying oven (0-250°C.)	2 (one vac. oven)
4.	Muffle furnace	1
5.	Karl Fischer apparatus	1
6.	Refractometer	1
7.	Spectro calorimeter	1
8.	T.L.C. equipment	1
9.	Vacuum pump	1
10.	Heating mantles	3
11.	Hot plates	3
12.	pH Meter	1
13.	UV - viewing cabinet	1

Glass Wares and other Laboratory Items :

1.	Burettes (10, 25 and 50 cc. capacity)		1 doz. each
2.	Pipettes (1,2,5,10,25 & 50 cc)		20 each
	Lamda pipettes (5,10 & 25)		3 each
	Graduated pipettes (1,5 & 10)		10 each
3.	Beakers (25,50,100,250,500 & 1000 cc)	1000	2 doz. each & 1 doz.
4.	Conical flasks (25,50,100,250,500 &		2 doz. each
	1000 cc) (Erlenmeyer		1 doz.
	Iodometric flask (250 ml.)		1 doz.

(ANNEXURE : A ..... Contd. .....)

		No.
5.	Kjeldhal distillation units (Kjeldhal flasks)	2 Nos.
	Kjeldhal flasks 500 ml.	6 Nos.
	Kjeldhal flasks 300 ml.	6 Nos.
6.	Platinum crucibles	2
	* Tongs with Pt. tip	2
7.	Nickel crucibles	2
8.	Silica (Vitreosol crucibles)	1 doz.
9.	Miscellaneous items (like stand, clamps, etc.)	
10.	Round bottom flask with Std. joints (B-24) (100, 250 & 500 ml.)	1 doz. each
11.	a) Thermometer (Ordinary 0-250°C)	6 Nos.
	b) Thermometer (Q.F. ,0-250°C)	3 Nos.
12.	Std. Glass joints, Adapters, Olassenheads, etc.	
13.	Separating funnel (50, 100, 750 & 500 cc)	6 each
	Ordinary funnels	1 doz.
14.	Weighing bottles	1 doz.
15.	Sintered glass crucibles	1 doz.
16.	Filteration flasks (50, 100, 250, 500, 1 lit.)	6 each
17.	Glass condensers of various types	1 doz.
	Coiled type	1 doz.
18.	Glass cylinders (10, 25, 100)	1 doz. each
19.	Neßler tubes (25,50, & 100	1 doz.
20.	Volumetric flasks (10,25,50,100,	1 doz. each
	250, 500 & 1 lit.	6 Nos.
	& 2 lit.)	3 Nos.

(ANNEXURE : A ..... Contd. .....)

			No.
21.	Test tubes ------- All sizes		2 doz.
22.	Desiccators ordinary		4
	Vac.		2
23.	Specific gravity bottle & Pyknometers	10	2 each
		25	
		50	
	Pyknometers		4
24.	100 Lit. All-glass Assembly		

Information mentioned hereunder has also been supplied.

1. Operation and Maintenance instructions for equipment.
2. Performance curves of pumps & Data available from the manufacturer.
3. Installation instructions.
4. Maintenance and operation manual.
5. Fire fighting and hazard handling arrangement.
6. Location of an optimum number of safety showers in the battery area.
7. Hazardous areas to be ear-marked and instructions for using such areas.
8. Information regarding the mode of anchoring each piece of equipment to be described and shown on the layout plan and details of the supports and fixtures.

ANNEXURE: B

LIST OF MANUALS, CIVIL AND MECHANICAL DRAWINGS, DATA SHEETS ETC., SUPPLIED

Operational Formula Part I & Part II and Quality Control Manual have been supplied.

The following 8 drugs are covered in Part I.

1. Aspirin
2. Nicotinamide
3. Methyl salicylate
4. Metronidazole
5. Procaine Hydrochloride
6. Clofibrate
7. Diphenylhydantoin &
8. Lignocaine Hydrochloride.

The following 7 drugs are covered in Part II.

1. Indomethacin
2. Nalidixic acid
3. Phenylbutazone
4. Paracetamol
5. Diazepam
6. Chlordiazepoxide &
7. Nikethamide.

All the details regarding operations for all the 15 drugs starting from the corresponding raw materials are given in the manuals.

Quality Control Manual contains the specifications of the finished products, local specifications for raw materials and intermediates. Details for carrying out the quality control tests are also indicated therein.

(ANNEXURE : B ..... Contd. .....)

Civil and Mechanical drawings have been supplied.

CIVIL DRAWINGS :

1. SHIP/UNIDO/CIV/6 R4 dated 18.1.80.
2. SHIP/UNIDO/CIV/7 R4 dated 5.2.80.
3. SHIP/UNIDO/CIV/16 R1 dated 5.3.80.
4. SHIP/UNIDO/CIV/8 R3 dated 15.2.80.
5. SHIP/UNIDO/CIV/9 R2 dated 25.2.80.

MECHANICAL DRAWINGS :

6. SHIP/UNIDO/01A/R6 dated 4.3.80.
7. SHIP/UNIDO/01B/R6 dated 7.3.80.
8. SHIP/UNIDC/12/R1 dated 13.3.80.

The above Civil & Mechanical drawings give details of site development, gutter layout, equipment layout, etc.

(ANNEXURE : B ..... Contd. .....)

Data Sheets have been supplied.

SR.NO.	DATA SHEET NO.	ITEM NO.	ITEM DESCRIPTION
1.	UNIDO/1001-A/2/15-9-79	UN-3-1	1000 L SS Reactor
2.	UNIDO/1001-B/2/15-9-79	UN-4-1	1000 L SS Reactor
3.	UNIDO/1001-C/2/15-9-79	UN-5-1	1000 L SS Reactor
4.	UNIDO/1001-D/2/15-9-79	UN-6-1	1000 L SS Reactor
5.	UNIDO/1002-A/2/15-9-79	UN-7-1	600 L SS Reactor
6.	UNIDO/1002-B/2/15-9-79	UN-8-1	600 L SS Reactor
7.	UNIDO/1002-C/2/15/9/79	UN-9-1	600 L SS Reactor
8.	UNIDO/1002-D/2/15-9-79	UN-10-1	600 L SS Vessel
9.	UNIDO/1003-A/2/15-9-79	UN-1-4	4 M^2 SS Condenser
10.	UNIDO/1003-B/2/15-9-79	UN-3-4	4 M^2 SS Condenser
11.	UNIDO/1003-C/2/15-9-79	UN-4-4	4 M^2 SS Condenser
12.	UNIDO/1003-D/2/15-9-79	UN-5-4	4 M^2 SS Condenser
13.	UNIDO/1003-E/2/15-9-79	UN-6-4	4 M^2 SS Condenser
14.	UNIDO/1004-A/2/15-9-79	UN-7-4	3 M^2 SS Condenser
15.	UNIDO/1004-B/2/15-9-79	UN-8-4	3 M^2 SS Condenser
16.	UNIDO/1004-C/2/15-9-79	UN-9-4	3 M^2 SS Condenser
17.	UNIDO/1005-A/2/15-9-79	UN-8-5	500 L SS Receiver
18.	UNIDO/1005-B/2/15-9-79	UN-9-5	500 L SS Receiver
19.	UNIDO/1006-A/2/15-9-79	UN-5-5	600 L SS Receiver
20.	UNIDO/1006-B/2-15-9-79	UN-6-5	600 L SS Receiver
21.	UNIDO/1006-C/2/15-9-79	UN-20-2	600 L SS Receiver
22.	UNIDO/1007-A/2/15-9-79	UN-11-1	600 L MSRL Vessel
23.	UNIDO/1007-B/2/15-9-79	UN-12-1	600 L MSRL Vessel
24.	UNIDO/1009-2/15-9-79	UN-13-1	500 L SS Pan
25.	UNIDO/1010-A/2/15-9-79	UN-15-1	SS Resin Column
26.	UNIDO/1010-B/2/15-9-79	UN-16-1	SS Resin Column
27.	UNIDO/1011-A/2/15-9-79	UN-21-1	600 L MSRL Filter box
28.	UNIDO/1011-B/2/15-9-79	UN-22-1	600 L MSRL Filter box

(ANNEXURE : B ..... Contd. .....)

SR.NO.	DATA SHEET NO.	ITEM NO.	ITEM DESCRIPTION
29.	UNIDO/1012-2/15-9-79	UN-20-1	600 L SS Filter Box
30.	UNIDO/1013-2/15-9-79	UN-14	200 L SS Distillation Unit
31.	UNIDO/1014-2/15/9/79	UN-24-1	Pressure filter
32.	UNIDO/1015-2/15-9-79	UN-23-1	SS KBC Filter
33.	UNIDO/1016-2/15-9-79	UN-30	Vacuum Dryer
34.	UNIDO/1017-A-2/15-9-79	UN-25	30 M^2 Tray Dryer
35.	UNIDO/1017-B-2/15-9-79	UN-26	30 M^2 Tray Dryer
36.	UNIDO/1017-C-2/15-9-79	UN-27	30 M^2 Tray Dryer
37.	UNIDO/1018-2/15-9-79	UN-28	15 M^2 Tray Dryer
38.	UNIDO/1019-2/15-9-79	UN-29	10 M^2 Tray Dryer
39.	UNIDO/1020-2/15-9-79	UN-45-1	SS Nutsche filter
40.	UNIDO/1021-2/15-9-79	UN-19-1	1000 mm ϕ SS Centrifuge.
41.	UNIDO/1022-A/2/15-9-79	UN-17-1	1200 mm ϕ SS Centrifuge.
42.	UNIDO/1022-B/2/15-9-79	UN-18-1	1200 mm ϕ SS Centrifuge.
43.	UNIDO/1023-2/15-9-79	UN-43	100 L Glass Reaction Unit.
44.	UNIDO/1024/A/2/15-9-79	UN-1-1	1000 L GL Reactor
45.	UNIDO/1024/B/2/15-9-79	UN-2-1	1000 L GL Reactor
46.	UNIDO/1025/2/15-9-79	UN-2-4	4.0 M^2 GL Condenser
47.	UNIDO/1026/2/15-9-79	UN-2-5	600 L GL Receiver
48.	UNIDO/1027/A/2/21.9.79	UN-35-1	SS Centrifugal Pump
49.	UNIDO/1027/B/2/21.9.79	UN-36-1	SS Centrifugal Pump
50.	UNIDO/1027/C/2/21.9.79	UN-37-1	SS Centrifugal Pump
51.	UNIDO/1027/D/2/21.9.79	UN-38-1	SS Centrifugal Pump
52.	UNIDO/1028/A/2/21.9.79	UN-39-1	MSRL Centrifugal Pump.
53.	UNIDO/1028/B/2/21.9.79	UN-40-1	MSRL Centrifugal Pump.
54.	UNIDO/1029/A/2/24.9.79	UN-31-1	Water Ring Vacuum Pump.
55.	UNIDO/1029/B/2/24.9.79	UN-32-1	Water Ring Vacuum Pump.

(Annexure : B ..... Contd. .....)

SR.NO.	DATA SHEET NO.	ITEM NO.	ITEM DESCRIPTION
56.	UNIDO/1029-C/2/24.9.79	UN-33-1	Water Ring Vacuum Pump
57.	UNIDO/1029-D/2/24.9.79	UN-34-1	Water Ring Vacuum Pump
58.	UNIDO/1030/2/24.9.79	UN-14-4	High Vacuum pump
59.	UNIDO/1031/2/24.9.79	UN-41-1	SS Pulveriser
60.	UNIDO/1032/2/3.11.79	UN-42-1	SS Mechanical Sieve
61.	UNIDO/1033/2/3.11.79		Gear Boxes
62.	UNIDO/1051/2/5.10.79	UN-51	Boiler
63.	UNIDO/1052/2/24.9.79	UN-55	Water Chilling Plant
64.	UNIDO/1053/2/24.9.79	UN-54	Brine Chilling Plant
65.	UNIDO/1054/2/21.9.79	UN-56	Cooling Tower
66.	UNIDO/1055/A/2/21.9.79	UN-56-5	Cooling Tower Pump
67.	UNIDO/1055/B/2/21.9.79	UN-56-7	Cooling Tower Pump
68.	UNIDO/1056-A/2/21.9.79	UN-57	Air Compressor
69.	UNIDO/1056-B/2/21.9.79	UN-60	Air Compressor
70.	UNIDO/1057/2/24.9.79	UN-59	Hot Oil Unit
71.	UNIDO/1058/2/21.9.79	UN-52	Demineralised Water Plant
72.	UNIDO/1059/2/21.9.79	UN-53	Water Softening Plant
73.	UNIDO/1060/2/2.11.79	-----	Flameproof Induction Motor
74.	UNIDO/1061/2/2.11.79	-----	T.E.F.C. Motors
75.	UNIDO/1062/2/1.11.79	-----	Variable speed Motor
76.	UNIDO/1063/2/3.11.79	-----	Furnace Oil Specifications.
77.	UNIDO/1064/2/3.11.79	-----	Raw Water Specifications
78.	UNIDO/1065/2/3.11.79	-----	DM/Soft Water Specifications
79.	UNIDO/1066/2/11.1.80	-----	Electrical Motors
80.	UNIDO/1201/24-12-79	UN-17-4	600 L Receiver
81.	UNIDO/1202/24-12-79	UN-18-4	600 L Receiver
82.	UNIDO/1203/24-12-79	UN-19-4	600 L Receiver

(Annexure : B - ..... Contd. .....)

SR.NO.	DATA SHEET NO.	ITEM NO.	ITEM DESCRIPTION
83.	UNIDO/1204/15-9-79	UN-20-2	600 L SS Jacketted Receiver
84.	UNIDO/1205/15-9-79	UN-21-2	600 L MSRL Receiver
85.	UNIDO/1206/15-9-79	UN-22-2	600 L MSRL Receiver
86.	UNIDO/1207/1-1-80	UN-30-7	Hot Water circulation pump
87.	UNIDO/1208/1-1-80	UN-46-1	Day Storage tank for methanol
88.	UNIDO/1209/1-1-80	UN-46-2	Day Storage tank for acetone
89.	UNIDO/1210/1-1-80	UN-46-3	Day Storage tank for ethanol
90.	UNIDO/1211/1-1-80	UN-46-4	Day Storage tank for benzene
91.	UNIDO/1212/1-1-80	UN-46-5	Day Storage tank for acetic anhydride
92.	UNIDO/1213/1-1-80	UN-46-6	Day Storage tank for acetic acid.
93.	UNIDO/1214/1-1-80	UN-46-7	Day Storage tank for Hydrochloric acid.
94.	UNIDO/1215/1-1-80	UN-47-1	Underground main storage tank for methanol
95.	UNIDO/1216/1-1-80	UN-47-2	Underground main storage tank for acetone
96.	UNIDO/1217/1-1-80	UN-47-3	Underground main storage tank for ethanol
97.	UNIDO/1218/1-1-80	UN-47-4	Underground main storage tank for benzene
98.	UNIDO/1219/-1-1-80	UN-47-5	Main Storage tank for Acetic anhydride
99.	UNIDO/1220/1-1-80	UN-47-6	Main storage tank for Acetic acid
100.	UNIDO/1221/1-1-80	UN-47-7	Main Storage tank for Hydrochloric acid

(Annexure : B ..... Contd. .....)

SR.NO.	DATA SHEET NO.	ITEM NO.	ITEM DESCRIPTION
101	UNIDO/1222/1-1-80	UN-48-1-1	Transfer pump for methanol
102	UNIDO/1223/1-1-80	UN-48-2-1	Transfer pump for acetone
103	UNIDO/1224/1-1-80	UN-48-3-1	Transfer pump for ethanol
104	UNIDO/1225/1-1-80	UN-48-4-1	Transfer pump for benzene
105	UNIDO/1226/1-1-80	UN-48-5-1	Transfer pump for acetic anhydride
106	UNIDO/1227/1-1-80	UN-48-6-1	Transfer pump for acetic acid.
107	UNIDO/1228/1-1-80	UN-48-7-1	Transfer pump for hydrochloric acid.
108	UNIDO/1229/2-1-80	UN-51-6	Intermediate oil tank
109	UNIDO/1230/2-1-80	UN-51-7	Main oil storage tank
110	UNIDO/1231/2-1-80	UN-51-8	Pump for furnace oil
111	UNIDO/1232/2-1-80	UN-51-10	Chimney
112	UNIDO/1233/2-1-80	UN-51-12	Water meter
113	UNIDO/1234/2-1-80	UN-51-20	Condensate holding tank
114	UNIDO/1235/2-1-80	UN-51-22	Condensate transfer pump
115	UNIDO/1236/2-1-80	UN-51-24	Feed water pump (standby)
116	UNIDO/1237/3-1-80	UN-52-1	Raw Water storage tank
117	UNIDO/1238/3-1-80	UN-52-2	Pump for raw water (2 Nos.)
118	UNIDO/1239/3-1-80	UN-52-3	Raw water feed pump for DM plant
119	UNIDO/1240/3-1-80	UN-52-10	Water meter
120	UNIDO/1241/3-1-80	UN-52-15	DM Water tank
121	UNIDO/1242/3-1-80	UN-52-16	Intermediate DM Water tank
122	UNIDO/1243/3-1-80	UN-52-17	DM Water pump
123	UNIDO/1244/3-1-80	UN-52-19	Intermediate raw water tank
124	UNIDO/1245/4-1-80	UN-53-1	Raw Water feed pump to water softening plant.
125	UNIDO/1246/4-1-80	UN-53-9	Water meter.

(Annexure : B ..... Contd. .....)

SR.NO.	DATA SHEET NO.	ITEM NO.	ITEM DESCRIPTION
126	UNIDO/1247/4-1-80	UN-53-10	Soft water tank
127	UNIDO/1248/4-1-80	UN-53-11	Raw water tank
128	UNIDO/1249/4-1-80	UN-53-13	Underground raw water storage tank
129	UNIDO/1250/4-1-80	UN-53-14	Soft water pump
130	UNIDO/1251/5-1-80	UN-54-12	Pump for brine circulation
131	UNIDO/1252/5-1-80	UN-54-14	Brine tank
132	UNIDO/1253/5-1-80	UN-54-15	Make up brine tank
133	UNIDO/1254/5-1-80	UN-55-12	Pump for chilled water circulation
134	UNIDO/1255/5-1-80	UN-55-14	Chilled water tank
135	UNIDO/1256/5-1-80	UN-59-2	Intermediate furnace oil storage tank
136	UNIDO/1257/5-1-80	UN-59-7	Pump for thermic fluid circulation
137	UNIDO/1258-A/18-12-79	-------	Hot insulation indoor
138	UNIDO/1258-B/18-12-79	-------	Hot insulation outdoor
139	UNIDO/1258-C/18-12-79	-------	Cold insulation
140	UNIDO/1258-D/18-12-79	-------	Cold & cold cum hot insulation indoor.
141	UNIDO/1258-E/18-12-79	-------	General specification for insulation
142	UNIDO/1259/18-12-79	-------	Globe valve
143	UNIDO/1260/18-12-79	-------	Gate valve
144	UNIDO/1261/18-12-79	-------	Needle valve
145	UNIDO/1262/18-12-79	-------	Audco plug valve
146	UNIDO/1263/18-12-79	-------	CI Non-return valve
147	UNIDO/1264/18-12-79	-------	Glass lined valve
148	UNIDO/1265/18-12-79	-------	Ball valve
149	UNIDO/1266/18-12-79	-------	C.I. gate valve
150	UNIDO/1267/18-12-79	-------	Rubberlined diaphragm valve
151	UNIDO/1268/18-12-79	-------	Vacuum guage
152	UNIDO/1269/18-12-79	-------	Pressure guage
153	UNIDO/1270/10-1-80	UN-53-16	Water meter
154	UNIDO/1271/11-1-80	-------	Electrical Motors.

ANNEXURE : C

ANNEXURE C.1 : LIST OF TECHNICAL CATALOGUE & DRAWINGS

A. CATALOGUE.

Sr.No.	Item	Qty.
1.	Instruction manual for Rotary Oil sealed vane type high vacuum pump - Tushniwal	1 No.
2.	Working and maintenance manual for DP Micro Pulveriser	1 No.
3.	Operation maintenance instruction manual of water-ring vacuum pumps J.B. Sawant Engg.	1 No.
4.	Maintenance overhaul instruction for bottom-Driven top discharge centrifuge	1 No.
5.	I.A.E.C. Steam Boiler instruction manual	1 No.
6.	Frick installation, operation service instruction for heavy duty industrial compressor	1 No.
7.	Frick, service parts list 2 cylinder size - 6" x 6" & 7" x 7"	1 No. + 1 No.
8.	Operator's manual spare parts catalogue - Khosla Air Compressor	1 No.
9.	Installation operation and maintenance instruction for permatower-Paharpur Cooling Tower	1 No.
10.	Machine - manual for glass lined equipments	1 No.
11.	Operating maintenance instruction manual for water softening DM Plant	1 No.
12.	General details of "Akay" Chemical pump	1 set
13.	Operation instruction manual for hot oil circulating unit-interest model TCE-126	1 No.
14.	Leaflet of 'Beacon' centrifugal pump type - 'L'	1 No.
15.	Catalogue on glass fittings	1 No.

(Annexure : C.1. ..... Contd. .....)

B. DRAWINGS:

Sr.No.	Item	Qty.
1.	GL. heat exchanger shell tube type Capacity - A M^2	78-GL-3857-00/4431C
2.	Agitator stuffing box for shaft dia 90 & 98	GL-406 Rev - 1
3.	Glasslined receiver Capacity - 500 ltr.	80-SM-4140/4431 B
4.	Glass lined reaction vessel Capacity - 100 ltr. flanged type	78 GL-3848 Rev-2 4431 A_1 & A_2
5.	Flowdiagram for water softening plant	TC/FD/FS/101/R_3
6.	Flowdiagram for water demineralising plant	TC/FD/DM/102/R_3
7.	100 ltr. glass assembly with tubular structure	Nil (Silica ware (P)Ltd)
8.	Details of service connection boiler type HN/10x10.5 kg/cm^2	BL-02-275
9.	1000 x 500 BO-To centrifuge	1200-001
10.	Line diagram for TCE-126 Thermic fluid heater	TCE-G-07E-80
11.	Thermic fluid heater-Electric model TCE-126	TCE-G-07A-80
12.	Isometric piping layout for D.M. Plant	TC/P/DM/106
13.	Isometric view for water softening plant	TC/P/FS/105
14.	Foundation details for water demineralising plant	TC/F/DM/104
15.	Steam heated 96 tray dryer for 100°C temp.	GPL/101/141
16.	General arrangement drg. DP Micro No. 1	2A-4623-32
17.	P & I Diagram for 10 TR brine chilling plant	C-2605

(Annexure C.1. ..... Contd.)

Sr.No.	Item	Qty.
18.	P & I Diagram for 60 TR water chilling plant	C-2603
19.	Plant Room layout refrigeration plant	C-2629
20.	Refrigeration pipes & pipe fittings	C-2654
21.	Distillation unit Sarabhai m/c.	$SMCH-A_3$ DS-1-Rev
22.	SVD - 12	$SMCH-A_1$-4546/A
23.	S.S. Nutche filter	$SMCH-A_1$-4547-Rev-1
24.	S.S. jucketed KBC filter	$SMCH-A_1$-4542-Rev-2
25.	Breather valve (Multitech services)	Nil
26.	Glass-lined piping layout	SHIP/UNIDO/53/Rev-2
27.	Equipment layout grid 1 to 5	SHIP/UNIDO/01A/rev-6
28.	Equipment layout grid 5 & 9	SHIP/UNIDO/013/Rev-6
29.	Utility-flow sheet	SHIP/UNIDO/04/Rev-2
30.	Flow sheet - chilled and brine chilling plant	SHIP/UNIDO/11/Rev-1
31.	Process flow sheet	SHIP/UNIDO/05/Rev-3
32.	Rycode electrical	8009-7
33.	Vacuum trap	

(Annexure : C.1. ..... Contd. .....)

DATE : 7-1-86

JOINT REPORT ON INSTALLATIONS AND TESTING OF MULTIPURPOSE PHARMACEUTICAL PILOT PLANT

Completed Civil/Mechanical/Electrical installations of all process and utilities plant's Equipments.

1. Steam boiler tested and commissioned in Nov - 85
2. Air compressors tested and commissioned in Oct - 85
3. Cooling tower system tested and commissioned in Dec. - 85.
4. Soft and D.M. water plants tested and commissioned in Dec - 85.
5. Hot oil unit tested mechanically and electrically in Jan - 86.
6. Vacuum pumps tested and commissioned in Dec - 85.
7. Circulation pumps of brine and chilling plants tested compressor motors tested.
8. Tray dryers tested with steam.
9. All reactor's/condenser's coil/jacket tested with water
10. All motors of equipments run on no-load for trial.
11. Service tank yard and transfer pumps installation over.

ANNEXURE : C.2

SUMMARY OF YIELDS OBTAINED IN EXPERIMENTAL BATCHES TAKEN IN CUBA BOTH IN LABORATORY & PILOT PLANT

1. ASPIRIN : (3 Batches) (Recycling of mother liquor)

Main Raw Material : Salicylic acid

Yield :

Yield of theory	Actual yield % of reported yield in docket	Guaranteed yield % of reported yield in docket
80.18%	94.5%	90.0%

Recovery (as per docket) :

	Reported	Obtained
Salicylic acid	6.4%	6.0%

Remarks :

Recovery of Salicylic acid has not been considered while computing the yield of Aspirin.

(Annexure : C.2. ..... Contd. .....)

2. DIPHENYL HYDANTOIN

Main Raw Material

Benzil

Batch No.	Yield (Theory)	Actual yield % of Rep. yield in docket	Guaranteed yield % of Rep. yield in docket
1	71.0%	91.7%	90.0%
2	71.0%	90.0%	90.0%

(Annexure : C.2. ..... Contd. .....)

3. DIAZEPAM

Main Raw Material : MCAB

Step and Batch No.	Product	Yield (Theory)	Actual yield % of Rep. yield in docket	Recovery (as per docket) Reported	Obtained
Step I :					
Batch 1	MCAB	76.2% (MCCAB)	99.0%	Benzene 66%	65%
Batch 2	MCAB	76.2% (MCCAB)	100.0%		
Step II :					
Batch 1	MCCAB	92.0% (Crude Diazepam)	89.4%		
Batch 2	MCCAB	92.0% (Crude Diazepam)	88.5%		
Step III :					
Batch 1	Crude Diazepam	77.0% (Pure Diazepam)	94.5%	Alcohol 78.5%	78.5%
Batch 2	Crude Diazepam	77.8% (Pure Diazepam)	95.9%		

YIELD OF DIAZEPAM ON BASIS OF STARTING RAW MATERIAL MCAB

Batch No.	Product	Yield (Theory)	Actual Yield % of Rep. yield in docket	Guaranteed Yield % of Rep. yield in docket
1.	MCAB	47.9%	94.6%	90.0%
2.	MCAB	47.9%	95.9%	90.0%

Remarks : Recovery of alcohol (50%) originally not planned. It has been reused in subsequent batches.

(Annexure : C.2. ..... Contd. .....)

4. PARACETAMOL

Main Raw Material : p-Aminophenol

Yield :

Yield of theory	Actual yield % of reported yield in docket	Guaranteed yield % of reported yield in docket
75.2%	90.0%	90.0%

(Annexure : C.2. ..... Contd. .....)

5. LIGNOCAINE HYDROCHLORIDE

Main Raw Material : m-Xylidine

Yield :

Step	Product	Yield (Theory)	Actual yield % of Rep. yield in docket
I	m-Xylidine	86.0% (Intermediate I)	100.0%
II	Intermediate I	90.0% (Lignocaine base)	93.7%
III	Lignocaine base	84.5% (Lignocaine HCl)	85.0%

Recovery as per docket

	Reported	Obtained
Benzene	75.0%	72.0%

Remarks :

By-product Acetone.

Lignocaine HCl

Main Raw Material	Yield (Theory)	Actual yield % of Rep. yield in docket	Guaranteed yield % of Rep. yield in docket
m-Xylidine	65.8%	85.0%	85.0%

(Annexure C.2. ..... Contd. .....)

6. METHYL SALICYLATE

Main Raw Material : Salicylic acid

Yield :

Yield (Theory)	Actual yield % of Rep. yield in docket	Guaranteed yield % of reported yield in docket
68.7%	95.0%	90.0%

Recovery (as per docket)

	Reported	Obtained
Salicylic acid	15.0%	13.6%

Remarks :

Recovery of salicylic acid is not calculated for the yield of Methyl salicylate.

By-product - Methanol.

(Annexure : C.2. ..... Contd. .....)

7. NICOTINAMIDE :

Main Raw Material : 3-Cyanopyridine.

Yield :

Batch No.	Starting material	Yield of theory	Actual yield % of Reported yield in dockets.	Guaranteed yield (Final product) in dockets.
1	3-Cyano-pyridine	62.0%	93.75%	90.0%
2.	3-Cyano-pyridine	62.0%	93.0%	90.0%

Recovery as per docket

Resin IRA-402 is recycled.

(Annexure : C.2. ..... Contd. .....)

8. NICKETEAMIDE

Main Raw Material : Nicotinic acid.

Yield :

Batch No.	Starting material	Yield of theory	Actual yield % of reported yield in dockets	Guaranteed yield (Final product) in dockets
1.	Nicotinic acid	77.0%	92.8%	85.0%
2.	Nicotinic acid	77.0%	98.0%	85.0%

Recovery (as per docket) :

	Reported	Obtained
Thionyl chloride	68.75%	98%
Toluene	83%	100%

(Annexure : C.2. ..... Contd. .....)

9. CLOFIBRATE

Main Raw Material : 1. p-Chlorophenol
2. Clofibric acid.

Yield :

Step & Batch No.	Starting Material	Yield of Theory	Actual Yield % of Reported yield in dockets
Step I :			
Batch 1	p-Chlorophenol	59.5% (Clofibric acid)	100%
Batch 2	p-Chlorophenol	59.5% (Clofibric acid)	104%
Step II :			
Batch 1	Clofibric acid	88.5% (Clofibrate)	92.8%
Batch 2	Clofibric acid	88.5% (Clofibrate)	100%

Recovery (as per docket) :

Step I :		Reported	Obtained	
Batch 1	Acetone	33%	100%	Both batches
Batch 2	$CHCl_3$	47%	100%	
Step II :				
Batch 1	Toluene	85%	100%	
Batch 2	Toluene	85%	100%	

Remarks :

Recovered acetone is to be used in two subsequent batches as per docket. (Recovered alcohol is by-product).

YIELD ON BASIS OF p-CHLOROPHENOL

Batch No.	Starting Material	Yield of theory	Actual Yield % of Rep. yield in dockets	Guaranteed yield (Final Product) in dockets
1	p-Chlorophenol	52.6%	99.2%	85.0%
2	p-Chlorophenol	52.6%	104.0%	85.0%

(Annexure : C.2. ..... Contd. .....)

10. PROCAINE HYDROCHLORIDE

Main Raw Material : Benzocaine

Yield :

Step	Starting Material	Yield of theory	Actual Yield % of Reported yield in dockets.
I	Benzocaine	68% (Procaine HCl crude)	95.5%
II	Crude Procaine HCl	76% (Pure Procaine HCl)	101%

Recovery (as per docket) :

		Reported	Obtained
Step I	DEAE	44.6%	44.6%
	Toluene	80%	80%
Step II	Mixed alcohol	74.0%	98.0%

PROCAINE HYDROCHLORIDE YIELD ON BASIS OF BENZOCAINE

Starting material	Yield of theory	Actual yield % of Rep. yield in dockets	Guaranteed yield (Final Product) in dockets
Benzocaine	51.7%	96.0%	95%

(Annexure : C. 2 ..... Contd. .....)

11. CHLORDIAZEPOXIDE

Main Raw Material : CAB

Yield :

Step and Batch No.	Starting Material	Yield of theory	Actual yield % of reported yield in dockets
Step I :			
B.No. 1	CAB	95.0% (Intermediate I)	100%
B.No. 2	CAB	95.0% (Intermediate I)	100%
Step II :			
B.No. 1	Intermediate I	65.7% (Intermediate II)	96%
B.No. 2	Intermediate I	65.7% (Intermediate II)	96%
Step III :			
B.No. 1	Intermediate II	78.0% (Intermediate III)	96.0%
B.No. 2	Intermediate II	78.0% (Intermediate III)	96.0%
Step IV :			
B.No. 1	Intermediate III	-	84.0%
B.No. 2	Intermediate III	-	84.0%

Recovery as per docket			Reported	Obtained
Step III	B.No. 1&2	Chloroform	61%	70%
Step IV	B.No. 1&2	Methanol	69%	95%

Remarks : 10% Extra chloroform recovery has been suggested. Recovery of acetone has been avoided.

CHLORDIAZEPOXIDE YIELD ON BASIS OF CAB

Starting material	Yield of theory	Actual yield % of Rep. yield in dockets	Guaranteed yield (Final product) in dockets	Recovery as per docket	
				Rep.	Obtained
CAB	40%	85%	80%	Ethanol 70%	75%

(Annexure : C.2. ..... Contd. .....)

12. NALIDIXIC ACID

Main Raw Material : 2-Amino-6-methyl pyridine

Yield :

Step and Batch No.	Starting Material	Yield of theory	Actual yield % of Rep. yield in dockets
Step I			
B.No. 1	2-Amino-6-methyl-pyridine	86.7% (Intermediate I)	100%
B.No. 2	2-Amino-6-methyl-	86.7% (Intermediate I)	100%
Step II :			
B.No. 1	Intermediate I	73.8% (Intermediate II)	90%
B.No. 2	Intermediate I	73.8% (Intermediate II)	90%
Step III :			
B.No. 1	Intermediate II	50.0% (Intermediate III)	100%
B.No. 2	Intermediate II	50.0% (Intermediate III)	100%
Step IV :			
B.No. 1	Crude Nalidixic acid (Int. III)	91.0% (Nalidixic acid)	85%
B.No. 2	Crude Nalidixic acid (Int. III)	91.0% (Nalidixic acid)	85%

Recovery (as per docket) :			Reported	Obtained
Step II.	B.No.1	Diphenyloxide	87%	82.6%
	B.No.2	Pet. ether	83%	74.7%
Step III.	B.No. 1	DMF	50%	50%
	B.No. 2	DMF	50%	50%
Step IV	B.NO. 1	Acetic acid	78%	74%
	B.No. 2	Acetic acid	78%	74%

Remarks : Xylene is recovered 80% of theory which was not planned as per docket.

YIELD OF NALIDIXIC ACID ON BASIS OF 2-AMINO-6-METHYL PYRIDINE

Batch No.	Main Raw Material	Yield of theory	Actual yield % of Rep. yield in docket	Guaranteed yield % of Rep. yield in docket
1.	2-Amino-6-methyl pyridine	29%	85.7%	80%
2.	2-Amino-6-methyl pyridine	29%	82.8%	80%

(Annexure : C.2 ..... Contd. .....)

13. METRONIDAZOLE

Main Raw Material : 2-Methyl-5-Nitroimidazole.

Yield :

Product	Main Raw material	Yield of theory	Actual yield % of reported yield in docket
Step I : (Crude Metronidazole)	2-Methyl-5-nitroimidazole	54%	100%
Step II (Pure Metronidazole)	Crude Metronidazole	71.4%	100%

Recovery (as per docket)

	Reported	Obtained
2-Methyl-5-nitroimidazole	18.8%	19.0%
Formic acid	73%	70.0%
Ethanol	70.8%	70.0%

Remarks : Recovered 2-Methyl-5-nitroimidazole is considered for the yield calculations.

YIELD OF METRONIDAZOLE ON BASIS OF 2-METHYL-5-NITROIMIDAZOLE

Product	Main raw Material	Yield of theory	Actual yield % of rep.yield in dockets	Guaranteed yield % of rep. yield in dockets
Metronimazole	2-Me-5-NO_2-imidazole	39.0%	100%	85%

(Annexure : C.2 ..... Contd. .....)

14. PHENYLBUTAZONE

Main Raw Material : Hydrazobenzene

Yield :

Product	Main Raw Material	Yield of theory	Actual yield % reported yield in dockets
Step I :			
Crude phenyl -butazone	Hydrazobenzene	68.57% (Crude Phenyl-butazone)	100%
STEP II :			
Purification	Crude Phenyl-butazone	80%	97.5%

Recovery (as per docket)

	Reported	Obtained
MCB	57.8%	58.0%
Methanol	62.0%	60.0%

YIELD OF PHENYLBUTAZONE ON BASIS OF HYDRAZOBENZENE

Product	Main raw material	Yield of theory	Actual yield % of rep.yield in dockets	Guaranteed yield % of rep. yield in dockets
Phenyl-butazone	Hydrazo-benzene	54.8%	97.5%	95.0%

(Annexure : C.2. ..... Contd. .....)

15. INDOMETHACIN

Main Raw Material : p-Anisidine

Yield :

Product	Main Raw Material	Yield of theory	Actual yield % of rep. yield in dockets.
Step I :			
NAPH	p-Anisidine	66.7% (NAPH)	100%
Step II :			
Crude Indomethacin	NAPH	43.0% (Crude Indomethacin)	98.8%
Step III :			
Pure Indomethacin	Crude Indomethacin	91.3% (Pure Indomethacin)	100%

Recovery (as per docket)

	Reported	Obtained
Toluene	76%	75%
Ethylacetate	71%	70%

YIELD OF INDOMETHACIN ON BASIS OF p-ANISIDINE

Product	Main raw material	Yield of theory	Actual yield % of rep. yield in docket	Guaranteed yield % of rep. yield in dockets.
Indomethacin	p-Anisidine	28.6%	90.0%	90.0%

(Annexure : C.2. ..... Contd. .....)

SOME TYPICAL EXAMPLES ARE GIVEN BELOW IN DETAIL

1. ASPIRIN :

3 Batches form a set. (Mother liquor from batch 1 is recycled in batch 2 and from 2 in batch 3).

Main Raw Material	Batch No. 1	Batch No. 2	Batch No. 3
Salicylic acid	125.0 kg.	112.5 kg.	112.5 kg.
Acetic anhydride	129.0 kg.	108.5 kg.	108.5 kg.
Acetic acid	221.0 kg.	-	-
Conc. Sulphuric acid	0.8 kg.	-	-
Mother liquor (Previous batch)	-	206.5 kg.	206.5 kg.
Acetic acid (Washings)	45.0 kg.	45.0 kg.	45.0 kg.

YIELD FOR A SET OF 3 BATCHES :

Theoretical yield	Reported Yield (Final product)		Obtained Yield		Guaranteed Yield (as per docket)	
	Weight	% of theory	Weight	% of report (as per docket)	Weight	%
456.5 kg. (Total)	366.0 kg.	80.18%	346.0 kg.	94.5%	327.0 kg.	90.0%

RECOVERY

Salicylic acid : 22.0 kg. (6.0% against 6.4% as per docket)

Acetic acid : 19.4% as a byproduct (as per docket)

REMARKS :

Recovery of salicylic acid has not been considered while computing yield of Aspirin.

(Annexure : C.2. ..... Contd. .....)

2. PARACETAMOL

p-Aminophenol . 160.3 kg.

YIELDS :

Theoretical yield	Reported yield (Final product)		Obtained yield		Guaranteed Yield (as per docket)	
	Weight	% of theory	Weight	% of report (as per docket)	Weight	%
221.6 kg.	166.6 kg.	75.2%	158.0 kg	90.0%	158.0 kg.	90.0%

(Annexure : C.2 ..... Contd. .....)

3. DIAZEPAM

Raw Material	Steps	Batch No. 1	Batch No. 2
MCAB	I	66.5 kg.	66.5 kg.
MCCAB	II	66.0 kg.	66.0 kg.
Crude Diazepam	III	48.0 kg.	47.5 kg.

YIELDS :

Step & Batch No.	Product	Theoretical yield	Reported yield Weight	Reported yield % of theory	Obtained yield Weight	Obtained yield % of report (as per docket)
Step I :						
B.NO. 1	MCCAB	87.2 kg.	66.5 kg.	76.2%	66.0 kg.	99.0%
B.NO. 2	MCCAB	87.2 kg.	66.5 kg.	76.2%	66.5 kg.	100.0%
Step II :						
B.NO. 1	Crude Diazepam	52.3 kg.	53.7 kg.	92.0%	48.0 kg.	89.4%
B.NO. 2	Crude Diazepam	52.3 kg.	53.7 kg.	92.0%	47.5 kg.	88.5%
Step III :						
B.No. 1	Pure Diazepam	48.0 kg.	37.0 kg.	77.0%	35.0 kg.	-
B.No. 2	Pure Diazepam	47.5 kg.	36.6 kg.	77.0%	35.8 kg.	-

RECOVERY

Step I : Benzene : 340 kg. (65.0% as per docket)
Step II : Alcohol : 300 kg. (50%)
Step III : Alcohol : 550 kg. (78.5% as per docket)

REMARKS

Recovery of alcohol (50%) originally not planned. It has been reused in subsequent batches.

DIAZEPAM YIELD ON BASIS OF MAIN RAW MATERIAL :

Main Raw Material	Batch No. 1	Batch No. 2
MCAB	66.5 kg.	66.5 kg.

YIELDS

Theoretical yield	Reported Yield Weight	Reported Yield % of theory	Obtained yield Weight	Obtained yield % of report (as per docket)	Guaranteed Yield Weight	Guaranteed Yield %
B.No. 1						
77.0 kg.	37.0 kg.	47.0%	35.0 kg.	94.6%	33.3 kg.	90%
B.No. 2						
77.0 kg.	37.0 kg.	47.9%	35.3 kg.	95.9%	33.3 kg.	90%

(Annexure : C.2. ..... Contd. .....)

4. LIGNOCAINE HYDROCHLORIDE

Raw Material :

Step I	m-Xylidine	:	64.0	kg.
Step II	Intermediate I	:	90.0	kg.
Step III	Intermediate II	:	96.0	kg.

YIELDS :

Product	Theoretical yield	Reported yield		Obtained yield		Recovery
		Weight	% of theory	Weight	% of report (as per docket)	
Step I						
m-Xylidine	104.5 kg.	90.0 kg.	86.0%	90.0 kg.	100%	Benzene 200 kg. (72% against 75% of docket)
Step II						
Intermediate I	136.7 kg.	96.0 kg.	90.0%	90.0 kg.	93.7%	Benzene 300 kg. (72 % of docket)
Step III						
Intermediate II	118.3 kg.	100.0 kg.	84.5%	85.0 kg.	85%	

LIGNOCAINE HYDROCHLORIDE YIELD ON BASIS OF MAIN RAW MATERIAL

m-Xylidine : 64.0 kg.

Theoretical yield	Reported yield		Obtained yield		Guaranteed yield	
	Weight	% of theory	Weight	% of report (as per docket)	Weight	%
152.0 kg.	100 kg.	65.8%	85.0 kg.	85.0%	85.0 kg.	85.0%

ANNEXURE : C.3. : Q.C. REPORTS OF A FEW PRODUCTS MANUFACTURED ACCORDING TO KNOW-HOW SUPPLIED

QUALITY CONTROL REPORT

PRODUCT : PARACETAMOL TESTED AS PER B.P.

Description	:	White crystalline powder, odourless, taste bitter.
Solubility	:	Conforms
Identification	:	Conforms
Melting point	:	169-170°C (Limit : 169-172°C)
Lead	:	Passes (Limit : 10 PPM)
4-Aminophenol	:	Passes (Limit : 0.005% w/v)
Loss on drying	:	0.5003 (Limit : Not more than 0.5%)
Sulphated ash	:	Negligible (Limit : Not more than 0.1%)
Assay	:	100.25% w/w (Limit not less than 98% on dry basis)

The sample conforms with B.P. tests in all respects.

(Annexure C.3. ..... Contd. .....)

PRODUCT : PROACINE HYDROCHLORIDE

		TESTED AS PER B.P.
Description	:	White crystalline powder, odourless, taste salty and bitter followed by local anaesthesia of the tongue.
Solubility	:	Conforms
Identification	:	A, B, C, conforms
Appearance of the solution	:	Clear and colourless, Passes the test.
pH	:	5.5 (Limit : 5.0-6.5)
Heavy metals	:	Passes (Limit : 1 PPM)
Iron	:	Passes (Limit : 10 PPM)
Readily carbonisable substances	:	Passes
Loss on drying	:	0.208% w/w (Limit : Not more than 0.5%)
Sulphated ash	:	0.07% w/v (Limit : Not more than 0.1%)
Assay	:	100.13% on dry basis (Limit : Not less than 99.0% on dry basis)

The sample conforms with B.P. Tests in all respects.

(Annexure : C.3. ..... Contd. .....)

PRODUCT : ASPIRIN

		TESTED AS PER USP
Description	:	White crystalline powder, and odourless.
Solubility	:	Conforms
Identification	:	Conforms
Loss on drying	:	0.0175% (Limit : Not more than 0.05%)
Residue on ignition	:	Negligible (Not more than 0.05%)
Chloride	:	Passes (Limit : 0.014%)
Sulphate	:	Passes (Limit : 0.04%)
Non-Aspirin salicylates	:	Passes the test (Limit : 0.1%)
Heavy metals	:	Passes (Limit : 0.001%)
Readily carbonizable substances	:	Passes
Assay	:	99.8% (on dry basis) (Limit : Not less than 99.5% and not more than 100.5% on the dried basis)

The sample conforms to USP tests in all respects.

(Annexure : C.3. ..... Contd. .....)

PRODUCT : LIGNOCAINE HYDROCHLORIDE

TESTED AS PER I.P.

Description	:	White crystalline powder, odourless, taste slightly bitter followed by a sensation of numbness.
Solubility	:	Conforms
Identification	:	A, B, C, Conforms
Acidity	:	Passes
Melting range	:	76°C (Limit 76 to 79°C.)
Water	:	5.73% w/w (Limit 5 to 7.5% w/w)
Sulphated ash	:	Negligible (Limit not more than 0.1%)
Assay	:	99.3% (Limit : not less than 99.0% and not more than 100.5%) on anhydrous basis.

The sample conforms with I.P. Tests in all respects.

(Annexure : C.3. ..... Contd. .....)

PRODUCT : NICOTINAMIDE

		TESTED AS PER U.S.P.
Description	:	White crystalline powder, Odourless and has a bitter taste. Its solution is neutral to litmus.
Solubility	:	Conforms
Identification	:	A and B conforms
Melting range	:	128-129°C. (Limit between 128 to 131°C.)
Loss on drying	:	Negligible (Limit : Not more than 0.5%)
Residue on ignition	:	Negligible (Limit : Not more than 0.1%)
Heavy metals	:	Passes (Limit : 0.003%)
Readily carbonizable substances	:	Passes
Assay	:	99.33% w/w (Limit : Not less than 98.5% and not more than 101.0%)

The sample conforms with U.S.P. tests in all respects.

(Annexure : C.3. ..... Contd. .....)

PRODUCT : NIKETHAMIDE

TESTED AS PER B.P.

Description	:	An oily slightly yellowish liquid with a slight characteristic odour and a slightly bitter, then burning taste leaving a faint warm sensation on the tongue.
Solubility	:	Conforms
Identification	:	A, B, C, conforms
Appearance of the solution in water	:	Passes
Freezing point	:	23°C. (Limit : 23 to 25°C.)
Relative density	:	1.06 (Limit : 1.06 to 1.066)
Refractive index	:	1.525 (Limit : 1.524 to 1.526)
pH	:	7 (Limit 6.5 to 7.8)
Heavy metals	:	Passes (Limit: 10 PPM)
Impurities with nitrated nucleus	:	Passes
Oxidisable substances	:	Passes
Water	:	0.06% (Limit : Not more than 0.2%)
Sulphated ash	:	Negligible (Limit not more than 0.1%)
Assay	:	99.4% w/w (Limit : not less than 98.5%)

The sample conforms with B.P. tests in all respects.

(Annexure : C.3. ..... Contd. .....)

PRODUCT : METHYL SALICYLATE :

TESTED AS PER U.S.P.

Description	:	Pale yellow liquid having characteristic odour and taste of Wintergreen.
Solubility	:	Conforms
Identification	:	Conforms
Solubility in 70% alcohol	:	Conforms
Specific gravity	:	1.1842 (Limit : 1.180 to 1.185)
Refractive index	:	1.5340 (Limit : 1.535-1.538 at 20°C.)
Heavy metal	:	Passes (Limit : 0.004%)
Assay	:	99.68% w/w (Limit not less than 98.0% and not more than 100.5%)

The sample conforms with USP tests in all respects.

(Annexure : C.3. ..... Contd. .....)

PRODUCT : METRONIDAZOLE

TESTED AS PER U.S.P.

Description	:	White to odourless crystalline powder.
Solubility	:	Conforms
Identification	:	A, B, C, conforms
Melting range	:	159°-160°C. (Limit 159 to 163°C.)
Loss on drying	:	0.31% (Limit not more than 0.5%)
Residue on ignition	:	Negligible (Limit not more than 0.1%)
Heavy metals	:	Passes (Limit : 0.005%)
Non basic substances	:	Passes
Assay	:	99.45% w/w (Limit : Not less than 99.0% and not more than 101.0% on dry basis)

The sample conforms with U.S.P. Tests in all respects.

ANNEXURE : C.4.

EXPLANATIONS FOR THE TECHNOLOGIES OFFERED; PROBLEMS LIKELY TO BE FACED; AND SOLUTIONS FOR THE PROBLEMS

ASPIRIN :

The proportions of AcOH, Salicylic acid and H_2SO_4 given for the manufacture of Aspirin were shown to be heavily weighted in favour of Aspirin at the end of the reaction. It was also shown that the whole of Aspirin would be in solution at the end of the reaction. It was further shown that the given rates of cooling ensures the formation of fine crystals of Aspirin free from salicylic acid crystallising out. It was also shown that the product coming out of the reaction was of pharmaceutical grade, after washing with cold water, and that the yields were never less than the guaranteed yields.

It was also demonstrated that rapid cooling would give Aspirin having higher than the permitted free salicylic acid content. It was pointed out that in the event of any breakdown of chilling arrangement, the batch is best heated back to the right temperature and the cooling process gone over again according to the docket. This was demonstrated in the laboratory. In one of the pilot plant batches in Cuba the problem of unregulated cooling was encountered and solved in the above manner. These were explained to the Cuban chemists and additional notes were incorporated in the manual.

(Annexure : C.4. ..... Contd.-.....)

PARACETAMOL :

In the case of paracetamol manufacture, some drums of p-aminophenol had suffered damages and the contents were found coloured and contaminated with metallic impurities.

A process of purification p-aminophenol which involved the isolation of its sulphate from aqueous medium thus ensuring the absence of metallic impurities, liberation of the base from the sulphate and subsequent acetylation of p-aminophenol to paracetamol was demonstrated. This was done to help the Cuban chemists to solve unforeseen problems. This should have given them added confidence that chemical problems can be solved with appropriate efforts. This will give them courage to undertake manufacture p-aminophenol in future, if they so desire.

NALIDIXIC ACID :

In the case of Nalidixic acid, the purification technique was designed to give almost colourless crystals. The technical trick of dissolving the crude acid in dilute ammonia solution and boiling off the excess of ammonia and preparing a supersaturated solution of nalidixic acid in water by adjusting the pH with acetic acid and allowing the product to crystallise out, was demonstrated. Similarly, the best technique to avoid formation of coloured by-products in the cyclisation step of the condensation product of ethoxymethylene malonate and 2-amino-6-methylpyridine, was demonstrated.

(Annexure : C.4. ..... Contd. .....)

METRONIDAZOLE :

In Metronidazole manufacture, the importance of pH during N-hydroxyethylation of 5-nitro-2-methylimidazole was explained to Cuban chemists. The safe handling of ethylene oxide was also demonstrated. Further, as a stimulus to indigenous metronidazole manufacture, a good simple technique for manufacturing 2-methylimidazole from ammonia, acetaldehyde and glyoxal was demonstrated without cumbersome concentrations and extractions. Further a safe method of manufacturing 5-nitro-2-methylimidazole from 2-methylimidazole, via. its easily-prepared nitrate salt, was demonstrated. The Cuban chemists took a batch on their own.

Even though, this was outside the purview of the contract, it was done with a view to stimulating the growth of basic industry in Cuba. 5-Nitro-2-methylimidazole has a considerable export potential and all the equipment required for its manufacture have been provided for. The Cuban technologists can at any time undertake the manufacture of 5-nitro-2-methylimidazole, if they so decide.

DIPHENYLHYDANTOIN :

Similarly, the feasibility of backward integration of technology in the manufacture of diphenylhydantoin has been explained to them. Instead of benzil, they can start from benzaldehyde.

(Annexure : C.4. ..... Contd. .....)

NICOTINAMIDE :

In Nicotinamide manufacture, the handling of ion-exchange resins with special emphasis on activation and regeneration has been explained and demonstrated. The importance of storing resins in the chloride form has also been explained. Detailed information regarding quantities of acids and alkalies and temperature and time to regenerate or reactivate resins has been supplied. This will help them to appreciate the use of ion-exchange resins in chemical technology. This will also help them to solve some problems faced in D.M. water plants.

INDOMETHACIN :

In Indomethacin, it was observed that some batches had lower melting point, This was analysed and could be attributed to minor amounts of p-chlorobenzoic acid present as an impurity. A process was designed to eliminate the p-chlorobenzoic acid impurity. The crude product is suspended in water (1:2). The slurry is neutralised to pH 7.3 with 20% NaOH carbon treated and filtered. It is then treated with 25% w/v calcium chloride solution. The precipitated calcium salt of Indomethacin is washed with water and then with acetone. A suspension of the calcium salt in t-butanol is then acidified to pH 2.5 with 2% HCl, cooled and filtered. The product is then crystallised from t-butanol.

In this manner, the technology transfer was not confined to demonstration of documented technology and reproduction of results. Experience and expertise of SRC was transferred to Cuban chemists using problems encountered during technology transfer.