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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

VIENNA INTERNATIONAL CENTRE

P.O.BOX 300, A-1400 VIENNA, AUSTRIA

TELEPHONE: 211 310 TELEGRAPHIC ADDRESS: UNIDO VIENNA TELEX: 135612 uno a FAX: 232156

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FINAL REPORT

Volume 1

Summary

ABOUT SERVICES RELATING TO THE

DETAILED STUDY FOR THE ESTABLISHMENT OF THE SHAHID MODARRES

INDUSTRIAL PHARMACEUTICAL COMPLEX

UNIDO CONTRACT NO 91/200
UNIDO PROJECT NO SF/IRA/90/901
ACTIVITYCODE:JI3422

prepared by

Univ. Doz. Dipl. Ing. Mag. Pharm.
Dr. Christian R. Noe
Zivilingenieur für Technische Chemie

A-1130 Wien, Stoessigasse 9
Tel. (0)222/877 55 33; (0)222/58 801 5019
Auto Tel. 663/17 223
Tlx. 135392 NOE A
Fax (0)222/58 60 573

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1. PREAMBLE

The present final report about services relating to the detailed study for the establishment of the SHAHID MODARRES Industrial Pharmaceutical Complex consists of the following volumes:

Volume 1: Summary -- Findings and Recommendations
Volume 2: Product Files
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Part 2: Sector 2
Part 3: Sector 3
Part 4: Sector 4
Volume 3: Unit Files
Annexes

The project team has appreciated the full support of UNIDO staff, above all of Dr.A.Tcheknavorian-Asenbauer, Director, Industrial Operations Technology Division, whose personal experience in the pharmaceutical sector has brought many decisive contributions in the implementation of the study. Dr.M.Sanchez-Osuna, Officer in the Pharmaceutical Sector, and Dr.Z.Csizer, Senior Interregional Adviser, have not only contributed through their technical knowledge, but also by co-ordinating the co-operation of the Iranian experts with the project team.

As a special feature this study was through most phases carried out in a co-operation between the expert team and the expert representatives of SHAHID MODARRES Drug Industries Company (SMDI), led by Dr.R.Ejeian, Managing Director of SMDI. During the time between the First and the Second Interim Meeting Mr.A.Hojaji, Deputy Managing Director of SMDI, and Prof.Dr.M.Fooladi stayed with the project team to work jointly on aspects of technology. In the time between Second Interim Meeting and submission of the Draft Final Report, Dr.R. Ejeian and Mr.A.F.Jahromi, Technical Manager of SMDI, joined the team which in this phase was working mainly on plant lay out and engineering aspects. As a result of the co-operation many strategic questions arising during the study could be discussed and brought to an immediate decision. Furthermore the careful study of the Iranian experts helped to delete weak points and mistakes from the report at an early stage. The technical competence of the Iranian experts was appreciated by the project team and has influenced the outcome of the study significantly.

2. EXECUTIVE SUMMARY - CONCLUSIONS AND RECOMMENDATIONS

Although all informations obtained during the study have been collected and presented in a condensed form, the final report comprises almost 3000 pages due to the complexity of the project. Even the Summary, which is presented in Volume 1, consists of more than 100 pages. Therefore it is difficult to present the essence of the study in a very short executive summary. This chapter therefore will cover only some of the most important aspects.

The results of the reassessed financial analysis indicate that an initial investment of more than 332 million US$ is required to set up the plant of which about 56% will be investment denominated in foreign exchange. The company is expected to receive about 59 million US$ for annual sales, operating cost will be almost 56 million US$. These figures indicate that there is only a small margin between operating cost and sales revenues, which will not cover depreciation.

From this analysis it can be seen that the economical aspects of the project are not yet perfect and require optimization. Financial analysis shows that out of 48 products only 24 earn their operating cost. Moreover only 8 products will be sufficiently profitable to cover their pertinent depreciation, in addition to operating cost. To improve this situation the following recommendations are given:

1. Eliminate products with unfavourable profitability figures. Based on the medical evaluation proposals have been made to introduce other products to the project, which should now be checked for their economic profitability.

2. Consider a change of the product mix by the introduction of new, high margin products, in case given even taking licenses for products still under patent protection.

3. As a result of the First Interim Meeting, capacities were increased, in many cases doubled. But even by doubling production quantities the scales would in several cases not reach economic levels. An increase of capacity of products exhibiting a good relation of their percentage of total sales versus their percentage of total operating cost and of total physical plant cost should be considered.

4. In case of an obligation of SMDI to take up production also of products with very bad figures of profitability, a change in plant utilization should be considered by reducing production quantities of such products to a required minimum and placing them into multi purpose plants. Products with better profitability could be placed in single lines instead.

5. As it can be seen from the sensitivity analysis of the internal rate or return (IRR) by COMFAR the profitability is not very much influenced by the initial investment. Even an alteration of investment by 30% will not change the IRR significantly. The most efficient measures for improving the profitability of the project are

- increase of sales revenues
- decrease of operating costs.

6. The effect of utilization of larger capacity equipment has been discussed at length. UNIDO in an analysis has laid particular emphasis to evaluate the effects of using larger reactors with the following result: In the capacity range of 0.5 to 20.0 m^3, the rule applies: the higher the capacity, the lower the relative investment. The same would be true for construction and installation costs and most of the upstream and downstream equipment except centrifuges and driers. Since however, most of the end products are solid and therefore bound to the use of centrifuges and driers, the overall economy of the project by further increasing reactor sizes would not be significantly changed.

7. In case of financing difficulties with respect to the initial investment consider a purchase of equipment from Central Eastern European and Indian manufacturers, which is as a rule cheaper than equipment from the established manufacturers in Western Europe.

8. A decrease of the raw material inventory from one year to 6 months would reduce the total investment by approximately 7%, would however increase the risk of continuous raw material supply.

9. A phase-wise implementation that would put into operation the units of highest margin first would result in better economics of the project as a whole, since these units would already generate revenues and trained personnel, both of which could be utilized at later stages.

10. Take a decision to work out a strategic profile for the SHAHID MODARRES Industrial Pharmaceutical Complex as proposed, which will allow to concentrate efforts to specific areas of interest. Once the decision for a profile has been met, planning measures should aim at improving further this profile.

11. Develop a long term research concept and co-operations based on the strategic profile of the company. Do not invest into research and development facilities before having a clear view on the long term benefits of these units. Since at the present stage no economy

could be made out with the research and development facilities, the investment requirements for these units were left out from the financial analysis of the subject study.

12. The objective of the project is the establishment of a pharmaceutical chemicals production in the SHAHID MODARRES complex. When the manufacture of pharmaceutical chemicals is well established, the Authorities of the Islamic Republic of Iran could consider a further step to create a fully integrated pharmaceutical industry. Based on industrial experience, it is well known that even with relatively small capacities, formulation and packaging has much higher margins than production of pharmaceutical chemicals. Therefore as a long term development goal, it is suggested that a fully integrated pharmaceutical industrial complex should be established in addition to the synthesis of pharmaceutical chemicals only.

3. GENERAL BACKGROUND INFORMATION AND OBJECTIVES OF THE PROJECT

The Islamic Republic of Iran has been all the time fully aware of the importance of supply of the population with medication. With this respect under the supervision of the Ministry of Industry, the National Iranian Industrial Organization (NIIO) has taken an important step by establishing SHAHID MODARRES Drug Industries Company and offering this company land and infrastructural facilities. The main aim of SHAHID MODARRES is to set up a pharmaceutical chemicals production complex, which will allow to satisfy the demand of the country for many of the most important drugs. The list of compounds to be manufactured amounts for 50 different products, so that the project of establishing this pharmaceutical company is one of the most ambitious pharmaceutical projects to the day. After a planning period, in which the requirements of the project were established, SMDI has decided to co-operate with UNDP/UNIDO in the implementation of the project. A contract was awarded to carry out the present detailed study.

The immediate objective of the subject project is to allow the Government of the Islamic Republic of Iran to take the appropriate decisions on the establishment of the SHAHID MODARRES Pharmaceutical Complex. The report shall provide the required data for the preparation of tender documents and for further planning by the SHAHID MODARRES staff.

The long term objective of the project is to contribute to the establishment of production of pharmaceutical chemicals in the Islamic Republic of Iran thus contributing to the

development of the country towards greater independence in an industrial field of very great social importance.

The contractor has had opportunity to gain experience in pharmaceutical project planning for many years. Among many other projects he has also been involved in UNIDO's Darou Paksh Project, a project which has the same general objective as the present project: to establish pharmaceutical production in the Islamic Republic of Iran. Although the Darou Paksh Project is very small compared to the activities foreseen in the present project, the experience from that project has provided a lot of help in the preparation of the present study. The Darou Paksh Project is almost implemented. Many aspects which have to be considered with transfer of technology to Iran have only come up during the implementation of that project. Therefore this unique situation allowed to have a very realistic and specific approach in the present study.

4. WORK PLAN

4.1. GENERAL CONSIDERATIONS

A special feature of the present project is its complexity. A typical pharmaceutical project would foresee the establishment and transfer of technology for the production of one or few pharmaceutical chemicals. The requirement to cover 50 products in this study, which is probably one of the most comprehensive requests in this field, is a great challenge, not only because of the size of the project and the investment concerned, but above all because of the complexity of the project, which renders the performance of the study as the most critical criterion. The great number of data and figures, which are required for evaluation of one product, is multiplied by 50, which does not only increase the complexity in all evaluations, but also has significant effects concerning time consumption. Thus 1200 patents had to be evaluated, which alone took 2 months of working time of a top expert. The print out of a 3000 pages report from the computer using a laser printer is also very time consuming. Such simple aspects posed an additional challenge, since it was requested that the report be prepared within an extremely short time period.

To be in a position to fulfill the Terms of Reference a strategy has been applied for the preparation of the report, by which a computer data base was structured and set up from the beginning of the work, which allowed immediate integration of arriving data to the report and which also has given the possibility to correlate data for evaluation purposes. This approach has not only allowed to submit Interim Reports on occasion of the technical

meetings at UNIDO Headquarters, but also has secured availability of up to date technical information at any phase of the project.

4.2. THE PROJECT GROUPS

Immediately after signing the contract the project team was established. Due to the complexity of the project and the broad scope of required technical experience it was decided to form several project groups. Responsibility in specific sub activities was assigned to the teams A to E. Group F was established to maintain local contacts to the Iranian counterpart. Group G is an Italian subcontractor, who has worked on several technologies and has prepared the lay - out for two production units.

Project Group Pharm/A:	Products and Technologies Vienna/Austria
Project Group Chem/B:	Chemical Processes and Patents Vienna/Austria
Project Group Tech/C:	Plant Lay - Out, Engineering Szazhalombatta/Hungary
Project Group /D	Medical Product Evaluation Frankfurt/Germany
Project Group Fina/E	Equipment, Financial Analysis Vienna/Austria
Project Group Iran/F	Local Situation Iran Teheran/Iran
Project Group Italy/G	Italian Sources Milan/Italy

4.3. TIME SCHEDULE

The project time schedule followed the lines given in the offer dated April 19th, 1991. Expert fielding started with assignment of the contract on October 1st, 1991. In the first phase of the work assessment of technologies was the central activity. This phase ended

with the First Interim Meeting at UNIDO, which took place from January 20th to 24th, 1992. In this meeting final decisions were met concerning selection of products, quantities and wherever feasible technologies. The next phase of the project resulted in a proposal for a general concept of the plant. Approval on this concept was achieved during the Second Interim Meeting held at UNIDO in the week from April 13th, 1992. The next phase of the study, concerning mainly engineering work and financial analysis ended only shortly before submission of the Draft Final Report, which was finalized in the time from May 11th to May 23rd. The Draft Final Report reflected already in a concise manner the structure of the Terms of Reference. There was a 104 page Summary, a second Volume in 4 parts, containing the product files of the 4 foreseen sectors, a third Volume consisting of the unit files and technical drawings and an Addendum having several volumes such as follows:

- Detailed Report on the Results of the Contacts to License Holders
- Cost and Revenue Estimates - Financial Analysis
- Quality Control and GMP
- List of Suppliers for Starting Materials
- Evaluation of Patents and Literature

The Draft Final Report altogether consisted of 2658 pages. It may be noted at this point that since the UNIDO Pharmaceutical Industries Technical Assistance Programme has been established, the submitted report has been the most extensive technical report in terms of its horizontal scope and length.

Extensive evaluation of the Draft Final Report by UNIDO and the Iranian experts led to a list of comments, which was submitted to the contractor on July 28th and was the basis for a comprehensive reevaluation of the study. Apart from technical aspects of report preparation, the most significant changes concerned the following aspects: Continued contacts to technology holders had allowed to include also the products missing in the draft report. Two products, Benzocaine and Metamizol, were deleted from the report. For one of the units the flow of chemicals was shown in more detail. Connection between different units of equipment and piping was shown in drawings. The plant lay - out was changed according to the comments. Many chapters of the report were rewritten, etc. Above all, a second financial analysis was carried out based on the results of the proposed changes. The resulting Final Report was submitted to UNIDO on October 15th, 1992.

In addition, immediately after submission of the Draft Final Report and before receiving the comments on that report, the project team worked on systematic answers to all

comments raised by Iranian experts and UNIDO during the whole project period. In total 40 pages of specific questions were considered and evaluated. The answers were collected in a report, which was submitted to UNIDO and is included to the Annex.

With respect to the complexity of the project and the extensive work of preparing, writing, reading, controlling and commenting such a comprehensive report it is not surprising that the duration of the project was significantly longer than scheduled. The expert team would however like to point out that it is proud to have achieved the specific steps of technical work within the foreseen time, although the delay in project progress, caused by several factors out of responsability and control of the project team, had made the implementation of the project difficult.

5. STRUCTURE OF THE REPORT

The present report was elaborated on basis of the Terms of References. Since it became clear already at an early stage of project implementation that it might become difficult to justify the project from the point of economics of investment, recommendation was made during the First Interim Meeting to improve economic prospects by changing products and production capacities. These recommendations also included the results of a medical evaluation, which had not been requested in the Terms of Reference, but was considered to be of crucial importance with respect to the choice of the product mix of the project. As a result of the Interim Meeting changes were made and accepted by the contractor concerning production quantities of several products. Agreement on a change in the product mix could not be met due to the lack of opportunities for funding the cost of additional work arising from such a change in the scope of the study. As a result the Draft Final Report was prepared based on the following criteria:

- Evaluation of all products requested in the terms of reference
- Increased production capacities according to the results of the First Interim Meeting

Simulating a project implementation process in the technical study first of all product files were established comprising all the data obtained for specific products. Based on data of the product files a general concept was worked out and proposed for the Shahid Modarres Industrial Pharmaceutical Complex. In the next phase unit files were established in which the data for the individual production units were collected. These data were subjected to financial analysis giving the following results as presented in the Draft Final Report:

The total initial investment was estimated to be 345,031,100 US$, of which 57.2% is foreign capital investment. The operating costs were expected to be 46,162,030 US$, of which 73.5% is foreign capital investment, the total sales revenues 48,496,900 US$, which gave compared to the operating costs a net income of 2,334,870 US$. This figure does however not include depreciation. These preliminary data gave a first impression on the economics of the project, which indicated the requirement for improvement of the terms of the projec..

Following the proposals and comments of UNIDO and the SHAHID MODARRES experts a reevaluation of the results of the Draft Final Report was carried out leading to improved data for financial analysis, which are now presented in the Final Report. In this report also options are indicated for further improvement of the economics of the project, the consideration of which would go beyond the scope of the present study.

To remain in line with the requirements of the project it was decided to structure the chapters of the Final Report in general along the lines given in the Terms of Reference.

6. PRODUCTION PROGRAMME, TECHNOLOGIES AND KNOW-HOW

6.1. DRUGS TO BE PRODUCED

According to the terms of reference the following 50 drugs were to be manufactured in the pharmaceutical complex:

	Product	Quantity tons/year
Unit No 1		
1	Cetrimide	500
2	Sulfamethoxazole	100
3	Ibuprofen	75
4	Metamizol-Natrium	65
5	Methyldopa	50
6	Cimetidine	50
7	Niacinamide	50

	Product	Quantity tons/year
Unit No 2		
1	Chlorhexidine	82
2	Trimethoprim	30
3	Chloramphenicol	16
4	Metronidazole	14
5	Vitamine E	13
6	Carbamazepine	9
7	Cetylpyridinium Chloride	8
8	Nalidixic Acid	8
9	Allopurinol	4.5
10	Dipyridamol	4.5
11	Propranolol	4
12	Calcium Panthothenate	4
13	Amytriptyline	3.5
14	Levamisole	3
15	Hydrochlorothiazide	2
16	Clomiphene Citrate	1*)
17	Albuterol Sulfate	0.5
18	Thiethylperazine Maleate	0.2
19	Clemastine Fumarate	0.1
20	Terbutaline Sulfate	0.1
Unit No 3		
1	Calcium Caseinate	140
2	Benzoic Acid	25
3	Isoniazide	12
4	Zinc Undecylenate	12
5	Sodium Benzoate	10
6	Pyridoxine	10
7	Riboflavine	9
8	Diphenhydramine Citrate	7
9	Isosorbide Dinitrate	2.5
10	Benzyl Benzoate	2.5
11	Undecylenic Acid	2.5
12	Miconazole Nitrate	2
13	Benzocaine	1.5
14	Clobutinol	1
15	Glibenclamide	1
16	Diethyltoloamide	1
17	Clidinium Bromide	0.5
18	Flurazepam	0.1

*) Due to a typing error the product Clopipten was considered instead of Clomifen in the first phase of the study. The error was corrected during the First Interim Meeting.

Product		Quantity tons/year
Unit No 4		
1	Magnesium Stearate	60
2	Zinc Stearate	540
3	Aluminum Hydroxide Gel	2,500
Unit No 5		
1	Mannitol	50
2	Ascorbic Acid	500

Unit No 6
Research and Development Center for Biotechnology and Genetic Engineering

Unit No 7
Multipurpose Medicinal Plant Processing Unit, including processing, extraction purification, solvent recovery and drying

Unit No 8
Pilot Plant for Technology Transfer in Synthetic Pharmaceuticals (related to the present project)

6.1.1. PRODUCT QUALITY STANDARDS

As a general requirement in the Terms of Reference qualities according to the United States Pharmacopoeia (USP XXII) are requested. Therefore an assignment to United States Pharmacopoeia monographs was attempted for all products in the project. However, not all the products are monographed in the United States Pharmacopoeia. Therefore other Pharmocopoeiae had to be used to define quality, *e.g.*, British Pharmacopoeia (BP 88) or Deutsches Arzneibuch (DAB 9). To one proposed bulk pharmaceutical compound no reference is made in any of the common Pharmacopoeiae. Its quality requirements are given only by the inventor company (Clobutinol - Boehringer Ingelheim). Calcium Caseinate does not appear in the Pharmacopoeiae. Table 1 indicates the specifications of the products as used in the evaluation.

The increased production quantities given in this list compared to the yearly production capacities given in the Terms of Reference result from a redefinition of production quantities by SHAHID MODARRES (letter of February 14th, 1991) as a result of the First Interim Meeting. The increase in foreseen production capacity on the one hand reflects the growth of population in Iran on the other hand it will improve the economics of the project.

Table 1: Specification of Product Quality and Production Capacity - Terms of Reference and Revised

Drug Bulk Chemicals (monography name)	capacity in tons/yr terms of reference	capacity in tons/yr revised after Feb 25
Albuterol Sulfate USP XXII (Salbutamol)	0.5	1.0
Allopurinol USP XXII	4.5	9.0
Aluminium Hydroxide Gel, Wet USP XXII	2,500.0	5,000.0
Amitriptyline Hydrochloride USP XXII	3.5	7.0
Ascorbic Acid USP XXII	500.0	500.0
Benzocaine USP XXII	1.5	0.0
Benzoic Acid USP XXII	25.0	50.0
Benzyl Benzoate USP XXII	2.5	5.0
Calcium Caseinate (food grade)	140.0	280.0
Calcium Panthothenate USP XXII	4.0	8.0
Carbamazepine USP XXII	9.0	18.0
Cetrimide 40 % BP 88	500.0	1,000.0
Cetylpyridinium Chloride USP XXII	8.0	16.0
Chloramphenicol USP XXII	16.0	16.0
Chlorhexidine Gluconate 20 % BP 88	82.0	164.0
Cimetidine USP XXII	50.0	50.0
Clemastine Fumerate USP XXII	0.1	0.2
Clidinium Bromide USP XXII	0.5	1.0
Clobutinol (Boehringer Mannheim)	1.0	2.0
Clomiphene Citrate USP XXII	1.0	2.0
Diethyltoluamide USP XXII	1.0	2.0
Diphenhydramine Citrate USP XXII	7.0	7.0
Dipyridamol USP XXII	4.5	4.5
Flurazepam USP XXII	0.1	0.2
Glibenclamide BP 88	1.0	2.0
Hydrochlorothiazide USP XXII	2.0	4.0
Ibuprofen USP XXII	75.0	150.0
Isoniazide USP XXII	12.0	24.0
Isosorbide Dinitrate, Diluted USP XXII	2.5	5.0
Levamisole Hydrochloride BP 88	3.0	6.0
Magnesium Stearate NF XVII	60.0	60.0
Mannitol USP XXII	50.0	100.0
Metamizol-Natrium DAB 9	65.0	0.0
Methyldopa USP XXII	50.0	100.0
Metronidazole USP XXII	14.0	28.0
Miconazole Nitrate USP XXII	2.0	4.0
Nalidixic Acid USP XXII	8.0	8.0
Niacinamide USP XXII	50.0	100.0
Propranolol USP XXII	4.0	8.0
Pyridoxine Hydrochloride USP XXII	10.0	20.0
Riboflavin USP XXII	9.0	18.0
Sodium Benzoate NF XVII	10.0	20.0
Sulfamethoxazole USP XXII	100.0	200.0
Terbutaline Sulfate USP XXII	0.1	0.2
Thiethylperazine Maleate USP XXII	0.2	0.4
Trimethoprim USP XXII	30.0	40.0
Undecylenic Acid USP XXII	2.5	5.0
Vitamin E USP XXII	13.0	26.0
Zinc Stearate USP XXII	540.0	540.0
Zinc Undecylate USP XXII	12.0	24.0
Overall Tonnage	4,987.0	8,635.5

6.1.2. THE PRODUCT FILES

As a first step in project implementation each of these compounds had to be evaluated separately. To achieve this in a most systematic manner, a file was established for each compound and incoming informations were collected systematically in these files, which in a completed form are part of this report (vol. 2/1 -- vol. 2/4):

1) General data of the compound:
   - Name according to USP XXII or BP 88
   - Chemical Structure
   - Molecular weight
   - CA - number of the final compound and of similar derivatives (e.g. salts, free base, razemate)
   - Names (CA, INN, Iran (as enlisted in the terms of reference), other names)
   - Indications
   - Tonnage (in the final document the revised quantities as enlisted in the fax received on 25.2.1992 are given)
   - Sales prices (most reasonable price obtained directly from producers)
   - Sales revenues of the product

2) Patents and literature dealing with the final compound
   - Patents enlisted in bibliographies
   - Patents obtained from computer assisted literature search

3) Methods for the preparation of the compound
   - Technology used in evaluation with formula flow sheet and brief description
   - Other methods for preparation with brief description or formula flow sheet

4) Possible suppliers of technologies

5) Brief description of the technological processes including a list, of unit reactions

6) Main equipment list, of products proposed for single line production

7) Estimated consumption indexes of basic raw materials in kg/kg and kg/year including molecular weights of raw materials when required

8) Utilities consumption and man power requirement proposed for single line production

9) Prices and possible suppliers for those starting materials, which are not for the production of any other product within the plant

10) Medical evaluation of the drug

11) Monograph of the compound according to the pharmacopoeia, in which the drug is cited (USP XXII as requested in the terms of reference, for compounds not enlisted in USP: BP 88, DAB 9, NF VII)

12) Basic block schemes, including yields

13) Block scheme evaluation: figures on inputs, recovered materials and waste

14) Basic flow diagrams

6.1.3. THE MEDICAL EVALUATION

The thesaurus of pharmaceutical compounds contains about 3000 products, half of them being of major importance. This thesaurus is subject to permanent change: Old products dissappear and new products come up. The changes usually come about slowly: Active products are replaced by more active products, so that in some cases we speak about products of the first, second or third generation. Side effects force a product out of the market. New therapautic concepts require new products. New classes of compounds appear. It is as a rule only a handful of new products that reach the market every year. The number of dissapearing products is almost the same.

Every product has its own history, sometimes a very long and old story, e.g. with acetylsalicylic acid. As a rule the history of a product nowadays is as follows: After a long development time of sometimes more than ten years the product is introduced into the market. If it is accepted by medical doctors and patients, the profit phase of the product starts: Its consumption increases and it can be sold at a high price. As a rule competitive products appear after some time, which reduce the economic prospects of the product. Such products frequently exhibit advantages in efficiency or have less side effects. After about ten years the phase of eventually big profits ends with the expiration of patents. Since generic companies that are specialized in selling free products are aware of changes in the patent situation, successful products with expiring patents are as a rule offered in a competitive manner, so that a decay in price results, which is stabilized only after some time, when the market shares of the different producers are settled. Research oriented companies at that stage have already put their efforts towards improved products, for which they can receive patent protection. Therefore a permanent survey on the situation of the market is required to be in a position to meet the right investment decisions in the pharmaceutical sector. Since prescription by medical doctors and new results in the medical research scene influence strongly future changes in the pharmaceutical market, a

study that wishes to evaluate the aspects of setting up an industrial complex for the manufacture of 50 products should also cover medical aspects.

Therefore, although not requested in the Terms of Reference, a medical evaluation was made for all 50 compounds: As a result of this evaluation 6 compounds were identified as antiquated because of clearly defined disadvantages compared to superior drugs available in the international market. These drugs are:

- Benzocaine
- Cimetidine
- Chloramphenicol
- Diphenhydramine
- Pyridamol
- Nalidixic acid

In addition, it has to be mentioned that another two drugs are the target of heavy critics:

- Metamizol, which due to cases of agranulocytosis has been withdrawn by WHO from the list of recommended drugs.
- Aluminum Hydroxide, which has been attacked due to the correlation between aluminum and Alzheimer's disease, a position which is still under discussion.

It must be pointed out that the result of the medical evaluation has to be seen only as a recommendation reflecting trends and development in the pharmaceutical sector. The products of the list of the Terms of Reference remain without any doubt established drugs.

The result of the medical evaluation was presented and discussed during the First Interim Meeting. To avoid delay in the execution of the study, it was decided to continue the study with the original set of drugs. Negotiations of the SMDI representatives with Iranian Authorities have led to the following proposal for changes:

- Astemizol in addition to Diphenhydramine Hydrochloride
- Cefotaxime Sodium in addition to Chloramphenicol
- Ciprofloxacine Hydrochloride in addition to Nalidixic Acid
- Diclofenac Sodium instead of Metamizol
- Ketorolac Trometamine instead of Metamizol
- Metoprolol Tatrate in addition to Dipyridamol
- Ranitidin Hydrochloride in addition to Cimetidine
- Benzocaine to be deleted and replaced by a substitute, which will be acknowledged

The contractor has indicated his readiness to evaluate these compounds and to discuss the consequence of their integration to the project, which could be done in an addendum to the present report. Preliminary figures indicate a very promising effect of these proposals.

6.1.4. PRODUCT PRICES

Product prices were directly requested from the suppliers usually from several sources. These prices together with the production quantities allowed to calculate the sales revenues expected for the foreseen production programme and also allowed to set up a ranking of products due to their sales volume.

From Table 2 it can be seen that few products are responsible for the main turn over and that one half of the products account for more than 90% of the turn over. It should however be pointed out that this list does not reflect the profitability of the specific products.

Considering possible sales revenues and comparing them with the great number of products to be manufactured, as well the choice as the number of products does not seem to be extremely promising from the economic point of view. Changes in production quantities as proposed and accepted during the progress of the study and even more replacement of economically bad products by better products, such as those which were proposed as a result of the medical evaluation, could improve the economic prospects of the project significantly. In addition during the First Interim Meeting it was pointed out that apart from financial investment aspects the main aim of the present project is to satisfy the demand of the Iranian population for pharmaceuticals.

Table 2: World Market Price and Estimated Yearly Sales Revenues

Drug Bulk Chemicals	world market prices in USD low	most resonable	high	most reasonable yearly sales revenues in USD	percent of the total yearly sales
Aluminium Hydroxide Gel, Wet USP XXII	1.90	1.90	1.90	9,500,000.00	16.08
Methyldopa USP XXII	35.80	80.00	85.00	8,000,000.00	13.54
Ascorbic Acid USP XXII	11.25	13.00	17.30	6,500,000.00	11.01
Cetrimide 40 % BP 88	3.00	3.28	3.52	3,280,000.00	5.55
Sulfamethoxazole USP XXII	12.00	16.00	17.28	3,200,000.00	5.42
Carbamazepine USP XXII	150.00	155.00	166.67	2,790,000.00	4.72
Cimetidine USP XXII	43.70	51.00	53.13	2,550,000.00	4.32
Ibuprofen USP XXII	13.19	16.00	23.00	2,400,000.00	4.06
Chlorhexidine Gluconate 20 % BP 88	9.50	10.00	12.00	1,640,000.00	2.78
Trimethoprim USP XXII	30.00	39.00	40.50	1,560,000.00	2.64
Riboflavin USP XXII	61.10	85.00	102.78	1,530,000.00	2.59
Niacinamide USP XXII	6.88	13.00	19.90	1,300,000.00	2.20
Calcium Caseinate (food grade)	2.81	4.00	5.42	1,120,000.00	1.90
Chloramphenicol USP XXII	62.17	70.00	85.00	1,120,000.00	1.90
Clobutinol (Boehringer Mannheim)	437.50	437.50	437.50	875,000.00	1.48
Pyridoxine Hydrochloride USP XXII	40.63	43.00	60.00	860,000.00	1.46
Vitamin E USP XXII	27.50	28.10	28.13	730,600.00	1.24
Clemastine Fumerate USP XXII	3,472.22	3,500.00	3,500.00	700,000.00	1.19
Dipyridamol USP XXII	91.50	145.00	188.30	652,500.00	1.10
Thiethylperazine Maleate USP XXII	1,625.00	1,625.00	1,625.00	650,000.00	1.10
Clomiphen Citrate USP XXII	237.00	315.00	335.00	630,000.00	1.07
Metronidazole USP XXII	17.00	22.00	24.38	616,000.00	1.04
Clidinium Bromide USP XXII	520.83	550.00	711.00	550,000.00	0.93
Zinc Stearate USP XXII	0.75	1.00	1.30	540,000.00	0.91
Amitriptyline Hydrochloride USP XXII	76.39	77.00	106.25	539,000.00	0.91
Nalidixic Acid USP XXII	59.38	65.00	86.70	520,000.00	0.88
Allopurinol USP XXII	45.00	50.00	83.20	450,000.00	0.76
Mannitol USP XXII	3.75	4.50	5.31	450,000.00	0.76
Levamisole Hydrochloride BP 88	75.00	75.00	75.00	450,000.00	0.76
Miconazole Nitrate USP XXII	96.88	105.00	188.00	420,000.00	0.71
Glibenclamide USP XXII	174.80	190.00	200.00	380,000.00	0.64
Zinc Undecylate USP XXII	10.31	15.00	21.88	360,000.00	0.61
Cetylpyridinium Chloride USP XXII	12.00	20.00	20.14	320,000.00	0.54
Albuterol Sulfate USP XXII (Salbutamol)	250.20	260.00	260.00	260,000.00	0.44
Propranolol USP XXII	21.41	30.00	34.72	240,000.00	0.41
Isoniazide USP XXII	6.88	9.70	9.78	232,800.00	0.39
Terbutaline Sulfate USP XXII	972.22	1,000.00	1,821.00	200,000.00	0.34
Diphenhydramine Citrate USP XXII	12.20	25.00	31.25	175,000.00	0.30
Calcium Panthothenate USP XXII	16.88	18.00	20.00	144,000.00	0.24
Benzoic Acid USP XXII	1.13	2.65	3.80	132,500.00	0.22
Isosorbide Dinitrate, Diluted USP XXII	13.10	25.00	25.00	125,000.00	0.21
Flurazepam USP XXII	450.00	460.00	520.83	92,000.00	0.16
Magnesium Stearate NF XVII	1.35	1.50	2.50	90,000.00	0.15
Hydrochlorothiazide USP XXII	15.50	20.00	31.25	80,000.00	0.14
Undecylenic Acid USP XXII	8.13	8.50	9.72	42,500.00	0.07
Sodium Benzoate NF XVII	1.10	1.40	1.57	28,000.00	0.05
Diethyltoluamide USP XXII	11.25	11.25	11.25	22,500.00	0.04
Benzyl Benzoate USP XXII	2.78	3.20	3.20	16,000.00	0.03
Overall Sum				59,063,400.00	100.00

6.2. PATENTS AND TECHNOLOGIES

A first analysis of the patent situation revealed that none of the products is still under patent protection. Although this fact at the first glance seems to be advantageous, it reflects also some negative effects: As said before product prices of pharmaceuticals as a rule drop to a low level after patent expiration. The analysis of the product prices of the present project shows that this fact holds in most cases true also here. Transfer of technology is a complex activity anyway and requires as a rule licensing agreements. The work for the transfer of a "young" product does not significantly differ from transfer of a product, where the patent is no more valid. The readiness to consider also new products should only be limited by negative results in licensing negotiations.

From the beginning of the project a systematic study of process patents started, which led to the selection of one "chosen process". Due to the limited time available for the study, in parallel to the negotiations with technology holders evaluation of the products was continued on the basis of this process, until it could be replaced or supplemented by data obtained from technology holders, a procedure which in many cases resulted in only minor changes. Taking into account that negotiations for supply of technologies are going on even at the time of the preparation of the Final Report, this strategy has been very efficient and successful in the implementation of the study.

As a result of the First Interim Meeting a comprehensive study on all patents of the products was requested, which was carried out by adding a systematic computer search. A total of 1200 references was obtained from this search and was analyzed to obtain a full picture of the patent situation.

6.3. TECHNOLOGIES

One of the specific requests in the Terms of Reference was that the study should be based upon offers requested from technology holders. Although this approach is excellent in principle, there were some constraints. These were on the one hand due to the short time in which the study had to be carried out. On the other hand, in a few cases, there was an extremely limited number of technology holders, so that no alternative was available in case of a negative reply. As previously mentioned for these reasons negotiations with technology holders have been continued throughout the time of the study and the study has been steadily adapted to consider all incoming results of negotiations with technology holders.

6.3.1. AVAILABILITY AND SUPPLY OF TECHNOLOGIES

Due to the complexity of the present project it can be said that there is not one company in the world and probably not even one country in the world holding know-how for the manufacture of all the 50 product. Therefore companies practically all over the world were contacted and informed about the project and the aim of the present study. Renowned technology holders of the manufacturing pharmaceutical industry, trading companies in the fields of bulk pharmaceuticals with direct contacts to producers and finally engineering companies active in the pharmaceutical sector in Europe, North America and the Far East were invited to cooperate in the realization of the SHAHID MODARRES Industrial Pharmaceutical Complex.

In the early phase of recruitment the first contacts were established by letter. Since in larger companies the internal organization may become rather complex causing long delays until the request reaches the relevant staff, direct first phone calls supported by a detailed presentation of the project via fax were preferred as contacting approach later on.

As a rule several divisions of a company are involved into activities related to transfer of technology (e.g., Export Division, R&D, Legal Branch, General Management). This fact leads to another considerable delay in the response, because offers cannot be readily submitted, but require some work in the engineering department. Therefore responding times of 2 to 3 months must be considered as common. A study period of less than 6 months -- as foreseen in the present project - requires a high degree of project organization to be in a position to consider incoming replies at any stage of the project.

Using international data bases and integrating experience and relations of the members of the project team, a list of suppliers of bulk pharmaceutical chemicals was set up. This list is given in the Annex and represents a more or less complete compilation of the bulk pharmaceuticals foreseen for production in the SHAHID MODARRES Industrial Pharmaceutical Complex.

Out of this list almost all companies have been contacted making reference to the present project. In addition to the above mentioned compilation UNIDO supplied a list of 7 companies, which had previously expressed their interest in Technology Transfer:

ChemServ - Chemie Linz AG, Austria
Hoechst AG, Germany
Ciba Geigy , Switzerland
Ficetec - Carlo Erba, Italy
Sicplant, Italy
Ekono Oy, Finland
Canedex, Canada

Answers were received from all companies with exception of Canedex. ChemServ (now part of Nycomed, Norway), Ciba Geigy and Hoechst informed about their decision not to coperate in a written form. The engineering companies Ficetec, which is a subcontractor in the present study, Sicplant and Ekono expressed their readiness to contribute to the project: Ficetec is in a position to supply technologies for Ascorbic Acid, Mannitol, Ibuprofen and others, Sicplant has negotiated to obtain agreements for Aluminum Hydroxide Gel, Zinc and Magnesium Stearate and Ekono Oy´s attempts to interest Nordic companies for the project are still ongoing (A great numbers of Nordic companies have already been recruited to the project by the project team).

Trading companies (broker companies) in Germany (*e.g.*, Transol, Schweitzerhall), Switzerland (Tiefenbacher) or Great Britain (Forum), who are insiders in the market of bulk pharmaceuticals due to their daily work, were asked to check with their partner companies for potential interest in the project. All efforts of these companies were however without success.

About some 200 producing companies all over the world were informed about the SHAHID MODARRES pharmaceutical project by the project team. In the case of no response to a first request further contacts - letter fax or phone calls - were attempted with almost all companies in Europe to come to a final written or oral answer. In the case of multinational companies requests were directed to the main quarter, affiliated companies were only contacted, when they have responsability in specific fields (*e.g.* Hoffmann-LaRoche, Switzerland acting in the Pharmaceutical area for all affiliated companies, but Givaudan-Lavirotte (a 100 % subsidiary of Hoffmann LaRoche) carries all activities in fatty acids).

With the date of September 10th, 1992 the following companies had expressed their readiness to cooperate in the realization of the SHAHID MODDARES Pharmaceutical Complex:

Ficetec (Engineering Company, Italy)

Ascorbic Acid	(from Polservice Warsaw)
Mannitol	(from Cerestar)
Chloramphenicol	(from Carlo Erba)
Ibuprofen	(from Carlo Erba)
Cimetidine	(One Person K.H.)
Dipyridamol	(One Person K.H.)
Allopurinol	(Secifarma)
Clidinium bromide	(Sifavitor)
Trimethoprim	(FIS)
Carbamazepine	(One Person K.H.)

Sicplant (Engineering Company, Italy)

- Aluminum Hydroxide Gel
- Zn and Mg Stearate

Antibioticos S.p.A. (Italy)

- Methyldopa

Francis (Italy)

- Sulfamethoxazole

Sibefat- Mediolast (Italy)

- Propranolol
- Amitryptiline
- Cimetidine
- Clidinium Chloride

Sivator (Italy)

- Clidiniuim Chloride

FIS (Italy)

- Trimethoprim

Pliva (Croatia)

- Cetylhexidine Acetate

Weiders (Norway)

- Cetylpyridinium Chloride

Fermion (Finland)

- Chlorhexidine Gluconate
- Ibuprofen
- Propranolol
- Trimethoprim
- Carbamazepine

Ferrosan (Denmark)
- Cetrimide

FAES (Spain)
- Trimethoprim

Meggle (Germany)
- Calcium Caseinate

Gerot (Austria)
- Flurazepam

Pharmaceutical Research Institute (Poland)
- Miconacole
- Pefloxacine (as a substitute for Nalidixic Acid)

Il-Yang (Korea)
- Aluminum Hydroxide

Ganesh Benzoplast (India)
- Benzoic Acid
- Sodium Benzoate
- Benzylbenzoate

Mirabh Pharmaceuticals PVT Ltd. (India)
- Propranolol
- Terbutaline Sulfate

Standard Organics Limited Ltd. (India)
- Albuterol
- Ibuprofen
- Sulfamethoxazole
- Trimethoprim

A few companies offered cooperation in a first reply, however withdrew the already envisaged supply of technologies later on:

Leiras (Finland)
- Albuterol

Pliva (Croatia)

- Ascorbic Acid
- Chlorhexidine
- Hydrochlorothiazide
- Methyldopa
- Pyridoxine Hydrochloride
- Sulfamethoxazole
- Trimethoprim

Upon a direct request from UNIDO, Pliva later offered a process for converting Chlorhexidine into Chlorhexidine Acetate.

For a group of bulk pharmaceuticals offers for development on contract are available:

- Benzoic Acid
- Sodium Benzoate
- Diethyltoluamide
- Undecylenic Acid
- Zinc Undecylenate
- Cyanopyridines as precursors for Niacinamide

At present a UNIDO project for the establishment of a multi purpose pilot plant for the manufacture of bulk chemicals in Iran is on the way including the following technologies:

- Metronidazol
- Propranolol
- Sulfamethoxazole
- Trimethoprim

Arrangements between Darou Paksh and SMDI would be very useful on the one hand to check options for cooperation and technology use by SHAHID MODARRES, on the other hand to avoid local competition.

Some companies offered technologies for bulk pharmaceuticals which are not in the list given in the Terms of Reference, but would represent reasonable substitutes for the requested compounds (*e.g.* Pefloxacine instead of Naldixic Acid).

Data of the present status of recruitment with entries for each foreseen bulk pharmaceutical compound are compiled in Table 3.

Table 3: Status of recruitment with entries for each foreseen bulk pharmaceutical compound

Bulk Pharmaceutical Chemical	Technology Supplier
Albuterol USP XXII	Standard Organics Ltd. (India) offers technology, details not disclosed Fees for TOT not disclosed
Aluminum Hydroxide Gel, Wet USP XXII	Sicplant (Italy) promised to supply a technology within May 1992. Il-Yang (Korea) promises a technology, but needs more time for working on the offer.
Allopurinol USP XXII	Secifarma (Italy) offers a process described in method A. Fees for TOT US$ 250,000
Amitriptyline Hydrochloride USP XXII	Sibefat (Italy) Fees for TOT not disclosed
Ascorbic Acid USP XXII	Polservice-Warsaw K.H. supplier, engineering by Ficetec (Italy) fees for TOT US$ 1,200,000
Benzoic Acid USP XXII	Today's Benzoic Acid plants have yearly production capacities between 30,000 to 100,000 tons/yr, producing mainly technical grade Benzoic Acid (which is in then converted to phenol) and a smaller quantities of pharma grade quality. Ganesh Benzoplast Ltd. (India) offers technology in principle without giving details. Fees for TOT not disclosed Development contract available (continuous oxidation with air oxygen)
Benzyl Benzoate USP XXII	K.H. purchase due to low value of foreseen sales revenues (US$ 16,000/yr) economically not feasible, development contract recommended
Calcium Caseinate	Meggle (Germany) offers TOT: starting with fresh milk Fees for TOT not disclosed DMV (NL) is in principle offering cooperation for the establishing of a production unit, however production capacity has to be 10-100 times higher to be economical feasible (raw material and pollution problems).
Calcium Panthothenate USP XXII	Extensive requests negative, limited market of suppliers (see comment on vitamins)
Carbamazepine USP XXII	Fermion (Finland) starts with Iminostilben, avoids the poisonous phosgene completely. Fees for TOT US$ 70,000 royalties US$ 1.90 /kg for 10 years
Cetrimide BP 88	Ferrosan (Denmark): TOT includes assistance during project stage Fees for TOT US$ 280,000
Cetylpyridinium Chloride USP XXII	Weiders Farmasoytiske A/S (Norway) envisaged offer for TOT (one-step reaction of cetyl chloride and pyridine). estimated price for equipment US$ 1,000,000 Fees for TOT will be agreed upon a later stage
Chloramphenicol USP XXII	Farmitalia Carlo Erba (Italy) Fees for TOT not disclosed

Table 3 (continued): Status of recruitment with entries for each foreseen bulk pharmaceutical compound

Bulk Pharmaceutical Chemical	Technology Supplier
Chlorhexidine Acetate BP 88	Fermion (Finland) starts with Hexamethylenediamine and p-Chloroaniline. Fees for TOT US$ 690.000 royalties US$ 4.10 /kg for 6 years US$ 2.50 /kg for 4 years
Clomiphene Citrate USP XXII	Only a very limited number of companies has K.H. for the production of Clomiphene, all of them refused to cooperate.
Cimetidine USP XXII	One-person K.H.: starting with 5-methylimidazole Fees for TOT US$ 100.000 Sibefat (It): Fees for TOT not disclosed
Clemastine Fumerate USP XXII	Only a very limited number of companies has K.H. for the production of Clemastine, all of them refused to cooperate. Development contract recommended
Clidinium Bromide USP XXII	Sifavitor S.p.A. (Italy) offers technology starting with benzylic acid methyl ester. Fees for TOT not disclosed Sibefat (It): Fees for TOT not disclosed
Clobutinol Hydrochloride (Boehringer Ingelheim)	Only a very limited number of companies has K.H. for the production of Clobutinol, all of them refused to co-operate. Development contract recommended
Diethyltoluamide USP XXII	K.H. purchase due to low value of foreseen sales revenues (US$ 22.500/yr) economically not feasible. Development contract recommended
Diphenhydramine Citrate USP XXII	No offers for this product
Dipyridamol USP XXII	One-person K.H.: starting with 5-aminoorotic acid Fees for TOT US$ 40.000
Flurazepam Hydrochloride USP XXII	Gerot Pharmaceutika (Austria): starting with 2-Amino-5-chloro-2'-fluorobenzophenone Fees for TOT US$ 30.000
Glibenclamide BP 88	No offer for TOT, but development on contract recommended
Hydrochlorothiazide USP XXII	No offer for TOT, but development on contract recommended
Ibuprofen USP XXII	Carlo Erba (Italy) process starting with Isobutylbenzene Fees for TOT not disclosed Fermion (Finland): starting with isobutylbenzene Fees for TOT US$ 180.000 royalties US$ 2.00/kg up to 250 tons Standard Organics Ltd. (India) offers technology without giving details. Fees for TOT not disclosed
Isoniazid USP XXII	No offer for TOT, but development on contract recommended
Isosorbide Dinitrate, Diluted USP XXII	No offer for TOT, but to our knowledge ISDN is already produced in the Islamic Republic of Iran.

Table 3 (continued): Status of recruitment with entries for each foreseen bulk pharmaceutical compound

Bulk Pharmaceutical Chemical	Technology Supplier
Levamisole Hydrochloride BP 88	Only a very limited number of companies holdes K.H. for the production of Levamisole, all of them refused to cooperate Development contract recommended
Magnesium Stearate NF XVII	Sicplant (Italy) promised to supply a technology within May 1992.
Mannitol USP XXII	Cerestar (Italy) offers technology. Fees for TOT not disclosed
Metamizol-Natrium DAB 9	No offers for this product
Methyldopa USP XXII	Antibiotics S.p.A. (Italy) starting from Veratralaldehyde Fees for TOT not disclosed
Metronidazole USP XXII	no offer for TOT, Metronidazol is already produced in the Islamic Republic of Iran
Miconazole USP XXII	Pharmaceutical Research Institute (Poland): starting with 2,4-Dichloroacetophenone Fees for TOT not disclosed Sibefat (Italy) offers technology without giving details Fees for TOT still under negotiation
Nalidixic Acid USP XXII	No offers for Nalidixic Acid Nalidixic Acid is already produced in the Islamic Republic of Iran Pharmaceutical Research Institute (Poland): offers a process for Pefloxacine, a third generation quinolone as a therapeutic substitute for Nalidixic Acid.
Niacinamide USP XXII	No offers for this product, but development offer for Cyanopyridine available
Propranolol USP XXII	Fermion (Finland): starts with α-Naphthol Fees for TOT US$ 55.000 royalties US$ 1.00/kg for 10 years Sibefat (Italy) gives no details of process Fees for TOT not disclosed Mirabh Pharmaceuticals PVT Ltd. offers technology starting with α-Naphthol, estimated equipment costs US$ 55.000 Fees for TOT US$ 35,000
Pyridoxine Hydrochloride USP XXII	No offers for this product Envisaged technology withdrawn (Pliva, Croatia)
Riboflavin USP XXII	Only a very limited number of companies holds K.H. for the production of Riboflavin , all of them refused to cooperate.
Sodium Benzoate NF XVII	Ganesh Benzoplast Ltd. offers technology without giving details. Fees for TOT not disclosed The expected sales return of US$ 28.000 do neither allow nor justify a TOT.

Table 3 (continued): Status of recruitment with entries for each foreseen bulk pharmaceutical compound

Bulk Pharmaceutical Chemical	Technology Supplier
Sulfamethoxazole USP XXII	Francis (It) Fees for TOT US$ 50.000 Standard Organics Ltd. (India) offers process without giving details Fees for TOT not disclosed
Terbutaline Sulfate USP XXII	Mirabh Pharmaceuticals PVT Ltd. offers technology starting with 3,5-Dimethoxy-Acetophenone . estimated equipment costs US$ 147.500 Fees for TOT US$ 35.000
Thiethylperazine Maleate USP XXII	No offers for this product Only available at Sandoz (Switzerland), rejected cooperation
Trimethoprim USP XXII	Fermion (Finland): starting with 3.4.5-trimethoxybenzaldehyde Fees for TOT US$ 75.000 royalties US$ 1.40/kg for 10 years FAES (Spain): starting with 3.4.5-trimethoxybenzaldehyde Fees for TOT US$ 40.000 FIS (Italy) starting with 3.4.5-trimethoxybenzaldehyde Fees for TOT US$ 250.000 Standard Organics Ltd. (India) offers technology without giving details Fees for not disclosed
Zinc Undecylenate USP XXII	No offers for this product, but offer for Development on Contract available
Undecylenic Acid USP XXII	No offers for this product, but offer for Development on Contract available
Vitamin E Acetate BP 88	No offers for this product, Development on Contract recommended Only a very limited number of companies holds K.H. for the production of Vitamin E, all of them refused to cooperate.
Zinc Stearate USP XXII	Sicplant (Italy) will supply a technology within May 1992 (written promise).

A detailed report on the recruitment efforts (positive and negative responses) is given in the Annex. Companies are arranged country by country, ownership is indicated as far as known. Bulk pharmaceuticals manufacturing know how expected to be with the company is enlisted. Following the heading 'contacts', the form of contacting and of the following response are given in addition to statements from the companies.

Negative results of negotiations were obtained for different reasons. First of all some of the products are produced in a very limited scale. Fees for transfer of technology (without assistance in the implementation phase and training) range between US$ 50,000 to 1,200,000 (see above). Bulk pharmaceuticals in the project with yearly sales revenues of less than US$ 100,000 to 200,000 are therefore not very attractive to companies for

transfer of technology, because the low expected sales revenues would not allow reasonable fees or royalties.

Another group of technologies is available only at a limited number of suppliers. Above all this holds true for vitamins, e.g. Riboflavin, Calcium Panthothenate or Vitamin E Acetate (Hoffmann LaRoche, BASF, Bayer or Takeda) and compounds like Clomiphen Citrate (Sandoz and Egis), Thiethylperazine (Sandoz) or Clobutinol (Boehringer Ingelheim and Farchemia). The problem of limited sources of know how is obvious. In the case of negative reactions from these suppliers a solution of this crucial problem may be found in establishing development contracts for these products. In a later phase the company should be in a position to develop such technologies through its own R&D department.

For some of the products modern plants are scaled some 100 to 1000 times larger than the foreseen capacities in the project (e.g. Benzoic Acid 50,000 - 100,000 tons/year compared to 50 tons of the present project). Technical grade are the main and pharma grade bulk chemicals are the minor output of these plants. Since the envisaged production scale of some of the products is far away from the usual technological level, international producers do not consider a request to be relevant. Technologies for pharma grade production only are not available on the market and have to be developed on contract or by the own R&D department. The situation is comparable for Benzoic Acid (mainly converted to phenol), Sodium Benzoate and Zinc and Magnesium Stearate (mainly used in plastics industry).

It has to be stated that unfortunately the huge majority of the companies which had been asked for cooperation refused to participate in the project. The reasons for negative responses were:

- Company already supplies bulk or formulated drugs to the Islamic Republic of Iran.
- Company is producing in capacities several times larger than the requested ones, down scaling would not be economically feasible.
- Company is convinced that at the end the Iranian Counterpart will have to export at low prices to cover the investments and in this way lower world market prices.
- Company holds the requested technology, but does not have enough capacity to work out the technical documentation which is required to offer the process.
- Company sells only products but not know how.
- Company only accepts models of cooperation (e.g. joint venture) which guarantee further control of the quality of the products.
- Company is concerned that know how will get out of control.

- Company is concerned about the seriousness of the project having evaluated the present list of proposed bulk pharmaceuticals (too many, in some cases low capacity and revenues).
- Company is only interested in joint ventures or direct investments.
- Company is convinced that an economical production under the present conditions is not possible and does therefore not want to get involved in the project.

It seems worth mentioning that some companies, which in the past have been involved in other similar project activities (e.g. some Indian or Hungarian companies) decided not to enter into the project.

Finally the present situation of most companies in East Europe after the change in the political system has to be taken into account. Many of these companies are at present in a phase of restructuring, including sometimes even takeovers by western companies. Although these companies may be considered as being potential technology suppliers, their situation is highly unclear at the present, so that sometimes decision makers cannot be reached.

6.3.2. PRICES FOR TECHNOLOGICAL KNOW-HOW

While the market for equipment for production of pharmaceutical chemicals is a very open and clear market, a common technology transfer market is not really established. Various payment models for transfer of technology have been proposed and requested by suppliers:

One time payment: Payment in 2 to 4 parts (*e.g.* after signing the contract, after submitting the first files, before and after installation)

Combinations of Fees and Royalties

In many cases companies indicated that they would negotiate fees and royalties only at a more advanced stage of cooperation. Therefore no figures for fees could be received in the course of the study . This situation is indicated in Table 3 with the term 'fees for TOT not disclosed'.

Further forms of agreements, which need direct negotiations of the counterparts, were considered to be not suitable for evaluation in a study like the present one, *e.g.* some companies asked for contracts for exclusively supplying starting materials (Siegfried, CH).

Price offers for technology (not covering assistance during implementation or training) range from US$ 40,000 (*e.g.* Trimethoprim) to US$ 1,200,000 (Ascorbic Acid) with higher figures for large scale (*e.g.* Chlorhexidine) or highly sophisticated process (*e.g.* Ascorbic Acid) and lower figures for know how which is widely available (*e.g.* Trimethoprim).

Having these figures in mind it is easy to realize that a transfer of technology for products with an estimated yearly sales revenue of less than about US$ 200,000 does not seem to be economically feasible for both sides. It is therefore proposed that the transfer of such technologies is carried out within technology development contracts set up with experienced companies, which should also include training and technical assistance in developing local capacities for development of pharmaceutical production processes.

6.3.3. RAW MATERIALS - PRICES - SUPPLIERS

There are two groups of chemicals required in pharmaceutical chemical production: basic chemicals and solvents on the one hand and specific starting materials for individual production processes. There is a big world market for basic chemicals and solvents with the pharmaceutical industry being one of the consumer industries. By far more specialized is the market for specific starting materials. Frequently, a limited number of specialized companies manufacture and offer such products, sometimes even several different intermediates for the production of one specific product. Buying companies will decide to start their production at that stage of the process, which is most economical for them. In fact, this market may be better called pharmaceutical intermediates market than starting materials market.

Bulk chemicals are commodities and their prices are established world market prices, usually subject only to minor and slow changes. Much more complicated is the situation with starting materials/intermediates. Here the number of suppliers is limited to very few specialized companies, frequently the supplier of the end product being supplier of the intermediate as well. Permanent careful observation of the market and good contacts between supplier and buyer are important in this market, in which it may happen that an intermediate is offered at a higher price than the end product.

There are about 250 different chemicals required in the project. For each of these starting meterials prices were collected using quotations from suppliers. The following list comprises the raw materials required to manufacture all products in the foreseen quantities. This figure was used as a basis for further evaluation (Table 4).

As far as the quality of starting materials and intermediates is concerned it was made clear that these chemicals are for use in pharmaceutical production. With specific intermediates it is self understanding that the qualities which are offered correspong to the requirements of the production of the pharmaceutical. Whenever a process will require a special quality of a chemical, the technology holder will have to indicate either the required purification process or a source where such a product of special quality can be purchased.

Suppliers for all raw materials required for the production of the 50 items of the project have been compiled. List of addresses are given in the Product Files. If a specific raw material is used in more than one process, the suppliers can be found in the Annex.

World market prices for the raw materials were collected by direct requests from the producers (no trading or broker companies) on the basis of the estimated yearly consumption. For most of the raw materials prices from at least two independent sources were obtained. Companies based their offers on the world wide accepted INCO terms and in most of the cases free main European port. Since prices for bulk chemicals are fluctuating, the offers reflect the present status and are subject to change.

It must be considered that the price quotations do not contain specific transport costs to Iran, since these costs will largely depend on the purchasing strategy of the management of SMDI.

It is not surprising that only few chemicals required are locally available in Iran. Since raw material costs constitute a significant part of the production cost, it will be extremely important and one of the most decisive factors for success of the project to secure an efficient purchase of starting materials.

A list of locally available raw materials is given in the Annex.

Table 4: Raw materials required to produce 48 items: amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
p-(acetamido)benzene sulfochloride	221.575	3.66	Sulfamethoxazole USP XXII
acetic acid	374.966	0.62	Albuterol Sulfate USP XXII Carbamazepine USP XXII Chloramphenicol USP XXII Cimetidine USP XXII Dipyridamole USP XXII Glibenclamide BP 88 Ibuprofen USP XXII Nalidixic Acid USP XXII Terbutaline Sulfate USP XXII
acetic aldehyde	30384	0.67	Chloramphenicol USP XXII
acetic anhydride	245.807	1.04	Albuterol Sulfate USP XXII Chloramphenicol USP XXII Methyldopa USP XXII Vitamin E Acetate USP XXII
acetone	1.154.036	0.49	Allopurinol USP XXII Ascorbic Acid USP XXII Chloramphenicol USP XXII Cimetidine USP XXII Clidinium Bromide USP XXII Dipyridamole USP XXII Glibenclamide BP 88 Levamisole Hydrochloride BP 88 Propranolol Hydrochloride USP XXII Sulfamethoxazole USP XXII Terbutaline Sulfate USP XXII
acetyl chloride	127.850	1.37	Amitriptyline Hydrochloride USP XXII Ibuprofen USP XXII
air	104.305	0.00	Benzoic Acid USP XXII
ß-alanine	3.245	7.33	Calcium Pantothenate USP XXII
D,L-alanin ethylester, hydrochloride	27.849	3.66	Pyridoxine Hydrochloride USP XXII
aluminium chloride	341.900	0.61	Aluminium Hydroxide Gel USP XXII
aluminium hydroxide	200.000	3.05	Aluminium Hydroxide Gel USP XXII
aluminium isopropoxide	5.424	0.93	Chloramphenicol USP XXII
aluminium sulfate	592.200	6.11	Aluminium Hydroxide Gel USP XXII
2-amino-5-chloro-2´-fluorobenzophenone	276	177.10	Flurazepam Hydrochloride USP XXII
(+)-3-(aminomethyl)pinane, hydrochloride	327	91.60	Calcium Pantothenate USP XXII
2-amino-6-methylpyridine	10.728	12.21	Nalidixic Acid USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
ammonium hydroxide, conc.	69.348	0.17	Chloramphenicol USP XXII Clemastine Fumarate USP XXII Flurazepam Hydrochloride USP XXII Glibenclamide BP 88 Hydrochlorothiazide USP XXII Sulfamethoxazole USP XXII Thiethylperazine Maleate USP XXII
ammonia gas	10.963	0.12	Chloramphenicol USP XXII Flurazepam Hydrochloride USP XXII
ammonium chloride	7.919	0.40	Amitriptyline Hydrochloride USP XXII Clemastine Fumarate USP XXII Clomiphen Citrate USP XXII
ammonium salt	46.000	0.40	Methyldopa USP XXII
aniline	5.494	0.85	Riboflavin USP XXII
antifoam agent	2.182	1.00	Sulfamethoxazole USP XXII
barbituric acid	8.076	9.16	Riboflavin USP XXII
benzene	19.425	0.38	Albuterol Sulfate USP XXII Amitriptyline Hydrochloride USP XXII Clemastine Fumarate USP XXII Clomiphen Citrate USP XXII Diphenhydramine Hydrochloride USP XXII Flurazepam Hydrochloride USP XXII Levamisole Hydrochloride BP 88 Pyridoxine Hydrochloride USP XXII Thiethylperazine Maleate USP XXII
benzene, dry	137	0.38	Terbutaline Sulfate USP XXII
benzilic acid	1.037	9.16	Clidinium Bromide USP XXII
benzoic aldehyde	57.456	0.72	Chloramphenicol USP XXII
benzoine	1.290	7.33	Clomiphen Citrate USP XXII
benzyl chloride	3.174	1.54	Benzyl Benzoate USP XXII
benzyl tert. butylamine	4.940	12.30	Albuterol Sulfate USP XXII Terbutaline Sulfate USP XXII
bromine	16.053	2.71	Albuterol Sulfate USP XXII Diphenhydramine Hydrochloride USP XXII Miconazole Nitrate USP XXII Terbutaline Sulfate USP XXII
bromoacetyl bromide	300	15.00	Flurazepam Hydrochloride USP XXII
3-bromonitrobenzene	445	98.39	Thiethylperazine Maleate USP XXII
4-bromophenol	3.639	20.00	Clomiphen Citrate USP XXII
butanol	4.086	0.90	Chlorhexidine Digluconate (20%) BP88
butanone	1.293	0.80	Clobutinol (boehringer ingelheim) Clomiphen Citrate USP XXII
2-buten-1,4-diol	10.502	3.66	Pyridoxine Hydrochloride USP XXII
calcium	722	18.32	Calcium Pantothenate USP XXII
calcium hydroxide	11.177	0.21	Calcium Caseinate (FOOD GRADE) Calcium Pantothenate USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
carbon dioxide	563.200	0.50	Aluminium Hydroxide Gel USP XXII
casein, acid	281.004	3.00	Calcium Caseinate (FOOD GRADE)
castor oil	110.249	1.98	Undecylenic Acid USP XXII
catalyst	57.000	1.80	Methyldopa USP XXII
catalyst n. 1	187.950	1.80	Ibuprofen USP XXII
catalyst n. 2	92.700	1.80	Ibuprofen USP XXII
cetyl chloride	12.324	6.72	Cetylpyridinium Chloride USP XXII
charcoal	100.975	3.15	Albuterol Sulfate USP XXII Allopurinol USP XXII Amitriptyline Hydrochloride USP XXII Ascorbic Acid USP XXII Carbamazepine USP XXII Chloramphenicol USP XXII Clemastine Fumarate USP XXII Clomiphen Citrate USP XXII Diphenhydramine Hydrochloride USP XXII Dipyridamole USP XXII Flurazepam Hydrochloride USP XXII Hydrochlorothiazide USP XXII Ibuprofen USP XXII Isoniazid USP XXII Isosorbide Dinitrate USP XXII Methyldopa USP XXII Metronidazole USP XXII Miconazole Nitrate USP XXII Nalidixic Acid USP XXII Niacinamide USP XXII Propranolol Hydrochloride USP XXII Pyridoxine Hydrochloride USP XXII Sulfamethoxazole USP XXII Thiethylperazine Maleate USP XXII
4-chloroacetophenone	956	12.17	Clemastine Fumarate USP XXII
3-chloroaniline	2.897	9.16	Hydrochlorothiazide USP XXII
4-chloroaniline, hydrochloride	23.305	5.27	Chlorhexidine Digluconate (20%) BP88
chlorobenzene	829	0.82	Clemastine Fumarate USP XXII
2-chlorobenzoic acid, potassium salt	440	7.33	Thiethylperazine Maleate USP XXII
4-chlorobenzyl chloride	2.664	8.43	Clobutinol (boehringer ingelheim)

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
chloroform	99.436	0.71	Albuterol Sulfate USP XXII Amitriptyline Hydrochloride USP XXII Calcium Pantothenate USP XXII Clemastine Fumarate USP XXII Clidinium Bromide USP XXII Clomiphen Citrate USP XXII Dipyridamole USP XXII Metronidazole USP XXII Pyridoxine Hydrochloride USP XXII Thiethylperazine Maleate USP XXII
5-chloro-2-methoxybenzoic acid methylester	1.726	3.05	Glibenclamide BP 88
1-(3-chloropropyl)-4-methylpiperazine	182	30.53	Thiethylperazine Maleate USP XXII
chlorosulfonic acid	35.885	0.35	Glibenclamide BP 88 Hydrochlorothiazide USP XXII
citric acid	1.064	1.61	Clomiphen Citrate USP XXII
cobalt naphthenate	130	80.00	Benzoic Acid USP XXII
copper(I)oxide	16	1.49	Thiethylperazine Maleate USP XXII
copper powder	189	3.05	Thiethylperazine Maleate USP XXII
N-cyanamido-dithiomethyl-carbonate	38.700	13.75	Cimetidine USP XXII
cyanoacetamide	9.450	22.24	Allopurinol USP XXII
4-cyanopyridine	26.696	5.50	Isoniazid USP XXII
3-cyanopyridine	137.900	4.89	Niacinamide USP XXII
cyclohexylisocyanate	680	6.11	Glibenclamide BP 88
cysteamine. hydrochloride	30.240	18.33	Cimetidine USP XXII
dibenzosuberone	5.028	50.53	Amitriptyline Hydrochloride USP XXII
dibenzoyl-L-tartaric acid	3.121	6.87	Chloramphenicol USP XXII Clemastine Fumarate USP XXII
3,5-di(benzyloxy)aceto-phenone	459	189.87	Terbutaline Sulfate USP XXII
2,4-dichloroacetophenone	5.840	17.51	Miconazole Nitrate USP XXII
2,4-dichlorobenzyl chloride	3.240	4.89	Miconazole Nitrate USP XXII
1,2-dichloroethane	600.000	0.49	Ascorbic Acid USP XXII
dichloromethane	647.714	0.63	Chloramphenicol USP XXII Flurazepam Hydrochloride USP XXII Levamisole Hydrochloride BP 88 Miconazole Nitrate USP XXII Pyridoxine Hydrochloride USP XXII Sulfamethoxazole USP XXII
diethanolamine	16.980	0.80	Dipyridamole USP XXII
diethylamine	5.288	1.07	Calcium Pantothenate USP XXII Diethyltoluamide USP XXII
diethylaminoethyl chloride. hydrochloride	3.801	12.98	Clomiphen Citrate USP XXII Flurazepam Hydrochloride USP XXII

Table 4 (continued): Raw materials required to produce 48 items: amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
diethyl malonate	19.990	2.02	Nalidixic Acid USP XXII
diethyl oxalate	246.750	4.67	Sulfamethoxazole USP XXII
dimethylamine, hydrochloride	528	3.85	Clobutinol (boehringer ingelheim)
2-(dimethylamino)ethanol	8.551	1.77	Diphenhydramine Hydrochloride USP XXII
3-(dimethylamino)propyl-chlorid, hydrochloride	7.634	13.43	Amitriptyline Hydrochloride USP XXII
3,4-dimethylaniline	8.383	8.55	Riboflavin USP XXII
dimethylformamide, dry	366	1.19	Flurazepam Hydrochloride USP XXII
dimethylsulfoxide	44.223	1.05	Levamisole Hydrochloride BP 88 Miconazole Nitrate USP XXII
dioxane	67.958	3.15	Dipyridamole USP XXII
diphenylether	2.716	2.54	Nalidixic Acid USP XXII
diphenylmethane	5.715	3.66	Diphenhydramine Hydrochloride USP XXII
disodium versenate	400	15.57	Ascorbic Acid USP XXII
epichlorhydrine	4.791	1.50	Propranolol Hydrochloride USP XXII
ethanol	710.269	0.40	Albuterol Sulfate USP XXII Amitriptyline Hydrochloride USP XXII Chlorhexidine Digluconate (20%) BP88 Cimetidine USP XXII Clemastine Fumarate USP XXII Clobutinol (boehringer ingelheim) Clomiphen Citrate USP XXII Diphenhydramine Hydrochloride USP XXII Flurazepam Hydrochloride USP XXII Hydrochlorothiazide USP XXII Isoniazid USP XXII Isosorbide Dinitrate USP XXII Nalidixic Acid USP XXII Pyridoxine Hydrochloride USP XXII Strong Cetrimide Solution (40%) BP 88 Thiethylperazine Maleate USP XXII
ethanol, dry	149.512	0.59	Allopurinol USP XXII Ascorbic Acid USP XXII Clobutinol (boehringer ingelheim) Clomiphen Citrate USP XXII Diphenhydramine Hydrochloride USP XXII Propranolol Hydrochloride USP XXII Pyridoxine Hydrochloride USP XXII Terbutaline Sulfate USP XXII Thiethylperazine Maleate USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
ether	54.483	3.04	Albuterol Sulfate USP XXII Amitriptyline Hydrochloride USP XXII Clemastine Fumarate USP XXII Clidinium Bromide USP XXII Clobutinol (boehringer ingelheim) Clomiphen Citrate USP XXII Diethyltoluamide USP XXII Diphenhydramine Hydrochloride USP XXII Flurazepam Hydrochloride USP XXII Hydrochlorothiazide USP XXII Isosorbide Dinitrate USP XXII Levamisole Hydrochloride BP 88 Riboflavin USP XXII Strong Cetrimide Solution (40%) BP 88 Terbutaline Sulfate USP XXII Thiethylperazine Maleate USP XXII
ether, dry	7.680	3.04	Clemastine Fumarate USP XXII Clobutinol (boehringer ingelheim) Terbutaline Sulfate USP XXII
ethoxyethanol	41.784	0.79	Chlorhexidine Digluconate (20%) BP88
ethyl acetate	46.152	0.83	Albuterol Sulfate USP XXII Cimetidine USP XXII Clemastine Fumarate USP XXII Dipyridamole USP XXII Metronidazole USP XXII
ethyl acetoacetate	99.145	2.34	Cimetidine USP XXII Dipyridamole USP XXII
ethyl bromide	2	2.80	Amitriptyline Hydrochloride USP XXII
ethyl chloroacetate	219.900	1.00	Ibuprofen USP XXII
ethylen oxide	62.496	2.50	Metronidazole USP XXII
ethyl formate	8.000	0.81	Chloramphenicol USP XXII
ferrous sulfate	32	0.08	Chloramphenicol USP XXII
filter aid	7.764	0.65	Chloramphenicol USP XXII Diphenhydramine Hydrochloride USP XXII Ibuprofen USP XXII Sulfamethoxazole USP XXII
formaldehyde, conc.	482.861	0.24	Albuterol Sulfate USP XXII Calcium Pantothenate USP XXII Cimetidine USP XXII Hydrochlorothiazide USP XXII Strong Cetrimide Solution (40%) BP 88
formamide	50.696	1.39	Allopurinol USP XXII Pyridoxine Hydrochloride USP XXII
formamidine, hydrochloride	11.250	2.44	Allopurinol USP XXII
formic acid, conc.	669.400	0.69	Metronidazole USP XXII Strong Cetrimide Solution (40%) BP 88
fumaric acid	510	1.46	Clemastine Fumarate USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
gluconic acid (50%)	45.635	0.86	Chlorhexidine Digluconate (20%) BP88
L-glutamic acid	4.673	4.89	Levamisole Hydrochloride BP 88
guanidine, hydrochloride	135.981	1.33	Trimethoprim USP XXII
heptane	5.099	0.22	Calcium Pantothenate USP XXII
hexamethylenetetramine	76	1.22	Flurazepam Hydrochloride USP XXII
n-hexane	21.061	0.36	Vitamin E Acetate USP XXII
hexane-1,6-diamine, dihydrochloride	19.084	5.50	Chlorhexidine Digluconate (20%) BP88
hydrazine hydrate	43.446	2.76	Allopurinol USP XXII Isoniazid USP XXII
hydrobromic acid (48%)	460.000	0.93	Methyldopa USP XXII
hydrochloric acid, conc.	1.808.178	0.06	Albuterol Sulfate USP XXII Ascorbic Acid USP XXII Calcium Pantothenate USP XXII Chloramphenicol USP XXII Cimetidine USP XXII Clemastine Fumarate USP XXII Clidinium Bromide USP XXII Clobutinol (boehringer ingelheim) Diethyltoluamide USP XXII Diphenhydramine Hydrochloride USP XXII Dipyridamole USP XXII Glibenclamide BP 88 Hydrochlorothiazide USP XXII Ibuprofen USP XXII Nalidixic Acid USP XXII Pyridoxine Hydrochloride USP XXII Riboflavin USP XXII Strong Cetrimide Solution (40%) BP 88 Terbutaline Sulfate USP XXII Thiethylperazine Maleate USP XXII Vitamin E Acetate USP XXII
hydrogen gas	282	10.85	Albuterol Sulfate USP XXII Dipyridamole USP XXII Riboflavin USP XXII
hydrogenated solution from hydrogenation plant of sorbitol (amount given as dry substance)	1.000.000	0.40	Mannitol USP XXII
hydrogen chloride gas	42.641	1.32	Ascorbic Acid USP XXII Calcium Pantothenate USP XXII Diphenhydramine Hydrochloride USP XXII Flurazepam Hydrochloride USP XXII Levamisole Hydrochloride BP 88 Propranolol Hydrochloride USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
hydrogen peroxide, conc.	128.650	1.04	Chloramphenicol USP XXII
			Ibuprofen USP XXII
4-hydroxyacetophenone	8.596	15.27	Albuterol Sulfate USP XXII
2-(2-hydroxyethyl)-1-methylpyrrolidine	1.286	4.89	Clemastine Fumarate USP XXII
hydroxylamine sulphate	139.029	2.20	Sulfamethoxazole USP XXII
3-hydroxyquinuclidine	455	351.51	Clidinium Bromide USP XXII
ice	508.146	0.00	Allopurinol USP XXII
			Clemastine Fumarate USP XXII
			Clidinium Bromide USP XXII
			Clobutinol (boehringer ingelheim)
			Dipyridamole USP XXII
			Flurazepam Hydrochloride USP XXII
			Glibenclamide BP 88
			Levamisole Hydrochloride BP 88
			Metronidazole USP XXII
			Thiethylperazine Maleate USP XXII
imidazole	5.840	6.72	Miconazole Nitrate USP XXII
iminostilbene	19.634	85.00	Carbamazepine USP XXII
2-imino-1,3-thiazolidine	9.307	9.16	Levamisole Hydrochloride BP 88
iodine	7	20.00	Amitriptyline Hydrochloride USP XXII
			Thiethylperazine Maleate USP XXII
iodomethane	3	24.41	Clomiphen Citrate USP XXII
iron	481	0.51	Thiethylperazine Maleate USP XXII
isobutanol	93.600	0.90	Riboflavin USP XXII
isobutylbenzene	169.200	4.50	Ibuprofen USP XXII
isobutyric aldehyde	12.923	1.04	Calcium Pantothenate USP XXII
			Pyridoxine Hydrochloride USP XXII
isophytol	21.109	34.00	Vitamin E Acetate USP XXII
isopropanol	47.466	0.61	Chloramphenicol USP XXII
			Cimetidine USP XXII
			Clemastine Fumarate USP XXII
			Clidinium Bromide USP XXII
			Levamisole Hydrochloride BP 88
			Miconazole Nitrate USP XXII
isopropanol, dry	5.271	0.61	Propranolol Hydrochloride USP XXII
isopropyl amine	3.624	3.26	Propranolol Hydrochloride USP XXII
isopropyl ether	571	1.74	Clemastine Fumarate USP XXII
magnesium	2.163	3.15	Amitriptyline Hydrochloride USP XXII
			Clemastine Fumarate USP XXII
			Clobutinol (boehringer ingelheim)
			Clomiphen Citrate USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
magnesium sulfate	68,934	0.33	Calcium Pantothenate USP XXII
			Clomiphen Citrate USP XXII
			Isosorbide Dinitrate USP XXII
			Magnesium Stearate NF XVII
			Miconazole Nitrate USP XXII
			Vitamin E Acetate USP XXII
maize starch	25,500	0.70	Ascorbic Acid USP XXII
maleic acid	160	3.20	Thiethylperazine Maleate USP XXII
methanol	378,946	0.15	Ascorbic Acid USP XXII
			Calcium Pantothenate USP XXII
			Carbamazepine USP XXII
			Chloramphenicol USP XXII
			Chlorhexidine Digluconate (20%) BP88
			Cimetidine USP XXII
			Clidinium Bromide USP XXII
			Clomiphen Citrate USP XXII
			Flurazepam Hydrochloride USP XXII
			Glibenclamide BP 88
			Hydrochlorothiazide USP XXII
			Metronidazole USP XXII
			Miconazole Nitrate USP XXII
			Pyridoxine Hydrochloride USP XXII
			Riboflavin USP XXII
			Terbutaline Sulfate USP XXII
			Thiethylperazine Maleate USP XXII
methanol, dry	75,276	0.15	Calcium Pantothenate USP XXII
			Flurazepam Hydrochloride USP XXII
			Terbutaline Sulfate USP XXII
			Thiethylperazine Maleate USP XXII
			Trimethoprim USP XXII
3-methoxypropionitrile	48,008	3.66	Trimethoprim USP XXII
methylamine (41%)	79,200	0.76	Cimetidine USP XXII
3-methylbenzoic acid	1,531	3.82	Diethyltoluamide USP XXII
methylbromide	90,292	1.70	Clidinium Bromide USP XXII
			Strong Cetrimide Solution (40%) BP 88
methyl 2-chloropropionate	127,000	3.42	Methyldopa USP XXII
methyl dichloroacetate	8,480	1.78	Chloramphenicol USP XXII
2-methylimidazole	36,450	11.57	Metronidazole USP XXII
4-methylpentan-2-ol	234	1.71	Thiethylperazine Maleate USP XXII
1-naphtol	6,783	3.99	Propranolol Hydrochloride USP XXII
nickel sulfate	46,000	5.18	Ascorbic Acid USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
nitric acid, conc.	340.234	0.71	Chloramphenicol USP XXII Dipyridamole USP XXII Isosorbide Dinitrate USP XXII Metronidazole USP XXII Miconazole Nitrate USP XXII
octanol	1	2.05	Dipyridamole USP XXII
oleum	965.000	0.07	Ascorbic Acid USP XXII
organic solvent	165.450	0.50	Ibuprofen USP XXII
palladium on charcoal	10	366.40	Dipyridamole USP XXII Terbutaline Sulfate USP XXII
paraformaldehyde	62.078	0.75	Cimetidine USP XXII Clobutinol (boehringer ingelheim)
perchloroethylene	2.907	0.35	Levamisole Hydrochloride BP 88
petrolether	1.978	0.29	Clomiphen Citrate USP XXII Nalidixic Acid USP XXII
2-phenethylamine	1.252	6.11	Glibenclamide BP 88
phosphoric acid	12.545	0.10	Calcium Caseinate (FOOD GRADE)
phosphor pentachloride	44.922	1.13	Clidinium Bromide USP XXII Clomiphen Citrate USP XXII Dipyridamole USP XXII
phosphor pentoxide	42.467	1.87	Pyridoxine Hydrochloride USP XXII
phosphor trichloride	2.512	0.90	Clomiphen Citrate USP XXII
piperidine	6.876	6.11	Dipyridamole USP XXII
pivalic acid	32.400	2.75	Riboflavin USP XXII
potassium carbonate	21.152	0.78	Diethyltoluamide USP XXII Dipyridamole USP XXII Levamisole Hydrochloride BP 88
potassium hydroxide	1.256.189	0.81	Ascorbic Acid USP XXII Clemastine Fumarate USP XXII Clobutinol (boehringer ingelheim) Diphenhydramine Hydrochloride USP XXII Dipyridamole USP XXII Miconazole Nitrate USP XXII
pyridine	105.838	6.11	Cetylpyridinium Chloride USP XXII Sulfamethoxazole USP XXII Thiethylperazine Maleate USP XXII
quinoline	1.924	3.28	Thiethylperazine Maleate USP XXII
raney nickel catalyst	1.746	24.43	Riboflavin USP XXII
rape oil	5.000	1.01	Ascorbic Acid USP XXII
D-ribose	10.487	112.97	Riboflavin USP XXII
salt n. 1	62.100	0.70	Ibuprofen USP XXII
salt n. 2, soln.	99.000	0.70	Ibuprofen USP XXII
salt n. 3	20.400	0.70	Ibuprofen USP XXII
silicic acid - aluminium oxide	11.409	15.27	Vitamin E Acetate USP XXII
silicon oil	2.000	6.11	Ascorbic Acid USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
sodium	82	3.26	Clidinium Bromide USP XXII
sodium acetate	163.553	1.37	Albuterol Sulfate USP XXII
			Riboflavin USP XXII
			Sulfamethoxazole USP XXII
			Terbutaline Sulfate USP XXII
			Vitamin E Acetate USP XXII
sodiumamide	267	7.33	Clemastine Fumarate USP XXII
sodium bicarbonate	1.124.239	0.28	Aluminium Hydroxide Gel USP XXII
			Chloramphenicol USP XXII
			Ibuprofen USP XXII
			Sulfamethoxazole USP XXII
sodium bisulfite	6.505	0.40	Chloramphenicol USP XXII
			Vitamin E Acetate USP XXII
sodium borhydride	280	48.39	Miconazole Nitrate USP XXII
sodium bromide	8.000	0.93	Chloramphenicol USP XXII
sodium carbonate	1.457.452	0.86	Albuterol Sulfate USP XXII
			Aluminium Hydroxide Gel USP XXII
			Amitriptyline Hydrochloride USP XXII
			Ascorbic Acid USP XXII
			Chloramphenicol USP XXII
			Cimetidine USP XXII
			Clemastine Fumarate USP XXII
			Diphenhydramine Hydrochloride USP XXII
			Isosorbide Dinitrate USP XXII
			Levamisole Hydrochloride BP 88
			Miconazole Nitrate USP XXII
			Thiethylperazine Maleate USP XXII
sodium chloride	71.175	0.52	Calcium Pantothenate USP XXII
			Diethyltoluamide USP XXII
			Diphenhydramine Hydrochloride USP XXII
			Hydrochlorothiazide USP XXII
			Vitamin E Acetate USP XXII
sodium cyanate	10.601	1.74	Carbamazepine USP XXII
sodium cyanide	47.097	1.87	Calcium Pantothenate USP XXII
			Methyldopa USP XXII
sodium dicyanamide	17.991	2.81	Chlorhexidine Digluconate (20%) BP88
sodium ethoxide	3.520	3.80	Propranolol Hydrochloride USP XXII
sodium hydride suspension (50%)	14.236	9.83	Levamisole Hydrochloride BP 88

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
sodium hydroxide (50%)	4.583.484	0.30	Aluminium Hydroxide Gel USP XXII Calcium Pantothenate USP XXII Chloramphenicol USP XXII Chlorhexidine Digluconate (20%) BP88 Cimetidine USP XXII Clidinium Bromide USP XXII Clomiphen Citrate USP XXII Diethyltoluamide USP XXII Diphenhydramine Hydrochloride USP XXII Dipyridamole USP XXII Flurazepam Hydrochloride USP XXII Glibenclamide BP 88 Hydrochlorothiazide USP XXII Ibuprofen USP XXII Isoniazid USP XXII Levamisole Hydrochloride BP 88 Magnesium Stearate NF XVII Metronidazole USP XXII Nalidixic Acid USP XXII Pyridoxine Hydrochloride USP XXII Sodium Benzoate NF XVII Strong Cetrimide Solution (40%) BP 88 Sulfamethoxazole USP XXII Thiethylperazine Maleate USP XXII Undecylenic Acid, Zinc Salt Vitamin E Acetate USP XXII Zinc Stearate USP XXII
sodiumhypochlorite (15%)	821.814	0.23	Sulfamethoxazole USP XXII
sodium hyposulfite	1.455	0.20	Sulfamethoxazole USP XXII
sodium methoxide	226.702	1.17	Allopurinol USP XXII Clomiphen Citrate USP XXII Flurazepam Hydrochloride USP XXII Pyridoxine Hydrochloride USP XXII Sulfamethoxazole USP XXII Trimethoprim USP XXII
sodium nitrite	49.755	0.92	Cimetidine USP XXII Riboflavin USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
sodium sulfate	91,513	0.13	Albuterol Sulfate USP XXII
			Calcium Pantothenate USP XXII
			Clemastine Fumarate USP XXII
			Clidinium Bromide USP XXII
			Clobutinol (boehringer ingelheim)
			Clomiphen Citrate USP XXII
			Dipyridamole USP XXII
			Flurazepam Hydrochloride USP XXII
			Hydrochlorothiazide USP XXII
			Miconazole Nitrate USP XXII
			Pyridoxine Hydrochloride USP XXII
			Sulfamethoxazole USP XXII
			Thiethylperazine Maleate USP XXII
			Undecylenic Acid USP XXII
sodium sulfite, soln.	5,091	0.20	Sulfamethoxazole USP XXII
solvent 1	466,000	0.50	Methyldopa USP XXII
solvent 2	148,000	0.50	Methyldopa USP XXII
solvent n. 1	270,000	0.50	Ibuprofen USP XXII
solvent n. 2	90,150	0.50	Ibuprofen USP XXII
D-sorbitol	1,037,984	1.13	Ascorbic Acid USP XXII
			Isosorbide Dinitrate USP XXII
steam	1,280,330	0.00	Benzoic Acid USP XXII
			Undecylenic Acid USP XXII
stearic acid	566,444	0.65	Magnesium Stearate NF XVII
			Zinc Stearate USP XXII
styrene oxide	10,935	4.27	Levamisole Hydrochloride BP 88
sulfur	107	0.29	Thiethylperazine Maleate USP XXII
sulfuric acid, conc.	1,948,618	0.08	Albuterol Sulfate USP XXII
			Allopurinol USP XXII
			Aluminium Hydroxide Gel USP XXII
			Calcium Pantothenate USP XXII
			Carbamazepine USP XXII
			Chloramphenicol USP XXII
			Dipyridamole USP XXII
			Ibuprofen USP XXII
			Isosorbide Dinitrate USP XXII
			Metronidazole USP XXII
			Sulfamethoxazole USP XXII
			Terbutaline Sulfate USP XXII
L-tartaric acid	240,428	3.64	Chloramphenicol USP XXII
			Methyldopa USP XXII
			Thiethylperazine Maleate USP XXII
1-tetradecaneamine	324,896	3.05	Strong Cetrimide Solution (40%) BP 88
tetrahydrofurane, dry	6,841	2.82	Amitriptyline Hydrochloride USP XXII
			Clomiphen Citrate USP XXII
thioethanol	206	3.66	Thiethylperazine Maleate USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
thionyl chloride	15,561	1.21	Clemastine Fumarate USP XXII Clomiphen Citrate USP XXII Diethyltoluamide USP XXII Levamisole Hydrochloride BP 88
thiourea	6,619	3.05	Dipyridamole USP XXII
toluene	1,434,167	0.30	Benzoic Acid USP XXII Cetylpyridinium Chloride USP XXII Chloramphenicol USP XXII Clidinium Bromide USP XXII Diethyltoluamide USP XXII Flurazepam Hydrochloride USP XXII Miconazole Nitrate USP XXII Pyridoxine Hydrochloride USP XXII Sulfamethoxazole USP XXII Thiethylperazine Maleate USP XXII Vitamin E Acetate USP XXII
toluene, dry	2,213	0.30	Clidinium Bromide USP XXII
p-toluene sulfonic acid	111	4.27	Isosorbide Dinitrate USP XXII Pyridoxine Hydrochloride USP XXII
p-toluene sulfonyl chloride	6,056	2.14	Levamisole Hydrochloride BP 88
trichloroethylene	199,000	0.72	Ascorbic Acid USP XXII Chloramphenicol USP XXII
triethoxymethane	15,548	2.44	Nalidixic Acid USP XXII
triethylamine	501	1.22	Benzyl Benzoate USP XXII Clomiphen Citrate USP XXII Levamisole Hydrochloride BP 88
triethyl phosphate	17,792	2.44	Nalidixic Acid USP XXII
3,4,5-trimethoxy-benzaldehyde	93,207	25.88	Trimethoprim USP XXII
2,3,5-trimethylhydroquinone	11,409	14.05	Vitamin E Acetate USP XXII
urea	58,475	0.21	Chloramphenicol USP XXII Dipyridamole USP XXII
veratraldehyde	147,000	5.70	Methyldopa USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
water	19.445.433	0.00	Albuterol Sulfate USP XXII
			Allopurinol USP XXII
			Amitriptyline Hydrochloride USP XXII
			Benzoic Acid USP XXII
			Benzyl Benzoate USP XXII
			Calcium Caseinate (FOOD GRADE)
			Calcium Pantothenate USP XXII
			Chlorhexidine Digluconate (20%) BP88
			Cimetidine USP XXII
			Clemastine Fumarate USP XXII
			Clidinium Bromide USP XXII
			Clobutinol (boehringer ingelheim)
			Clomiphen Citrate USP XXII
			Diethyltoluamide USP XXII
			Diphenhydramine Hydrochloride USP XXII
			Dipyridamole USP XXII
			Flurazepam Hydrochloride USP XXII
			Glibenclamide BP 88
			Hydrochlorothiazide USP XXII
			Isoniazid USP XXII
			Isosorbide Dinitrate USP XXII
			Levamisole Hydrochloride BP 88
			Magnesium Stearate NF XVII
			Metronidazole USP XXII
			Miconazole Nitrate USP XXII
			Nalidixic Acid USP XXII
			Propranolol Hydrochloride USP XXII
			Riboflavin USP XXII
			Strong Cetrimide Solution (40%) BP 88
			Sulfamethoxazole USP XXII
			Terbutaline Sulfate USP XXII
			Thiethylperazine Maleate USP XXII
			Trimethoprim USP XXII
			Undecylenic Acid USP XXII
			Undecylenic Acid, Zinc Salt
			Vitamin E Acetate USP XXII
			Zinc Stearate USP XXII

Table 4 (continued): Raw materials required to produce 48 items; amount in [kg/year]; prices in [US$/kg]; and for which product they are needed.

Starting materials	kg/year	prices	Product
water, dist.	1.663.672	0.01	Albuterol Sulfate USP XXII
			Benzyl Benzoate USP XXII
			Carbamazepine USP XXII
			Cetylpyridinium Chloride USP XXII
			Chlorhexidine Digluconate (20%) BP88
			Dipyridamole USP XXII
			Hydrochlorothiazide USP XXII
			Niacinamide USP XXII
			Trimethoprim USP XXII
xylene	6.490	0.29	Chloramphenicol USP XXII
			Isosorbide Dinitrate USP XXII
			Thiethylperazine Maleate USP XXII
zinc chloride	140.915	1.22	Undecylenic Acid, Zinc Salt
			Vitamin E Acetate USP XXII
			Zinc Stearate USP XXII
zinc powder	1.880	1.47	Vitamin E Acetate USP XXII

It must however be pointed out that many companies refused to place offers for chemicals bound for Iran, due to fears that they might be involved into affairs of chemical weapons production. Therefore for some critical chemicals no offer for export to Iran could be obtained. As a result of the present international situation it must be stated that it seems a prerequisite for the implementation of the present project to establish a control system for the plant, following the Geneva convention on the ban of chemical weapons, which will guarantee technology, equipment and raw materials suppliers that their activities might not have negative effects. This concern was found with most of the companies contacted. It must be pointed out that most companies relied on the involvement of UNIDO, so that it has to be doubted, whether the proposed project could be carried out without participation of an International Organization.

6.3.4. INTERRELATION: RAW MATERIALS - ECONOMIC EFFICIENCY - OPERATING MARGIN

A first impression of the economical feasibility of a process can be achieved by a comparison of raw material costs and expected sales revenues (= Operating Margin) (Table 5).

Table 5: Cost of Starting Materials in Percent of Sales Revenues and Operating Margin

Products	produced quantity [t/year]	sales revenues [US$/year]	costs of starting materials [US$/year]	cost of starting materials in percent of sales revenues	operating margin [US$/year]
Methyldopa USP XXII	100.0	8.000.000	3.264.511	41	4.735.489
Ascorbic acid USP XXII	500.0	6.500.000	3.788.412	58	2.711.588
Aluminium hydroxide gel USP XXII	5.000.0	9.500.000	6.918.904	73	2.581.096
Cetrimide BP 88	1.000.0	3.280.000	1.886.086	58	1.393.914
Chlorhexidine gluconate BP 88	164.0	1.640.000	399.359	24	1.240.641
Carbamazepine USP XXII	18.0	2.790.000	1.744.459	63	1.045.541
Cimetidine USP XXII	50.0	2.550.000	1.661.648	65	888.352
Clobutinol HCl (Boehr. Ingel.)	2.0	875.000	46.826	5	828.174
Clemastine fumarate USP XXII	0.2	700.000	47.371	7	652.629
Chloramphenicol USP XXII	16.0	1.120.000	483.913	43	636.087
Niacinamide USP XXII	100.0	1.300.000	700.805	54	599.195
Thiethylperazine maleate USP XXII	0.4	650.000	66.463	10	583.537
Pyridoxine hydrochloride USP XXII	20.0	860.000	422.089	49	437.911
Clomiphen citrate USP XXII	2.0	630.000	202.355	32	427.645
Mannitol USP XXII	100.0	450.000	47.000	10	403.000
Clidinium bromide USP XXII	1.0	550.000	184.025	33	365.975
Glibenclamide BP 88	2.0	380.000	27.076	7	352.924
Calcium caseinate (food grade)	280.0	1.120.000	846.565	76	273.435
Nalidixic acid	8.0	520.000	301.034	58	218.966
Cetylpyridinium chloride USP XXII	16.0	320.000	107.889	34	212.111
Miconacole nitrate USP XXII	4.0	420.000	246.240	59	173.760
Zinc undecylenate USP XXII	24.0	360.000	193.001	54	166.999
Propranolol USP XXII	8.0	240.000	80.317	33	159.683
Amitriptyline hydrochloride USP XXII	7.0	539.000	420.736	78	118.264
Benzoic acid USP XXII	50.0	132.500	27.463	21	105.037
Allopurinol USP XXII	9.0	450.000	353.534	79	96.466
Terbutaline sulfate USP XXII	0.2	200.000	112.123	56	87.877
Isosorbide dinitrate, diluted USP XXII	5.0	125.000	41.475	33	83.525
Levamisole hydrochloride BP 88	6.0	450.000	382.861	85	67.139
Magnesium stearate NF XVII	60.0	90.000	48.873	54	41.127
Dipyridamole USP XXII	4.5	652.500	616.418	94	36.082
Ibuprofen USP XXII	150.0	2.400.000	2.364.150	99	35.850
Flurazepam USP XXII	0.2	92.000	60.763	66	31.237
Diphenhydramine HCl USP XXII	7.0	175.000	144.385	83	30.615
Calcium panthothenate USP XXII	8.0	144.000	119.315	83	24.685
Sodium benzoate NF XVII	20.0	28.000	14.346	51	13.654
Zinc stearate USP XXII	540.0	540.000	527.364	98	12.636
Diethyltoluamide USP XXII	2.0	22.500	16.204	72	6.296
Benzyl benzoate USP XXII	5.0	16.000	10.533	66	5.467
Hydrochlorothiazide USP XXII	4.0	80.000	76.555	96	3.445
Undecylenic acid USP XXII	5.0	42.500	39.544	93	2.956
Albuterol USP XXII	1.0	260.000	258.780	100	1.220
Isoniazid USP XXII	24.0	232.800	332.899	143	-100.099
Riboflavin USP XXII	18.0	1.530.000	1.669.425	109	-139.425
Metronidazole USP XXII	28.0	616.000	1.002.399	163	-386.399
Vitamine E acetate USP XXII	26.0	730.600	1.301.705	178	-571.105
Sulfamethoxazole USP XXII	200.0	3.200.000	4.547.613	142	-1.347.613
Trimethoprim USP XXII	40.0	1.560.000	2.933.489	188	-1.373.489
sum (without negative products)		**51,194,000**	**29,301,772**		**21,892,228**

It can be seen that in many cases the raw material price constitutes a very high percentage of the end product price (a situation which would be even worse, if transport costs of

chemicals would be included). This low margin is not surprising in the case of established "old" bulk pharmaceutical chemicals. It makes clear that such products can only be manufactured economically with optimized production know how. In some cases even negative values were obtained. This reflects that either technologies are starting from too expensive starting materials (Trimethoprim, Metronidazole). In this case technology suppliers should be requested to include the manufacture of the starting material into their offer. In other cases it reflects the fact that the technological know how applied by the manufacturers is significantly superior to the level of technology available for this study. This refers mainly to the vitamins, for which there is a rather closed market of manufacturers with a high production standard.

In relation to the investment required for the implementation of the project the operating margin is rather low. Maintaining the production programme as it is at present means that the justification of this project has to be strongly supported by the fact that it is carried out for the social benefit of the Nation.

Taking into account operating margins it can also be stated that these margins as a rule are much better for "younger" products. Although it must be expected that for such products costs of technological know how will be higher, it is recommended that some flexibility with respect to product alternatives is introduced into the requests for technologies to improve the situation concerning operating margins in the plant. A first step into this direction has been taken by the proposal of the 7 new compounds quoted in chapter 6.1.3..

6.3.5. TECHNICAL PROCESSES - PRODUCTION

The different steps of the selected technologies were analyzed to identify the unit reactions used in the plant. The result is given in Table 6.

The list reflects a great variety of unit reactions to be performed. Their implementation would mean that a broad technical know how in chemical synthesis will be available in the plant.

Table 6: Unit reactions used in the plant

Unit reactions	Product
Acetal formation	Pyridoxine Hydrochloride USP XXII
Acetylation	Vitamin E Acetate USP XXII
Aldol condensation	Calcium Pantothenate USP XXII
	Chloramphenicol USP XXII
Alkylation	Cimetidine USP XXII
	Clemastine Fumarate USP XXII
	Levamisole Hydrochloride BP 88
	Metronidazole USP XXII
Amide degradation	Sulfamethoxazole USP XXII
Amide formation	Diethyltoluamide USP XXII
	Glibenclamide BP 88
Amine-Cyanamide addition	Chlorhexidine Digluconate (20%) BP88
Amino nitrile formation	Methyldopa USP XXII
Aminolysis	Chloramphenicol USP XXII
Azo coupling	Riboflavin USP XXII
Bromination	Albuterol Sulfate USP XXII
	Diphenhydramine Hydrochloride USP XXII
	Miconazole Nitrate USP XXII
	Terbutaline Sulfate USP XXII
Carbonyl addition reaction	Glibenclamide BP 88
Chlorination	Clemastine Fumarate USP XXII
	Clidinium Bromide USP XXII
	Clomiphen Citrate USP XXII
	Diethyltoluamide USP XXII
	Dipyridamole USP XXII
Condensation	Allopurinol USP XXII
	Chlorhexidine Digluconate (20%) BP88
	Hydrochlorothiazide USP XXII
	Methyldopa USP XXII
	Sulfamethoxazole USP XXII
	Trimethoprim USP XXII
	Vitamin E Acetate USP XXII
Crack-Reaction	Undecylenic Acid USP XXII
Cyanohydrine formation	Calcium Pantothenate USP XXII
Decarboxylation	Thiethylperazine Maleate USP XXII
Dehydration	Amitriptyline Hydrochloride USP XXII
	Isosorbide Dinitrate USP XXII
Diels-Alder-reaction	Pyridoxine Hydrochloride USP XXII
Elimination	Clomiphen Citrate USP XXII
Enolization	Ascorbic Acid USP XXII
Ester formation	Albuterol Sulfate USP XXII
	Benzyl Benzoate USP XXII
	Clidinium Bromide USP XXII
Ester hydrolysis	Albuterol Sulfate USP XXII
Formation of free base	Chlorhexidine Digluconate (20%) BP88
Formylation	Ibuprofen USP XXII

Table 6 (continued): Unit reactions used in the plant

Unit reactions	Product
Friedel-Crafts acylation	Ibuprofen USP XXII
Friedel-Crafts alkylation	Albuterol Sulfate USP XXII
Grignard formation	Amitriptyline Hydrochloride USP XXII Clobutinol (boehringer ingelheim) Clomiphen Citrate USP XXII
Grignard reaction	Amitriptyline Hydrochloride USP XXII Clemastine Fumarate USP XXII Clobutinol (boehringer ingelheim) Clomiphen Citrate USP XXII
Hydrazide formation	Isoniazid USP XXII
Hydrobromation	Chloramphenicol USP XXII
Hydrogenation	Albuterol Sulfate USP XXII Mannitol USP XXII Riboflavin USP XXII Terbutaline Sulfate USP XXII
Hydrolysis	Ascorbic Acid USP XXII Calcium Pantothenate USP XXII Methyldopa USP XXII Nalidixic Acid USP XXII Niacinamide USP XXII Pyridoxine Hydrochloride USP XXII Sulfamethoxazole USP XXII
Ketal formation	Ascorbic Acid USP XXII Chloramphenicol USP XXII
Lactonisation	Ascorbic Acid USP XXII
Liberation of the base	Clemastine Fumarate USP XXII
Mannich reaction	Clobutinol (boehringer ingelheim)
N-Acylation	Chloramphenicol USP XXII Flurazepam Hydrochloride USP XXII
N-Alkylation	Albuterol Sulfate USP XXII Cetylpyridinium Chloride USP XXII Clidinium Bromide USP XXII Flurazepam Hydrochloride USP XXII Miconazole Nitrate USP XXII Nalidixic Acid USP XXII Strong Cetrimide Solution (40%) BP 88 Terbutaline Sulfate USP XXII Thiethylperazine Maleate USP XXII
N-Arylation	Thiethylperazine Maleate USP XXII
N-Formylation	Pyridoxine Hydrochloride USP XXII
Nitration	Chloramphenicol USP XXII Dipyridamole USP XXII Isosorbide Dinitrate USP XXII Metronidazole USP XXII
Nucleophilic substitution	Cimetidine USP XXII Dipyridamole USP XXII Hydrochlorothiazide USP XXII

Table 6 (continued): Unit reactions used in the plant

Unit reactions	Product
O-Alkylation	Clomiphen Citrate USP XXII
	Diphenhydramine Hydrochloride USP XXII
	Miconazole Nitrate USP XXII
	Propranolol Hydrochloride USP XXII
Oxidation	Ascorbic Acid USP XXII
	Benzoic Acid USP XXII
	Ibuprofen USP XXII
Purification	Albuterol Sulfate USP XXII
	Allopurinol USP XXII
	Ascorbic Acid USP XXII
	Benzoic Acid USP XXII
	Carbamazepine USP XXII
	Clomiphen Citrate USP XXII
	Ibuprofen USP XXII
	Isoniazid USP XXII
	Methyldopa USP XXII
Quaternisation	Strong Cetrimide Solution (40%) BP 88
Racemate resolution	Calcium Pantothenate USP XXII
	Chloramphenicol USP XXII
	Clemastine Fumarate USP XXII
	Levamisole Hydrochloride BP 88
	Methyldopa USP XXII
Razemisation	Calcium Pantothenate USP XXII
	Levamisole Hydrochloride BP 88
	Methyldopa USP XXII
Reaction with beta-alanine	Calcium Pantothenate USP XXII
Recovery of resolution agent	Calcium Pantothenate USP XXII
Recrystallisation	Clemastine Fumarate USP XXII
	Glibenclamide BP 88
	Metronidazole USP XXII
Reduction	Chloramphenicol USP XXII
	Dipyridamole USP XXII
	Miconazole Nitrate USP XXII
	Thiethylperazine Maleate USP XXII
Ring Closure	Allopurinol USP XXII
	Cimetidine USP XXII
	Dipyridamole USP XXII
	Flurazepam Hydrochloride USP XXII
	Nalidixic Acid USP XXII
	Pyridoxine Hydrochloride USP XXII
	Riboflavin USP XXII
	Sulfamethoxazole USP XXII
	Vitamin E Acetate USP XXII
S-Alkylation	Thiethylperazine Maleate USP XXII
S-Arylation	Thiethylperazine Maleate USP XXII

Table 6 (continued): Unit reactions used in the plant

Unit reactions	Product
Salt formation	Albuterol Sulfate USP XXII
	Aluminium Hydroxide Gel USP XXII
	Amitriptyline Hydrochloride USP XXII
	Calcium Caseinate (FOOD GRADE)
	Chlorhexidine Digluconate (20%) BP88
	Cimetidine USP XXII
	Clemastine Fumarate USP XXII
	Clemastine Fumarate USP XXII
	Clobutinol (boehringer ingelheim)
	Clomiphen Citrate USP XXII
	Diphenhydramine Hydrochloride USP XXII
	Flurazepam Hydrochloride USP XXII
	Magnesium Stearate NF XVII
	Propranolol Hydrochloride USP XXII
	Sodium Benzoate NF XVII
	Thiethylperazine Maleate USP XXII
	Thiethylperazine Maleate USP XXII
	Undecylenic Acid, Zinc Salt
	Zinc Stearate USP XXII
Schiff base formation	Riboflavin USP XXII
Solution formation	Strong Cetrimide Solution (40%) BP 88
Sulfonamide formation	Glibenclamide BP 88
	Hydrochlorothiazide USP XXII
	Sulfamethoxazole USP XXII
Urethane - formation	Carbamazepine USP XXII

Concerning the plant lay-out it was decided that some specific reactions, which appear in different productions, should be carried out in the same unit, both to save investment for specific equipment and to be in the position to perform the production with personnel specialized on these reactions. The reactions which were identified for performance at one specific place were:

- Hydrogenations
- Grignard reactions
- Oxidations

Isosorbide dinitrate which is an explosion hazardous compound should be manufactured in a specific unit apart from the other production units. Metronidazole production, in which ethylene oxide is used, should be placed in a single line. The final decisions on the required distance to other production units should be subject to a risk analysis in the implementation phase of the project.

6.3.6. PROCESS FLOW SHEETS AND BLOCK SCHEMES

Process flow-sheets were prepared for all steps of production of each of the products. These flow sheets can be found in the product file of each product. Since in most cases - as mentioned earlier - detailed process data were not supplied by technology holders, these flow sheets were worked out as basic process flow sheets. They reflect the equipment requirements for production. Since these flow sheets were also required for decision whether a product would be placed in a single line or a multi product line, they had to be drawn before this decision was met. Therefore in several cases, especially for multi purpose plant products, the reactor sizes indicated in the flow sheet do not correspond to the actually considered capacities.

Block schemes were also drawn for each product and added to the product file. These schemes reflect the material flow and were the basis for the evaluation of raw material and solvent requirements, solvent recovery , energy demand and estimation of generated waste.

6.3.7. OPTIONS TO ADOPT THE BEST TECHNO-ECONOMICAL PRODUCTION PROGRAM BASED ON SINGLE AND MULTI PRODUCT LINES

As mentioned before the main aim of the project is to satisfy the demand of the Iranian population for pharmaceuticals. This requirement is reflected in the foreseen production quantities. The approach of this project is differing from that of most pharmaceutical manufacturers who try to target the world market and therefore have no restrictions in increasing their production capacity to the most economic level. The contacts to technology suppliers revealed that in many cases the project production capacities are considerably lower than usual and in several cases even so low that an economically feasible production would be practically impossible. In such cases only production in a multi purpose plant will secure that the investment is not lost, because the option to change production will leave the decision open to which degree non profitable productions are carried out.

Advantages and disadvantages of single line production versus multi purpose plant production are well known and have frequently been discussed. There is general agreement that both strategies of production are acceptable, differences in opinions appear mainly on the question, when a product should be placed into a multi purpose plant. The decisions in this project were met along the following criteria:

1. A maximum reactor size of 6 m^3 was foreseen for the multi purpose units, because bigger reactors would reduce the flexibility of the plant.

2. Products, which in a multi purpose plant would occupy one line for about one year, were considered for single line production, for the following reasons: Production organization is much easier. Conditions of a technology supplier concerning equipment can be met more easily. The additional investment required mainly refers to local investment for the building.

3. For reasons of production organization the number of products to be manufactured in one multi purpose production unit was kept below 10 products, with an optimum of about only 2 products to be manufactured at one time (production campaigns).

4. Products with bad parameters concerning economy of production were allocated to a multi purpose production unit, wherever feasible.

6.4. PRODUCTION PROGRAMME FOR EACH UNIT AND THE WHOLE COMPLEX

With 48 products to be synthesized this project is certainly one of the most ambitious pharmaceutical projects ever carried out. It also differs from usual ventures in the investment sector by the fact that its main goal is not maximizing profit, but satisfying the demand of a nation.

Technically speaking the goal of the project is to establish in a big effort a pharmaceutical complex, which in terms of economy is medium size, in terms of complexity and perspective is large size. A pharmaceutical company is a living body that requires short term, medium term and long term planning from the beginning. Short term success is determined by the products foreseen in the planning phase. Prerequisites for long term success, such as establishment of research centers, have also been considered in this project. Medium term success is however closely related with the interrelation of the company to the international sector, because there is a steady development in products, prices and markets, which requires permanent activities in planning. As a matter of fact the complex situation of the pharmaceutical sector has led to a significant specialization of most companies, such specialization being either correlated to special fields of indication or to specialized technical know how.

It could be seen from the answers of many companies to the request for technology supply that an unstructured mix of 50 products makes it difficult for outsiders to understand the dedication and strategy of a pharmaceutical company. Much more decisive seems however the fact that it is extremely difficult for the strategic planning staff to cover the whole range of pharmaceutical production without setting strategic medium term development goals.

Bearing in mind the dedication of the plant and the requirements of structuring, it was found in an analysis that about each 25% of the products could be associated to two main fields on indication: analgesics and other pharmaceuticals acting on the central nervous system on the one hand and chemotherapeutics and antiseptics on the other hand. Another 25% of the products were related to natural product chemistry, either using natural products as starting materials or producing natural products, such as vitamins. The remaining 25% consisted of synthetic pharmaceuticals with differing field of indication. This finding was the basis to work out a strategic profile for the plant, which will reduce its complexity by the formation of 4 operating sectors as follows:

A. Sectors with pharmaceutical profile

Sector 1: Analgesics and Central Nervous System Compounds
Sector 2: Chemotherapeutics and Antiseptics

The products of these sectors would satisfy the demand of the country for pharmaceuticals in two of the most important fields of indication. Flexibility in the choice of products, active readiness to improve the product mix in these two fields of indication by licensing of young products and concentrating development work on these fields would secure the future development.

Profitability in pharmaceutical industry is much more related to formulation than to active compound production. The fact that the SHAHID MODARRES project at present does not foresee any formulation will certainly be a disadvantage of the established company, because it will be depending upon a few formulating companies instead of the whole market of pharmaceutical distributors. It is therefore strongly recommended that in a second phase of development the Sectors 1 and 2 also should integrate formulation to their profile thus becoming fully integrated pharmaceutical manufacturing companies.

As far as the technical concept is concerned, these unit will have their emphasis in production following highest quality of manufacturing standards. Apart from the

hydrogenation unit, which will be placed in sector 1 (practically all hydrogenations are connected with products of this sector) no specific chemical technological profile is foreseen.

B. Sector 3: Natural Product Chemistry

Although not integrated into the present project, a sorbitol plant at the site of SHAHID MODARRES is by far the biggest unit in the industrial complex. Sorbitol, such as some other products, like Mannitol and the Stearates, is manufactured from natural products. Industries of this type are specialized and as a rule not necessarily connected with pharmaceutical production. The specific situation that this type of chemistry is included in a pharmaceutical complex represents an interesting challenge, because there is a considerable number of pharmaceuticals based on this family of products. It seems therefore to be advisable to use this opportunity as a nucleus to develop the profile of the company further into the production of pharmaceuticals from natural sources. This development could include the following long term lines:

- carbohydrate based pharmaceuticals
- carbohydrates as building blocks for synthetic pharmaceuticals
- semisynthetic pharmaceuticals from Iranian natural products
- biotechnological manufacturing processes
- (synthesis of natural products from other sources)

As a matter of fact such development has been considered already in the Terms of Reference by integrating a Multi Purpose Medicinal Plant Extraction and a Research and Development Center for Biotechnology and Genetic Engineering to the project. Both units will be attached to sector three to strengthen the development capacity in this field.

Sector three also contains a synthetic multi purpose plant, which is mainly used for the manufacture of vitamins. Although the investment into a multi purpose plant in this sector seems justified in principle, it must be stated that technologies for the production of the vitamins foreseen in this plant could not be obtained for the project till now.

C. Sector 4: Intermediates Manufacturing

Development and up-scaling of chemical synthetic processes as well as the manufacture of intermediates constitute an important element in a fully integrated pharmaceutical company. It is recommended to concentrate these activities to one sector. Broad chemical

synthetic know how together with flexible infrastructure and equipment are characteristic for such units. With reference to the importance of this part of pharmaceutical manufacturing it is recommended to dedicate the sector, in which at present those products are manufactured, which do not fit into the profiles of the other sectors, to process development and intermediates manufacturing. It is obvious that this dedication would be a long term goal and that manufacture of the present set of pharmaceuticals could continue also in this sector, but it is expected that a highly versatile chemical synthetic profile of this sector could render the SHAHID MODARRES plant competitive in product development. For this reason also the Pilot Plant for Technology Transfer will be placed in this unit.

It is recommended that as a special feature of the pilot plant it should include a unit for development and up-scaling of continuous processes. Some of the products foreseen in the project, e.g. benzoic acid, are bulk pharmaceuticals manufactured in continuos processes. The quantities for foreseen production correspond to pilot scale in continuos processes. Thus the investment into such a pilot plant for up-scaling of continuous processes would on the one hand come up to the requirement of the proposed production and would on the other hand without considerable further investment install one of the most versatile chemical development centers.

A look on the production programme of the 4 sectors of the SHAHID MODARRES Industrial Pharmaceutical Complex reveals that the sectors are also well balanced concerning their expected sales revenues (Fig. 1 - 6).

SECTOR 1: ANALGESICS AND CENTRAL NERVOUS SYSTEM COMPOUNDS

Unit 1.1.	Ibuprofen	150	t/y
Unit 1.2.	Methyldopa	100	t/y
Unit 1.3.	Multi - purpose Plant		
	Carbamazepine	18	t/y
	Propranolol	8	t/y
	Dipyridamole	4,5	t/y
	Clomiphene	2	t/y
	Albuterol	1	t/y
	Thiethylperazine	0,4	t/y
	Terbutaline	0,2	t/y
	Flurazepam	0,2	t/y
	Hydrogenation part:		
	Dipyridamole		
	Albuterol		
	Terbutaline		

SECTOR 2: CHEMOTHERAPEUTICS AND ANTISEPTICS

Unit 2.1.	Cetrimide (40%)	1000	t/y
	Metronidazole	28	t/y
Unit 2.2.	Sulfamethoxazole	200	t/y
	Trimethoprim	40	t/y
Unit 2.3.	Multi - purpose Plant		
	Chlorhexidine (20%)	164	t/y
	Isoniazid	24	t/y
	Cetylpyridinium-chloride	16	t/y
	Chloramphenicol	16	t/y
	Nalidixic acid	8	t/y
	Levamisole	6	t/y
	Miconazole	4	t/y

SECTOR 3: NATURAL PRODUCT CHEMISTRY + VITAMINS + FATTY ACID DERIVATIVES

Unit 3.1.	Ascorbic acid	500	t/y
Unit 3.2.	Ca - caseinate	200	t/y
Unit 3.3.	Nicotinamide	100	t/y
Unit 3.4.	Zn - stearate	540	t/y
	Mg - stearate	60	t/y
Unit 3.5.	Mannitol	100	t/y
Unit 3.6.	Isosorbide dinitrate (explosion protected area)	5	t/y
Unit 3.7.	Multi - purpose Plant		
	Vitamins:		
	Vitamine E	26	t/y
	Pyridoxine	20	t/y
	Riboflavin	18	t/y
	Ca - panthothenate	8	t/y
	Fatty acid derivatives:		
	Undecylenic acid	24	t/y
	Zn - undecylenate	5	t/y
Unit 3.8.	Medicinal Plant Extraction		
Unit 3.9.	Biochemical Engineering and Generic Development Center		

SECTOR 4: PHARMACEUTICAL INTERMEDIATES AND GENERAL PHARMACEUTICAL CHEMICALS

Unit 4.1.	Aluminum-hydroxide (10%)	5000	t/y
Unit 4.2.	Cimetidine	50	t/y
Unit 4.3.	Multi - purpose Plant		
	Allopurinol	9	t/y
	Diphenhydramine	7	t/y
	Hydrochlorothiazide	4	t/y
	Diethyltoluamide	2	t/y
	Glibenclamide	2	t/y
	Clidinium bromide	1	t/y
	Clemastine	0,2	t/y
	Grignard - reaction part:		
	Amitriptyline	7	t/y
	Clomiphen		
	Clobutinol	2	t/y
	Clemastine		
Unit 4.4.	Multi - purpose Plant Development Center		
	Oxidation part:		
	Benzoic acid	50	t/y
	Sodium - benzoate	20	t/y
	Benzylbenzoate	5	t/y
	including development facilities for:		
	Nicotinic acid (beta, gamma)		
	m-Methylbenzoic acid		

6.5. MATERIAL INPUT AND RECOVERY

As it can be seen from Chapter 6.3.3. there is as well a great variety as also a great quantity of chemicals to be handled, which requires a well organized material management, handling and storage system. In the storage of solid materials it has to be considered that enough storage units are available to enable required separation of products.

Most of the solid chemicals will be stored in a general store, in addition small storage units will be attached to the production units to allow storage of immediately required raw materials and intermediates. In Chapter 14.2. a comprehensive survey on the storage facilities is given.

Table 7: Estimated yearly sales revenues for sector 1

Sector	Unit	Drug Bulk Compound	Capacity tons/yr	estimated sales revenues in US$ minimum	most likely	maximum
1	1	Ibuprofen USP XXII	150.00	1,979,166.67	2,400,000.00	3,450,000.00
1	2	Methyldopa USP XXII	100.00	3,580,000.00	8,000,000.00	8,500,000.00
1	3	Albuterol Sulfate USP XXII	1.00	250,200.00	260,000.00	260,000.00
1	3	Carbamazepine USP XXII	18.00	2,700,000.00	2,790,000.00	3,000,000.00
1	3	Clomiphen Citrate USP XXII	2.00	474,000.00	630,000.00	670,000.00
1	3	Dipyridamol USP XXII	4.50	411,750.00	652,500.00	847,350.00
1	3	Flurazepam USP XXII	0.20	90,000.00	92,000.00	104,166.67
1	3	Propranolol USP XXII	8.00	171,280.00	240,000.00	277,777.78
1	3	Terbutaline Sulfate USP XXII	0.20	194,444.44	200,000.00	364,200.00
1	3	Thiethylperazine Maleate USP XXII	0.40	650,000.00	650,000.00	650,000.00
		sum over sector	284.30	10,500,841.11	15,914,500.00	18,123,494.44

Fig. 1: Estimated yearly sales revenues for sector 1

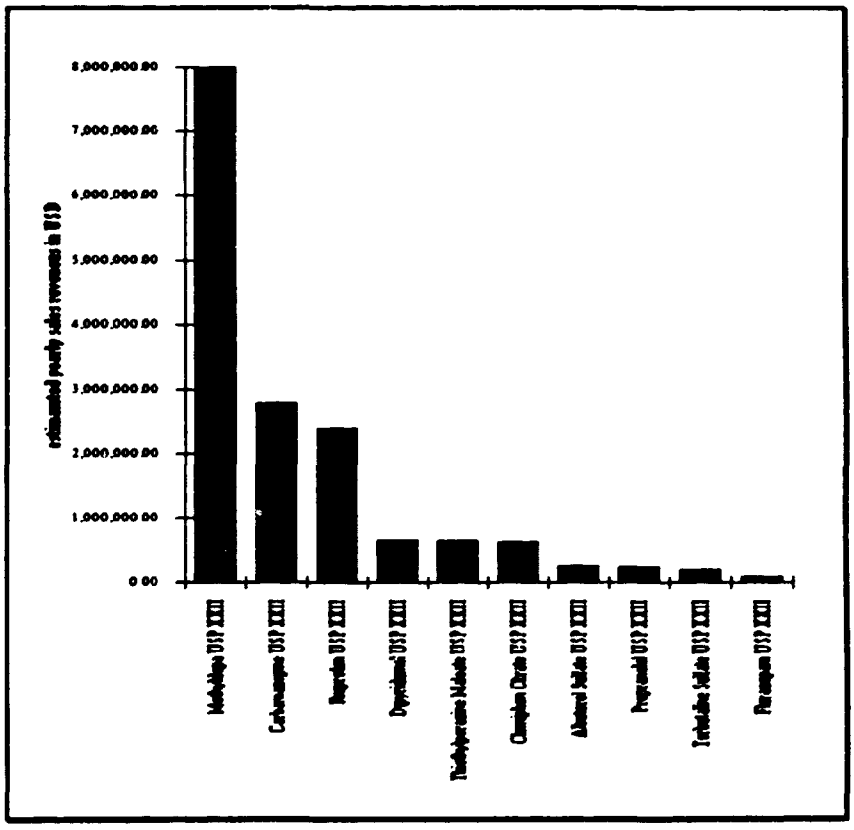


Table 8: Estimated yearly sales revenues for sector 2

Sector	Unit	Drug Bulk Compound	Capacity tons/yr	estimated sales revenues in US$ minimum	most likely	maximum
2	1	Cetrimide 40 % BP 88	1,000.00	3,000,000.00	3,280,000.00	3,520,000.00
2	1	Metronidazole USP XXII	28.00	476,000.00	616,000.00	682,500.00
2	2	Sulfamethoxazole USP XXII	200.00	2,400,000.00	3,200,000.00	3,456,000.00
2	2	Trimethoprim USP XXII	40.00	1,200,000.00	1,560,000.00	1,600,000.00
2	3	Cetylpyridinium Chloride USP XXII	16.00	192,000.00	320,000.00	322,222.22
2	3	Chlorhexidine Gluconate 20 % BP 88	164.00	1,558,000.00	1,640,000.00	1,804,000.00
2	3	Chloramphenicol USP XXII	16.00	994,720.00	1,120,000.00	1,360,000.00
2	3	Isoniazide USP XXII	24.00	165,000.00	232,800.00	234,720.00
2	3	Levamisole Hydrochloride BP 88	6.00	450,000.00	450,000.00	450,000.00
2	3	Miconazole Nitrate USP XXII	4.00	387,500.00	420,000.00	752,000.00
2	3	Nalidixic Acid USP XXII	8.00	475,000.00	520,000.00	693,600.00
		sum over sector	1,506.00	11,298,220.00	13,358,800.00	14,875,042.22

Fig. 2: Estimated yearly sales revenues for sector 2

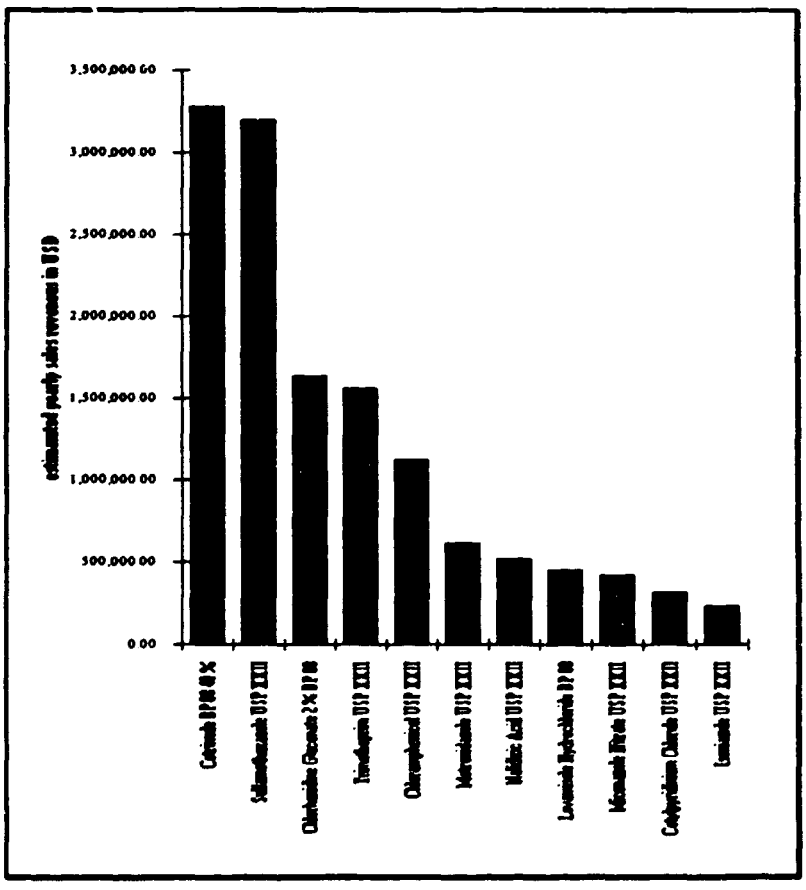


Table 9: Estimated yearly sales revenues for sector 3

Sector	Unit	Drug Bulk Compound	Capacity tons/yr	estimated sales revenues in US$ minimum	most likely	maximum
3	1	Ascorbic Acid USP XXII	500.00	5,625,000.00	6,500,000.00	8,650,000.00
3	2	Calcium Caseinate (food grade)	280.00	787,500.00	1,120,000.00	1,517,600.00
3	3	Niacinamide USP XXII	100.00	687,500.00	1,300,000.00	1,990,000.00
3	4	Magnesium Stearate NF XVII	60.00	81,000.00	90,000.00	150,000.00
3	4	Zinc Stearate USP XXII	540.00	405,000.00	540,000.00	702,000.00
3	5	Mannitol USP XXII	100.00	375,000.00	450,000.00	531,250.00
3	6	Isosorbide Dinitrate, Diluted USP XXII	5.00	65,500.00	125,000.00	125,000.00
3	7	Vitamin E USP XXII	26.00	715,000.00	730,600.00	731,250.00
3	7	Calcium Panthothenate USP XXII	8.00	135,000.00	144,000.00	160,000.00
3	7	Pyridoxine Hydrochloride USP XXII	20.00	812,500.00	860,000.00	1,200,000.00
3	7	Riboflavin USP XXII	18.00	1,099,800.00	1,530,000.00	1,850,000.00
3	7	Undecylenic Acid USP XXII	5.00	40,625.00	42,500.00	48,611.11
3	7	Zinc Undecylate USP XXII	24.00	247,500.00	360,000.00	525,000.00
		sum over sector	1,686.00	11,076,925.00	13,792,100.00	18,180,711.11

Fig. 3: Estimated yearly sales revenues for sector 3

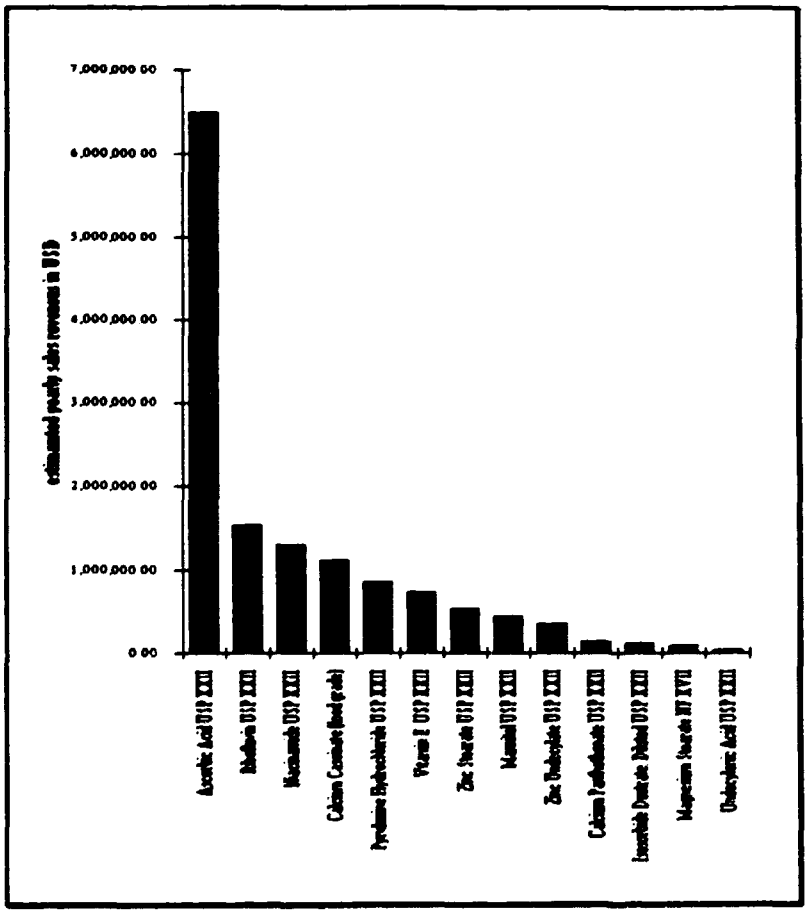


Table 10: Estimated yearly sales revenues for sector 4

Sector	Unit	Drug Bulk Compound	Capacity tons/yr	estimated sales revenues in US$ minimum	most likely	maximum
4	1	Aluminium Hydroxide Gel, Wet USP XXII	5,000.00	9,500,000.00	9,500,000.00	9,500,000.00
4	2	Cimetidine USP XXII	50.00	2,185,000.00	2,550,000.00	2,656,250.00
4	3	Allopurinol USP XXII	9.00	405,000.00	450,000.00	748,800.00
4	3	Amitriptyline Hydrochloride USP XXII	7.00	534,722.22	539,000.00	743,750.00
4	3	Clemastine Fumerate USP XXII	0.20	694,444.44	700,000.00	700,000.00
4	3	Clidinium Bromide USP XXII	1.00	520,833.33	550,000.00	711,000.00
4	3	Clobutinol (Boehringer Mannheim)	2.00	875,000.00	875,000.00	875,000.00
4	3	Diethyltoluamide USP XXII	2.00	22,500.00	22,500.00	22,500.00
4	3	Diphenhydramine Hydrochloride USP XXII	7.00	85,400.00	175,000.00	218,750.00
4	3	Glibenclamide BP 88	2.00	349,600.00	380,000.00	400,000.00
4	3	Hydrochlorothiazide USP XXII	4.00	62,000.00	80,000.00	125,000.00
4	4	Benzoic Acid USP XXII	50.00	56,500.00	132,500.00	190,000.00
4	4	Benzyl Benzoate USP XXII	5.00	13,900.00	16,000.00	16,000.00
4	4	Sodium Benzoate NF XVII	20.00	22,000.00	28,000.00	31,400.00
		sum over sector	5,159.20	15,326,900.00	15,998,000.00	16,938,450.00

Fig. 4: Estimated yearly sales revenues for sector 4

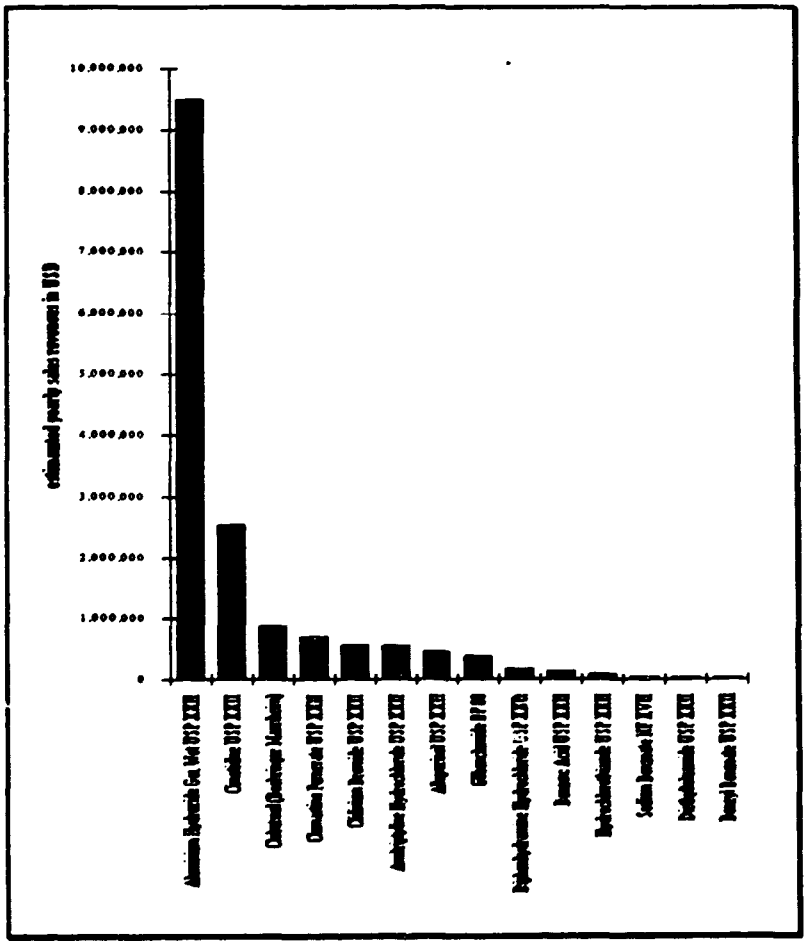


Table 11: Estimated yearly sales revenues arranged by Units

Sector	Unit	Drug Bulk Compound	Capacity tons/yr	estimated sales revenues in US$ minimum	most likely	maximum
1	1	Ibuprofen USP XXII	150.00	1,979,166.67	2,400,000.00	3,450,000.00
1	2	Methyldopa USP XXII	100.00	3,580,000.00	8,000,000.00	8,500,000.00
1	3	Multiple Purpose Plant 1.3.	34.30	4,941,674.44	5,514,500.00	6,173,494.44
2	1	Cetrimide & Metronidazole	1,028.00	3,476,000.00	3,896,000.00	4,202,500.00
2	2	Trimethoprim & Sulfamethoxazole	240.00	3,600,000.00	4,760,000.00	5,056,000.00
2	3	Multiple Purpose Plant 2.3.	238.00	4,222,220.00	4,702,800.00	5,616,542.22
3	1	Ascorbic Acid USP XXII	500.00	5,625,000.00	6,500,000.00	8,650,000.00
3	2	Calcium Caseinate (food grade)	280.00	787,500.00	1,120,000.00	1,517,600.00
3	3	Niacinamide USP XXII	100.00	687,500.00	1,300,000.00	1,990,000.00
3	4	Zink & Magnesium Stearate	600.00	486,000.00	630,000.00	852,000.00
3	5	Mannitol	100.00	375,000.00	450,000.00	531,250.00
3	6	Isosorbide Dinitrate, Dilluted USP XXII	5.00	65,500.00	125,000.00	125,000.00
3	7	Multiple Purpose Plant 3.7.	101.00	3,050,425.00	3,667,100.00	4,514,861.11
4	1	Aluminium Hydroxide Gel, Wet USP XXII	5,000.00	9,500,000.00	9,500,000.00	9,500,000.00
4	2	Cimetidine USP XXII	50.00	2,185,000.00	2,550,000.00	2,655,250.00
4	3	Multiple Purpose Plant 4.3.	34.20	3,549,500.00	3,771,500.00	4,544,800.00
4	4	Multiple Purpose Plant 4.4.	75.00	92,400.00	176,500.00	237,400.00

Fig. 5: Estimated yearly sales revenues arranged by Units

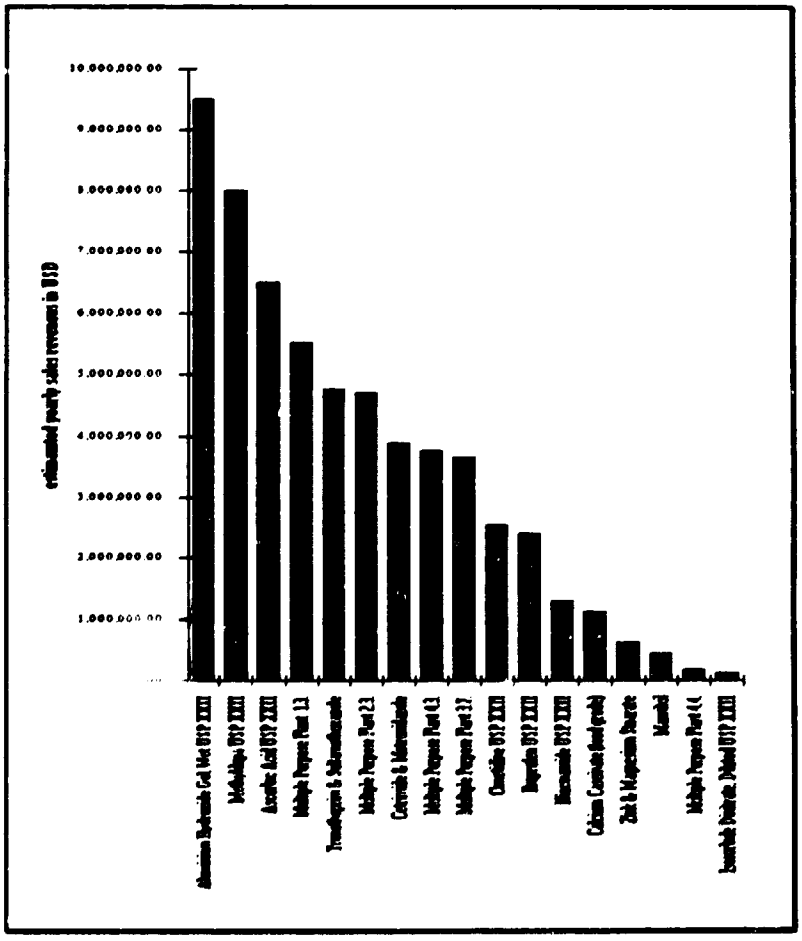
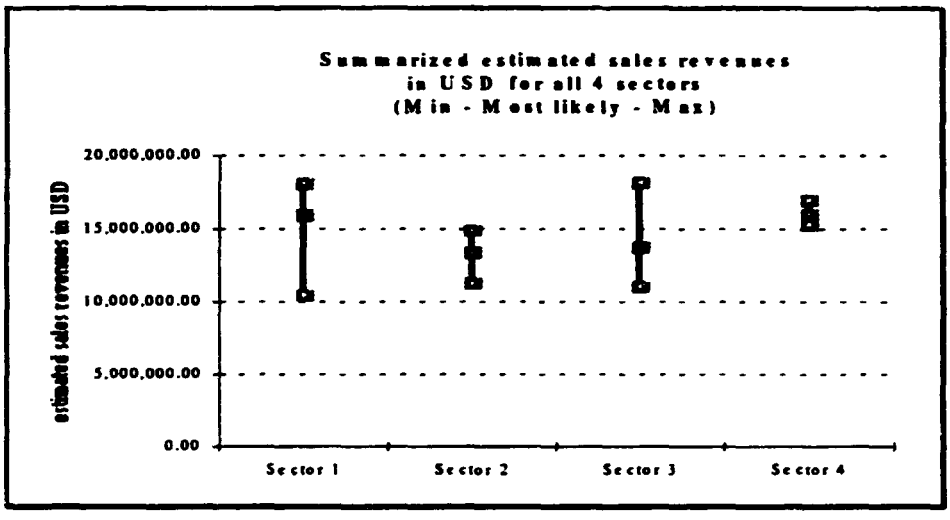


Table 12: Estimated yearly sales revenues - Sectors and Total Pharmaceutical Complex

	Capacity	estimated sales revenues in US$		
	tons/yr	minimum	most likely	maximum
Sector 1	284.30	10,500,841.11	15,914,500.00	18,123,494.44
Sector 2	1,506.00	11,298,220.00	13,358,800.00	14,875,042.22
Sector 3	1,686.00	11,076,925.00	13,792,100.00	18,180,711.11
Sector 4	5,159.20	15,326,900.00	15,998,000.00	16,938,450.00
overall sum	8,635.50	48,202,886.11	59,063,400.00	68,117,697.78

Fig. 6: Estimated yearly sales revenues - Sectors and Total Pharmaceutical Complex



6.5.1. SOLVENTS

It was a specific request of the Iranian counterparts to provide a storage capacity of one year for liquids and to have the storage facilities in a remote place about 4 km from the production units. Due to the variety of chemical processes this request will result in a rather complex tank storage system. Storage capacities near the manufacturing units can therefore be kept rather low just to meet the daily demand, which is a positive effect with respect to plant safety. In order to supply the different sectors with the required solvents just in time, logistics for an internal transportation service have to be established.

Solvents arriving in tank trucks always should be considered as one batch and stored apart from other batches in the corresponding suitable tanks. The filling operation should be supervised by qualified personnel, and a representative sample for analysis drawn from the tank. These operations should be carried out in explosion-proofed and defined areas using adequate equipment (transfer, pumps etc.) and sufficient ventilation.

It is important that all solvents never loose their identification, which means that correct labeling is required at all times including dangerous characteristics. Because of extreme temperatures in summer and winter, supply and storage of solvents cannot be performed at any time (freezing or danger of explosions).

The internal transportation should take place under the same precautions using suitable containers or barrels. In all operations it is extremely important to avoid a mix up of different solvents.

It is recommended that the solvents foreseen for use in the plant should be checked, whereby highly toxic or inflammable solvents should be replaced by less dangerous solvents.

6.5.2. GASES

Gases, either in compressed or liquefied form should be handled and stored also in accordance to the general safety regulations. Gas cylinders should be stored under cover and not subjected to extreme temperature. Storage areas should be well ventilated. All cylinders and gas pipe lines should be colour-coded and clearly marked or labeled with product names. Also the valves must be marked accordingly in order to prevent a mix up and severe consequences.

6.5.3. AUXILIARY AND SANITARY MATERIAL

Auxiliary materials used in the plant range from office supply, to production auxiliaries, e.g. filters of different permeability and maintenance and repair materials, e.g. cleaning material, detergents. Of course also sufficient facilities have to be foreseen for these purposes. A survey on auxiliary and service aspects is given in chapter 12.5..

6.5.4. MATERIAL RECOVERY

Taking into account the significant portion of raw material cost in the economics of the plant it is clear that recovery and reuse of solvents is of significant importance. Also recovery and reuse must be well organized. If possible, solvents should be reused for the same step of the chemical reaction only, after being checked by the Quality Control Department to guarantee that they will meet the specifications. The same applies to solvents recovered from the dryers. Therefore it is proposed to establish distillation units within each sector, which will allow reprocessing of the solvents near to the production unit. The recovered solvents should be interim stored within the sectors in tanks.

Table 13 indicates the quantities of material which will be recovered in the production foreseen.

Table 13: Recovery of materials in [kg/year]: In the case a material is recovered in several units also the sum for all units is given.

Unit	substance	amount [kg/year]	sum [kg/year]
Unit 4.3.	acetic acid	8,813	
Unit 1.3.	acetic acid	139,657	
Unit 2.3.	acetic acid	227,340	**375,810**
Unit 2.3.	acetone	7,543	
Unit 1.3.	acetone	49,348	
Unit 4.3.	acetone	74,200	
Unit 4.2.	acetone	180,642	**311,733**
Unit 2.2.	ammonium hydroxide, conc.	190,909	**190,909**
Unit 3.7.	benzene	14,893	
Unit 1.3.	benzene	23,605	
Unit 2.3.	benzene	72,476	
Unit 4.3.	benzene	81,195	**192,169**
Unit 1.3.	benzyl tert. butylamine	5,016	**5,016**
Unit 2.3.	butanol	70,822	**70,822**
Unit 1.3.	butanone	5,458	**5,458**

Table 13 (continued): Recovery of materials in [kg/year]: In the case a material is recovered in several units also the sum for all units is given.

Unit	substance	amount [kg/year]	sum [kg/year]
Unit 4.3.	chloroform	102.549	
Unit 2.1.	chloroform	103.286	
Unit 3.7.	chloroform	247.967	
Unit 1.3.	chloroform	256.545	**710,347**
Unit 1.3.	dichloromethane	3.338	
Unit 2.3.	dichloromethane	133.740	
Unit 3.7.	dichloromethane	417.579	
Unit 2.2.	dichloromethane	1.124.240	**1,678,897**
Unit 1.3.	dimethylformamide, dry	1.736	**1,736**
Unit 2.3.	diphenylether	50.917	**50,917**
Unit 3.6.	ethanol	4.800	
Unit 1.3.	ethanol	21.443	
Unit 3.7.	ethanol	32.652	
Unit 4.2.	ethanol	73.070	
Unit 4.3.	ethanol	140.607	
Unit 2.3.	ethanol	472.698	**745,271**
Unit 3.7.	ethanol, dry	15.594	
Unit 1.3.	ethanol, dry	42.862	
Unit 4.3.	ethanol, dry	79.560	**138,016**
Unit 3.6.	ether	9.600	
Unit 3.7.	ether	11.578	
Unit 2.3.	ether	16.155	
Unit 1.3.	ether	49.813	
Unit 4.3.	ether	213.174	
Unit 2.1.	ether	1.370.600	**1,670,920**
Unit 1.3.	ether, dry	1.902	
Unit 4.3.	ether, dry	6.852	**8,754**
Unit 2.3.	ethoxyethanol	122.408	**122,408**
Unit 4.3.	ethyl acetate	1.855	
Unit 1.3.	ethyl acetate	25.978	
Unit 1.3.	ethyl acetate	36.409	
Unit 2.1.	ethyl acetate	40.320	
Unit 4.2.	ethyl acetate	187.706	**292,268**
Unit 3.7.	heptane	25.884	**25,884**
Unit 4.3.	hydrogen chloride gas	1.440	**1,440**
Unit 4.3.	isopropanol	947	
Unit 2.3.	isopropanol	40.219	
Unit 4.2.	isopropanol	43.085	**84,252**
Unit 1.3.	isopropyl amine	7.482	**7,482**
Unit 4.3.	isopropyl ether	5.136	**5,136**
Unit 2.1.	methanol	35.840	
Unit 4.3.	methanol	45.167	
Unit 1.3.	methanol	77.891	
Unit 4.2.	methanol	188.843	
Unit 2.3.	methanol	235.268	
Unit 3.7.	methanol	777.615	**1,360,624**

Table 13 (continued): Recovery of materials in [kg/year]: In the case a material is recovered in several units also the sum for all units is given.

Unit	substance	amount [kg/year]	sum [kg/year]
Unit 1.3.	methanol. dry	6.793	
Unit 3.7.	methanol. dry	17.553	
Unit 2.2.	methanol. dry	207.969	232,315
Unit 2.1.	methylbromide	95.788	95,788
Unit 1.3.	4-methylpentan-2-ol	850	850
Unit 3.7.	n-hexane	188.045	188,045
Unit 1.3.	palladium on charcoal	148	148
Unit 2.3.	perchloroethylene	58.383	58,383
Unit 1.3.	petrolether	5.312	
Unit 2.3.	petrolether	19.715	25,028
Unit 4.3.	2-phenethylamine	834	834
Unit 1.3.	phosphoroxy trichloride	564.173	564,173
Unit 2.3.	pyridine	10.164	10,164
Unit 4.3.	tetrahydrofurane. dry	34.377	34,377
Unit 4.3.	thionyl chloride	2.766	2,766
Unit 1.3.	toluene	1.590	
Unit 4.3.	toluene	12.811	
Unit 2.3.	toluene	33.760	
Unit 4.4.	toluene	65.191	
Unit 3.7.	toluene	225.302	
Unit 2.2.	toluene	725.453	1,064,108
Unit 4.3.	toluene. dry	5.707	5,707
Unit 4.3.	water	55.176	
Unit 1.3.	water	184.195	
Unit 4.2.	water	637.910	
Unit 2.2.	water	727.269	1,604,550
Unit 3.3.	water. dist.	600.000	600,000
Unit 1.3.	xylene	496	
Unit 3.6.	xylene	6.400	6,896

7. UTILITIES

The following utilities must be available in the plant:

- Water of different quality
- Compressed air
- Nitrogen
- Steam
- Brine
- Heating and cooling oil
- Electricity

Concerning energy supply the infrastructure of the plant site comes up to the requirements of the project. As far as utilities for the plant are concerned, it is proposed to set up an Energy Center located in the middle of the plant site. All the required utilities could be produced in the Energy Center and supplied to the production units.

7.1. WATER

In the water plant the incoming water is filtered and treated to produce water of different quality as required.

The following types of water are produced:
- drinking water
- soft water
- deionized water
- make-up water for the cooling water system

Although there is sufficient water supply in principle, measures have to be considered for reuse of water. First of all cooling water should be reused after passing the cooling towers. Furthermore, in connection with the effluent treatment concept, it should be examined, whether reuse of water coming from the effluent treatment plant is economically and technically feasible.

7.2. AIR AND NITROGEN

Two different qualities of compressed air will be required:

- Oil, water and microorganism free air to be used in the fermenters is produced using filters and oil free (screw) compressors.
- Compressed air for the instruments and technologies is produced in standard air compressors.

It is proposed to produce compressed air centrally in the Energy Center.

Although the installation of an air liquefier in the plant might be considered, the present study is based on the assumption of purchase of liquid nitrogen in tank trucks. In this case it is not necessary to install a centralized service for compressed nitrogen. The liquid nitrogen, which is arriving in tank trucks, is transferred into cooled local nitrogen tanks, from which the required amount of nitrogen is vaporized to produce nitrogen of required pressure.

An alternative solution would be to foresee a central air liquefier, which allows local production of liquid nitrogen. This solution in the long run would be more economical, because it may be assumed that purchase and transportation cost for liquid nitrogen will be a significant factor in production cost.

7.3. STEAM

Steam constitutes a major source of energy in a chemical plant, because it is the standard heating medium in chemical reactors. Overheated steam is generated in a central boiler plant. The burners operate with natural gas, but in the case of lack of gas should have a design, which allows use of oil burners.

It is recommended that the plant carries as a second function the production of emergency electric energy. The high pressure, high temperature steam, produced in the boilers could run a back pressure turbine, to which a generator is connected. The output of electric power of this generator should be about 3 MW, which is enough to allow operation of the plant at a reduced level in the case of breakdown of electric energy supply. The steam coming from the turbine is fed into the technological service network system and is utilized as heating steam. Boiler water production and utilization of the heat of emitted hot

gases also have to be considered in the boiler plant lay out. The plant should operate fully automatized.

7.4. HEATING - COOLING

As said before the equipment in the manufacturing units is heated with the steam coming from the boiler plant. In few cases, where extremely high temperatures are required or heating and cooling of a reaction must take place within very short time, oil heating is used. Heating oil and cooling oil should be of the same type. Using electricity the heating oil should be produced locally in the unit, where it is required.

The standard cooling media are water and brine. Great quantities of cooling water are used in the condensers. Therefore cooling towers have to be set up to recool the warmed up effluent cooling water. After compensation of evaporation losses the cooling water is recycled.

Brine is mainly used for cooling of reactors. It is produced in a central cooling system and transported to the units in isolated pipes. The cooling plant also includes an ice manufacturing unit, which produces block ice for the technologies and all other purposes.

7.5. ELECTRICITY

The required electrical energy can be obtained from the 20 kV transmission passing by the plant site. It is transformed and distributed into the sectors in the Electric Energy Center.

As described earlier, because of safety requirements, a back pressure turbine integrated into the boiler plant serves as emergency electric energy source. In the case of lack of electricity it can guarantee operation of the sectors at a reduced level.

In addition, it is suggested to install Diesel-generators directly nearby units where critical or dangerous production processes (e.g. nitration, oxidation). are carried out as an additional security measure in cases of power cuts.

7.6. REQUIREMENTS FOR UTILITIES

Table 14 shows the demand of utilities for the whole plant.

Table 14 Utility consumption

Utility	Sector 1	Sector 2	Sector 3	Sector 4	Four sectors
Steam [t/h]					
p=7 bar, t=165°C	6.7	8.7	7.7	5.1	28.2
p=10 bar, t=180°C	0.5	0.5	0.7	0.8	2.5
sum	**7.2**	**9.2**	**14.3**	**9.4**	**40.9**
Brine [m3/h]					
p=4 bar, t(max)=-20°C, Δt=5°C	171.7	186.5	399.8	167.8	925.8
Electric energy [kW]					
0.4 kV, 50 Hz					
for power transfer	530.0	905.2	618.0	510.0	2563.2
for internal lighting	60.0	111.7	53.6	70.0	295.2
for external lighting	10.0	18.6	21.8	30.0	80.4
sum	**762.5**	**1035.5**	**1508.5**	**846.1**	**4152.6**
Nitrogen [m3/h]					
p=4 bar	60.8	11.2	12.7	14.5	99.2
Cooling water, rec. [m3/h]					
p=4 bar, t(max)=25°C, Δt=10°C	335.0	337.7	521.1	441.1	1634.9
Ice [t/h]	0.2	0.3	0.5	0.3	1.3
Compressed air [m3/h]					
p=7 bar	8.5	17.9	2569.4	9.5	2605.4
Compressed air for instruments [m3/h]					
p=7 bar, t(dew temp)=-20°C	9.5	10.3	13.9	9.5	43.2
Drinking water [m3/h]					
p=4 bar, t=12-14°C					
for techn. purp.	2.5	16.1	1.8	1.8	22.2
for social purp.	1.7	2.2	1.1	0.5	5.6
sum	**4.2**	**18.3**	**10.4**	**23.2**	**56.2**
Deionized water [m3/h]					
p=4 bar, 10 μS	2.8	2.7	3.3	0.7	9.4

Table 14 (continued): Utility consumption

Utility	Boiler plant	Brine plant	Cooling water plant	Deionized water plant	Compressed air plant
Brine [m3/h]					
p=4 bar, t(max)=-20°C, Δt=5°C					13.3
Electric energy [kW]					
0.4 kV, 50 Hz					
for power transfer	622.0	2336.0	900.0	10.0	115.0
for internal lighting					
for external lighting					
sum	**622.0**	**2336.0**	**900.0**	**10.0**	**115.0**
Cooling water, rec. [m3/h]					
p=4 bar, t(max)=25°C, Δt=10°C		61300.0			20.0
Drinking water [m3/h]					
p=4 bar, t=12-14°C					
for techn. purp.	35.6	80.0	90.0	12.0	
for social purp.					
sum	**35.6**	**80.0**	**90.0**	**12.0**	
Gas [m3/h]	**1100.0**				

Table 14 (continued): Utility consumption

Utility	per hour	per year
Steam [t]		
p=7 bar, t=165°C	28.16	202.736
p=10 bar, t=180°C	2.50	18.000
sum	**40.83**	**288,236**
Brine [m3]		
p=4 bar, t(max)=-20°C, Δt=5°C	**939.06**	**6,761,198**
Electric energy [kWh]		
0.4 kV, 50 Hz		
for power transfer	6,546.17	47,132,390
for internal lighting	295.24	2,125,694
for external lighting	80.39	578,815
sum	**8,135.59**	**58,576,240**
Nitrogen [m3]		
p=4 bar	**99.20**	**714,224**
Cooling water, rec. [m3]		
p=4 bar, t(max)=25°C, Δt=10°C	**62,954.90**	**453,275,313**
Ice [t]	**1.25**	**9,016**
Compressed air [m3]		
p=7 bar	**2,605.35**	**18,758,537**
Compressed air for instruments [m3]		
p=7 bar, t(dew temp)=-20°C	**43.20**	**311,065**
Drinking water [m3]		
p=4 bar, t=12-14°C		
for techn. purp.	239.83	1,726,768
for social purp.	5.56	40,048
sum	**273.76**	**1,971,087**
Deionized water [m3]		
p=4 bar, 10 µS	**9.45**	**68,017**
Gas [m3]	**1,100.00**	**7,920,000**

8. RESEARCH AND DEVELOPMENT UNITS

According to the Terms of Reference the pharmaceutical complex of SMDI will include to a significant degree research and development facilities. This is a clear commitment to the approach of an integrated pharmaceutical company.

8.1. THE RESEARCH CONCEPT

The development of a new pharmaceutical product and its introduction to the international market is nowadays considered to be a venture requiring investment of more than 100 million US$. With respect to the time required such a development project is a long term activity, which nevertheless is required in a modern integrated pharmaceutical company.

Therefore it is not surprising that the pharmaceutical industry is one of the industries with the highest percentage of expenditures for research and development.

In the present project several research facilities are foreseen, which would require significant investment. Since at the present stage there is no specific research programme from which an economic impact of these units on the future development of the company might be estimated, it was decided not to consider the research units in the economic evaluation. Nevertheless lay out and equipment proposals are presented in the study for these units.

With respect to the importance of research it is strongly recommended that as soon as possible a research programme based on a company development concept should be worked out. A prerequisite would be that a long term development plan for the company is established. Development targets should be defined. The concept proposed in chapter 6.4. might be an useful basis for such a development plan. As soon as an agreement has been met on such a development plan, all research efforts should be directed towards long term implementation of the development plan.

Following these lines general research fields could be:

- Development of new products in the main lines of company activity
- Improvement of production efficiency by introduction of new production processes and technologies
- Evaluation of fields of potential future interest of the company
- Strengthening of local production by increasing use of locally available natural products and chemicals

It is strongly recommended that after establishment of the research programme contracts should be awarded to local and international partners to carry out such research activities jointly. Research contracts with Iranian Universities and other research institutions might be useful to evaluate the prospects of specific research projects and by this measure to contribute to the integration of the national pharmaceutical research scene.

As a matter of fact the research units in the plant should be established and equipped only after a suited research programme has been set up to avoid unnecessary investment.

At the present stage only the pilot plant for technology transfer placed in sector 4 seems to be economically justified because its research activities can be easily related directly to

activities of the manufacturing plant: Process development is an activity directly connected to pharmaceuticals production. The importance of permanently optimizing production to be competitive, as well as introducing new production processes cannot be overseen. The efficiency of such development work will be reflected quickly in the company performance.

In the following chapters some indications are given on potential subjects of research to be carried out in the specific research units. However, as it was said before, only a clear commitment to long term research targets and clear and detailed research programmes based on these commitments will be the basis for successful implementation of research and development work.

8.2. THE PILOT PLANT FOR TECHNOLOGY TRANSFER

The target of this plant is to establish and develop processes. As a rule technologies considered for production in the manufacturing plants will first be evaluated in this pilot plant. It was said before that establishment of this unit is already justified at the present stage, because improvement of established production processes is a promising development target.

Technology transfer can mean transfer of the manufacture of established products. It can also mean transfer of production of most up to date pharmaceuticals. From the technical point of view the complexity of technology transfer is similar in both cases. Therefore profitable new products fitting into the range of interest of the company should be targets for technology transfer.

To be in a position to step into product development it is also recommended to consider licensing of development products, which are not yet on the market, but still at the stage of development, mostly in the clinical phase. This approach would allow to carry out product development, without having too long periods of development. Also the financial risk connected with the development of a new product could be reduced by this approach.

The plant will be placed in the sector 4 aiming at intermediates. The recommendation to concentrate activities on intermediates has also a research aspect. Development of a new product takes much less time with intermediates than with pharmaceutical end products, because neither pharmacological nor clinical testing is required. New products can be established within a short period of sometimes less than one year. Intermediates production

will reduce dependence from raw material suppliers, but might also in itself be targeted to participate in the international intermediates market.

The equipment of this plant reflects versatility and up-scaling facilities, starting from glass equipped laboratories. As a special feature it is foreseen to install scaling-up units for development of continuous processes. This will increase the versatility of this unit dramatically and will allow even development of large scale bulk chemical processes.

8.3. THE RESEARCH CENTER FOR BIOTECHNOLOGY AND GENETIC ENGINEERING

This research center in its present dedication is not at all directly connected to the production of one of the sectors. This means that it could aim primarily at basic research and development, with only long term perspectives as far as economic efficiency is concerned. It will however serve as an internal focus to step into new activities of biotechnological production.

It was decided to place this unit in sector three for the following reasons: Sector three is dedicated to natural products, the main processes requiring natural products as starting materials, comparable to biotechnological production. Furthermore sector three could accomodate biotechnological production without change of its market orientation.

Production processes of pharmaceuticals, e.g. vitamins, and of intermediates may frequently be carried out using biotechnological processes. This option should be kept open in the pharmaceutical complex.

With genetic engineering the situation concerning the introduction of new products is seen much less optimistic nowadays than a few years ago. In pharmaceutical industry the general approach to this area is usually to buy an established small research company, which is experienced in this field, expectations on return of investment shift more and more to the importance of molecular biology and genetic engineering as a new set of tools in pharmacology.

At this stage it must also be mentioned that in a pharmaceutical company sophisticated research work, e.g. genetic engineering research, without pharmacological and toxicological research laboratories will not be very effective and that establishment of such units seems to be a major prerequisite before starting any sophisticated research and development activities.

Therefore it is recommended to keep only a low profile and low investment in this part of the research unit. In Volume 3 design and equipment are given for such a biotechnology research center consisting of

- Fermenter laboratory
- Downstream processing laboratory
- Genetic engineering laboratory.

8.4. MULTI PURPOSE MEDICINAL PLANT EXTRACTION UNIT

Establishment of multipurpose units for extraction of medicinal plants has been one of the most efficient project strategies of UNIDO. It is therefore recommended that the foreseen unit in its structure will be oriented to follow the successful UNIDO approach. In the UNIDO Report "Design Options for a Polyvalent Pilot Plant Unit for the Distillation and Extraction of Medicinal and Aromatic Plants" (IPCT.143(SPEC.), 15 September 1991) detailed data are presented for a unit, which in the first phase of such activites would be well suited for erection in the SHAHID MODARRES plant. Data on a multi purpose medicinal plant extraction unit are also found in Volume 3 of the present report.

Most obvious targets for research work in this unit would be compounds from local Iranian plants (see Table 15). Since the products extracted from these plants also constitute pharmaceuticals, which have to be placed on the market and which increase the present number of about 50 products, it is recommended to step into this specific field of pharmaceutical activity only after establishing a detailed development and work programme at a later stage of project implementation.

Since, based on available information, at present a decision cannot be met, which products might be suitable for production in industrial scale, it is recommended that a co-operation with a company specialized in plant extraction be set up, which might be useful to help SHAHID MODARRES to take decisions on further activities. Interest in such co-operation has been indicated by one company.

As far as the development programme is concerned it is recommended not only to aim at known pharmaceuticals from plants, but to consider also synthetic transformation of extracted products to semisynthetic pharmaceuticals.

More and more natural products are used as starting materials and intermediates for structurally complex drugs (e.g. chiral pool). Extracting and transforming natural products to obtain building blocks for chemical and pharmaceutical compounds could be a promising long term development target in a pharmaceutical company having the structure of the SHAHID MODARRES Industrial Pharmaceutical Complex.

Table 15: List of medicinal plants common in Iran

Item No.	Scientific name	Common name
01	Atropa Belladonna	Beladona
02	Mentha Piperita L.	Mentha
03	Claviceps Purpurea	Ergo
04	Camelia Sinensis	Tee
05	Ephedra Vulgaris	Ephedra
06	Cephaelis Ipecacuanha	Ipeca
07	Ricinus Communis	Ricinus
08	Papaver Somniferum	Papavera
09	Pilocarpus Jaborandi	Pilocarpus
10	Plantago Psyllium	Plantago
11	Amygdalus Communis L.	Amygdalus
12	Arachis Hypogaba	Arachis
13	Pinus Paxustris	Pine
14	Astragalus Gummifer	Astragalus
15	Eucalyptus Globulus	Eucalyptus
16	Acacta Arabica	Acacta
17	Pimpinella Anisum	Anise

9. QUALITY CONTROL

Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act edited by Food and Drug Administration (US Department of Health and Human Services) requires that all drugs be manufactured, processed, packed, and held in accordance with current good manufacturing practice. No distinction is made between bulk pharmaceutical chemicals (BPC's) and finished pharmaceuticals.

Although there are basic differences between the processes used in production of BPC's and the processes used in manufacturing finished pharmaceuticals, the need for the assurance of quality is still the same.

In the case of a plant producing bulk pharmaceutical chemicals it will be necessary to establish a system of quality assurance and quality control to ensure that the substances produced will meet the specifications required.

Quality assurance should be the department for coordination of the different divisions in the company having influence on the quality of the product:

Production Management
Quality Control with the sections: Chemical Analysis and Microbiology
Packaging
Storage
etc.

This results in the edition of sampling plans, hygiene plans, written operating procedures for analysis, stability testing programs, cleaning, storage, packing etc., so called Standard Operating Procedures (SOP's).

Quality Assurance is also responsible for the observation of the rules of Good Manufacturing Practice in the whole plant.

Furthermore Quality Control is responsible for the analytical and microbiological testing written down in the SOP's for each product - raw material or finished product. Also procedures for control of the hygienic status, efficiency of cleaning procedures, stability testing etc. have to be carried out. The Quality Control Manager is the only person who may decide about the release or rejection of a starting material or finished product - of course he may delegate some of his responsibilities.

Production Management is resoponsible only for testing the intermediates of the production (in-process control, IPC).

All results of testing procedures (raw material, IPC, final product, cleaning procedures, packing procedures etc.) have to be laid down in a written form, so that at the end of a production Quality Control has a basis for decision about the release or rejection of a BPC.

For further information refer to:

Quality Control and GMP File: "Good Manufacturing Practice (GMP) in Production of Bulk Pharmaceutical Chemicals"
"Organigramm of QA/QC Organization" "The Scope of the Warehouse Laboratory"
"The Scope of the In-Process-Control Laboratory"
"The Scope of the Central Laboratory in BPC Production"
"The Scope of a Microbiological Laboratory in BPC Production"

10. ENVIRONMENTAL PROTECTION INCLUDING EFFLUENT TREATMENT

10.1. GENERAL CONCEPT

Conceiving a general long term concept for environmental protection means to take into account that the requirements for environmental safety will increase in future. It is therefore not only necessary to consider existing regulations but to aim at the best technological solution which is economically feasible.

A specific distinction between an Iranian and an European chemical company lies in the fact that in Iran neither rivers are available to dilute effluents nor an existing infrastructure of organizations dealing with regular disposal of the wastes either by incineration or dumping may be expected. Planning therefore should aim at an eventually waste free manufacturing plant.

Steps for environmental protection start with the selection of technologies. Resulting wastes have to be examined painstakingly with regard to further treatment. Also measures to reduce the amount of waste through changes in processes should be considered. A first and effective action in this respect would be an extensive recovery of solvents. As recovery of solvents only makes sense, if further utilization is guaranteed, it was proposed earlier in this report that a couple of medium sized solvent recovery units are set up in the different sectors, so that the recovered solvents always remain in the same areas of the production plant.

10.2. INCINERATION

Residues of distillation and various organic materials have to be removed by incineration, whereby special attention has to be directed to possible emissions of highly toxic compounds (dioxins, furanes). Such problems can be avoided either by installation of an efficient exhaust gas purification plant or by dumping of critical wastes instead of incineration. It seems desirable to combine the incineration unit with heat or energy recovery systems thus reducing the cost of environmental protection activities.

10.3. EFFLUENT TREATMENT

Discharge of effluents into a river for further dilution is not feasible at the plant site. For this reason great care has to be attributed to the aspect of effluents.

Each effluent after individual treatment (if necessary) in the relevant production unit is fed to a biological effluent treatment unit, which should be kept in an encasement, which allows the collection of the air emitted from the basin. Bubbling of air through the effluents as a positive side effect will also strip volatile organic compounds from the water, which should be collected and fed preferably to the incinerator air. With respect to the great distance between the treatment plant and the incinerator, long distance piping of the collected exhausting air might be economically not feasible. In this case use of bio filter should be considered as an alternative.

According to the planning of the Iranian experts the water from the effluent treatment plant should be fed into a pool for evaporating. This concept is well conceived and technically simple. It must be considered that safe sealing of the bottom of the pool by means of layers of clay and plastic foils is required in order to avoid contamination of the ground water. It may be assumed that in the first phase of operation the evaporating pond might become a biosphere of considerable ecological value providing an additional water purification effect. However it is obvious that soon biotop function will disappear due to the concentration of salts in the effluents.

Concerning this technical concept of effluent treatment it is recommended that at least two separated ponds should be foreseen, to provide the possibility to remove and dump the wastes from the dried up sections of the pools. A substantially more expensive, but economically superior solution, would be the installation of a desalination step after the biological treatment. The desalinated water would not effect the ecological system of the

ponds and could furthermore be reused in the plant as process water, thus reducing the requirements for water supply.

10.4. DUMPING

Last not least it is necessary to install a dumping site for chemical waste to be used for dumping of inorganic salts, non combustible organic wastes and wastes from the filters of the incinerator. Here again a safe sealing of the floor is required to avoid ground water contamination.

Furthermore it must be considered that such a dumping site, as well as the other units of environmental safety, requires an organizational and operational concept to allow secure operation, observation and control.

10.5. QUANTITIES OF WASTE TO BE EXPECTED

Table 16 represents a list of waste produced in each unit. The waste is attributed according to the foreseen treatment procedure.

Table 16: Waste produced in each unit, attributed according to the foreseen treatment procedure

Unit	dumping kg/year	incineration kg/year	waste water kg/year
Unit 1.1.		120.000	6.105.000
Unit 1.2.		550.000	10.000.000
Unit 1.3.	19.469	140.823	2.254.467
Unit 2.1.		410.399	2.397.222
Unit 2.2.	50.909	191.060	9.125.089
Unit 2.3.	104.301	349.333	3.221.549
Unit 3.1.		1.845.000	22.374.000
Unit 3.2.	1.504		2.627.636
Unit 3.3.		6.000	797.900
Unit 3.4.			7.206.456
Unit 3.5.	40.500		21.000.000
Unit 3.6.	480	4.680	138.512
Unit 3.7.	139.215	419.395	2.821.683
Unit 4.1.			2.564.684
Unit 4.2.	41.831	96.225	2.164.899
Unit 4.3.	21.707	122.809	1.502.214
Unit 4.4.	373		1.526.985
sum	**420,289**	**4,255,725**	**97,828,296**

10.6. EMISSION

Since most of the reactions in the plant will be carried out in closed equipment, emission of organic vapours into the air will have to be expected mainly in those areas, where gases are blown into the reaction mixtures or formed during the reactions. In those cases, where the normally installed scrubbers will not be sufficient, the units will have to be equipped with special scrubbers.

Significant solvent emissions have to be expected from the dryers, where rather big quantities of solvents are set free. It is recommended to use dryers with solvent recovery system. In case of a negative cost benefit analysis of these devices the exhaust gas from the dryers should be fed to the scrubbers.

11. MAINTENANCE AND SAFETY

11.1. SURVEY ON MAINTENANCE ACTIVITIES

Maintenance and repair units will have to be established securing all required services. Repair shops will have to be equipped for mechanical, electrical, electronical and glass working techniques (see Chapter 12.5.) and must be run by skilled personnel. More general services, like construction, masonry, painting or car service, must be considered as well. Although with respect to the remote location of the plant it may not be expected to find local repair shops, in case given repair contracts with locally established companies should be considered.

11.2. SAFETY PROCEDURES - REQUIREMENTS AND REGULATIONS

Safety aspects gain more and more attention and importance in chemical industry. Since it is important to consider safety aspects from the beginning of the planning phase of a project, the present report is giving some comments on this topic.

11.2.1. AIMS OF SAFETY PROCEDURES

Aim of the following measures is to increase safety in chemical synthesis by means of an action plan in the case of fire, accident or other troubles, to minimize risks for humans and environment.

Already in the phase of project planning and construction of buildings and equipment, national regulations and international standards must be taken into consideration. For the start up period of operation, written instructions and regulations have to be issued by the Safety Committee under chairmanship of the Safety Commissioner (Head of Security, Fire & Pollution) including representatives of the fire brigade and medical doctors.

Safety in chemical plants is a multi-dimensional problem including not only hardware and process aspects, but also training, documentation and management. A recent major accident investigation report (Monitoring Safety published by Health & Safety Executive, UK 1986) gives a survey about the reponsability for fatal accidents in the years 1981-1983 in the UK: In 61 % of the accidents senior mangagement was to blame for the incidents and only in 17 % of the events the operators themselves. These figures demonstrate that a reliable safety mangagement will be the basis for safe operation of the plant.

11.2.2. SAFETY COMMITTEE

Starting from the very early phase of planning the fully authorized Safety Commissioner has to assist the Project Management with his knowledge and experience. The tasks of the Safety Commissioner comprise the establishment of the fire fighting brigade and the Safety Committee which has the following tasks:

Dividing the plant into safety areas, safety zones and safety sections; preparing a concept for safety analysis; first aid concept; concept for information and announcement in case of accident; alarm plan and stand by measures etc.

A hazard and risk assessment process should be part of all activities in the planning phase. Safety has to be planned and built in in all installed equipment and processes. The slogan 'what you haven't got, can't leak' summarizes the concept of Inherent Safety: lower inventory, safer materials, less hazardous process routes (cooler, lower pressure, less dangerous chemicals) and the use of semi-batch methods).

11.2.3. SAFETY ANALYSIS OF THE PLANT

DANGEROUS MATERIALS - RECORDING: SAFETY DATA SHEET

All starting materials, intermediates and finished products should be enlisted alphabetically according to their dangerous characteristics: explosive, inflammable, toxic etc.; according to their chemical and physical properties: melting point, flash point, solubility in water,

temperature of decomposition, precautions in transportation etc.. It is recommended to use the forms of ADR (= European convention of the international transportation of dangerous goods on the road). Those safety data sheets already exist for several hundreds of chemicals substances, including safety aspects in the case of accidents.

SAFETY SECTIONS; SAFETY ZONES - COMPILATION AND CLASSIFICATION OF MATERIALS, EQUIPMENT AND METHODS

For the different sections, areas etc. a detailed list of the maximum quantities in store has to be worked out. Together with the risks of the processes, a classification of the sources of danger in the corresponding area has to be given. (Classification 1 - 10 = no - high risk of safety). This assessment of risks is of utmost importance in the provision of safety aspects. All the actions should be revised regularly in the Safety Committee.

REQUIRED SAFETY PROCEDURES

Safety procedures are applied at different levels. Without being exhaustive the following topics have to be considered:

- Organization: first aid; medical provision; fire brigade; alarm plan; instructions of personnel; training of personnel; check list for safety analysis.

- Buildings: burning sections; fire proof walls; installations and equipment; precautions in joint storage (-peroxides !); extinguishing equipment; smog abatement-ventilation; firewater network system and firewater stores.

- Equipment: protective clothes; safety goggles; working boots; oxygen apparatus; neutralizing agents; bonding material; fire extinguisher.

- Other: double energy input for the technologies, which in the case of lack of energy can cause fire and/or explosion.

CHECK LIST FOR SAFETY ANALYSIS

It is recommended to enlist the different safety criteria according to the following aspects. A revision should be performed periodically to include the findings into the obligatory safety procedures of the plant. A raw survey of a check list should contain among many others:

- Process and material
  - type of reaction: exothermic gas formation, delayed starting, reaction progress,
  - starting materials, reaction mixtures, wastes, safety data sheets, effects on health

- Plant and transportation system:
  - Construction: open, closed, hall, floor,
  - surroundings: offices, crowds of people, gasoline tanks, pipe lines, power stations,
  - equipment: construction material, electric and electronic installations, safety system, safety valves, earthing, energy breakdown, control devices, alarm system, exhaustors
  - transportation: facilities, pumps, containers, leakage, roads.

- Manpower:
  - personnel: training, knowledge, false reaction, stress, occupational disease.
  - instructions: written manufacturing procedures, written alarm and information plan, written check lists for supervision of critical actions.
  - outfit: working clothes, helmet.
  - training: programme on behaviour in emergency situations, fire fighting, first aid, respiratory masks.

- External influence:
  - day/night, temperature, wind, dust
  - sabotage, strike, war
  - natural disasters
  - earthquakes

- Environment:
  - air, soil, water, pollution, burning, dumping, collecting reservoirs in case of leakage.

ORGANIZATION AND ARRANGEMENTS

Establishment of a Safety Committee including staff and workers from all sectors and administrative buildings, who implement the results of the safety analysis by means of the check lists into the obligatory safety plans, alarm plans and training arrangements, is an absolute necessity in a chemical plant of this size. A medical care center and first aid

rooms are foreseen within this project with sufficient space and personnel. A well equipped fire brigade including a vehicle fleet must also be established.

12. EQUIPMENT AND PROJECT ENGINEERING

12.1. PRODUCTION EQUIPMENT - TYPES AND PRICES

The equipment foreseen in the plant is standard equipment as used in pharmaceutical industry both from the point of view of size and structural material.

Selection of material was carried out along the following criteria.:

- Structural material has to resist to corrosion during the process.
- In case of alternatives of suited materials, the cheapest was proposed.

According to this, the following structural materials are used:

- steel
- enamelled/glass lined steel
- stainless steel
- halar coated steel
- graphite (korobon)
- glass

The installation of teflon coated or glass lined equipment was only foreseen when required by any means, since prices for this type of material are rather high.

The scope of application of the different structural materials is as follows::

Enamelled steel:	useful under acidic, neutral and mildly basic conditions up to 300°C alkaline solutions corrode
Stainless steel:	useful under acidic, neutral and basic conditions Chlorine containing solutions, oxidizing acids corrode at higher temperatures. Hydrogen chloride solution corrodes even at low temperatures.
Graphite:	useful practically under all sorts of conditions, except the oxidizing mediums at high temperatures
Halar coated steel:	useful under acidic, neutral and alkaline conditions
Teflon coated steel:	useful practically under all sort of conditions*)
Glass:	useful under acidic, neutral and mildly alkaline conditions alkaline solutions corrodes at higher temperatures

12.2. PRODUCTION EQUIPMENT QUANTITY

For each unit the main equipment was established . The complete list of the equipment can be seen in Volume 3 of this report.

Table 17 gives a summary over all equipment parts foreseen in the complex, without equipment for research and development centers (Unit 3.8., Unit 3.9., Unit 4.4. Upscaling part) and prices for all parts.

Table 17: Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
absorber	1		absorber (methyl amine)		500
	2		absorber (methyl mercaptane)		500
	1	1000 mm	absorber (NOX)		1000
	4		gas absorber	enamelled	164

*) Teflon coated materials are mainly used in reactions with hydrogen fluoride, such as hydrofluorination, halofluorination, nitrofluorination and conversion of alcohols to alkylhalides.

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
autoclave	4	0.63 m3	hydrogenation autoclave	stainless steel	123
blender	1	4 m3	blender	stainless steel	447
boiler	2	3.15 m2	backboiler	stainless steel	500
	1	3.25 m2	backboiler	stainless steel	500
	1	12.5 m3	reboiler	stainless steel	346
calorifer	16		steam heated calorifer		50
centrifuge	2	1000 mm	basket centrifuge	carbonated steel / rubber	2239
	1	1000 mm	basket centrifuge	stainless steel	2239
	6	1200 mm	basket centrifuge	stainless steel	2556
	4	1000 mm	bottom discharged centrifuge	halar coated	2239
	1	1600 mm	bottom discharged centrifuge	halar coated	3001
	17	1000 mm	bottom discharged centrifuge	stainless steel	2239
	15	1600 mm	bottom discharged centrifuge	stainless steel	3001
	1	1500 mm	centrifuge		2878
	1	1500 mm	centrifuge	acid resistent	2878
	1	1200 mm	centrifuge	enamelled	2556
	7	1250 mm	centrifuge	stainless steel	2556
	5	1500 mm	centrifuge	stainless steel	2878
	4	1000 mm	top discharged centrifuge	halar coated	2239
	3	1200 mm	top discharged centrifuge	halar coated	2556
	40	1000 mm	top discharged centrifuge	stainless steel	2239
	2	1200 mm	top discharged centrifuge	stainless steel	2556
column	1	5 m	extraction column	stainless steel	144
	1		ion exchanger column	stainless steel	500
	1	250x6000 mm	oxidation column	stainless steel	1000
	2	250x6000 mm	rectification column	stainless steel	1000
	1	3 t/h	rectification column	stainless steel	1000
condenser	22		condenser		70
	8	3.75 m2	condenser	enamelled	39
	1	10 m2	condenser	graphite	143
	8	12 m2	condenser	graphite	167
	2	12.5 m2	condenser	graphite	167
	3	14 m2	condenser	graphite	180
	44	16 m2	condenser	graphite	197
	3	17 m2	condenser	graphite	206
	1	0.5 m2	condenser	stainless steel	14
	5	1 m2	condenser	stainless steel	22
	8	3.15 m2	condenser	stainless steel	48
	1	4 m2	condenser	stainless steel	56
	2		condenser	stainless steel	70
	7	6 m2	condenser	stainless steel	76
	14	6.3 m2	condenser	stainless steel	79
	60	8 m2	condenser	stainless steel	90
	1	10 m2	condenser	stainless steel	105
	31	12 m2	condenser	stainless steel	122
	11	12.5 m2	condenser	stainless steel	122
	5	17 m2	condenser	stainless steel	150

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
condenser	1	20 m2	condenser	stainless steel	168
(continued)	2	25 m2	condenser	stainless steel	196
	1	40 m2	condenser	stainless steel	405
	1	50 m2	condenser	stainless steel	442
	1	80 m2	condenser	stainless steel	610
	8		tube packet condenser		100
container	8	0.5 m3	mobil container	halar coated	109
	40	0.5 m3	mobil container	stainless steel	109
cooler	1		cooler		345
	1	2 m2	cooler	stainless steel	35
	2	20 m2	cooler	stainless steel	168
	2	35 m2	cooler	stainless steel	345
	1	50 m2	cooler	stainless steel	605
	1	3.15 m2	exit gas cooler	stainless steel	48
	1	10 m3	slurry cooler	stainless steel	314
crystallizer	2	1 m3	crystallizer	glass lined	320
	2	2 m3	crystallizer	glass lined	462
	1	3.2 m3	crystallizer	glass lined	593
	3	2.5 m3	crystallizer	stainless steel	520
cyclone	2	2200 mm	cyclone	stainless steel	50
decanter	1	1 m3	decanter	stainless steel	130
	1	2 m3	decanter	stainless steel	167
decomposer	8	25 l	steam decomposer	glass lined	25
demister	2		demister	teflon	50
distiller	1	0.2 m3/h	distilling apparatus	stainless steel	100
	1	6 m3	distilling apparatus	stainless steel	360
	1	10 m3	distilling apparatus	stainless steel	600
	15	0.25 m3	vacuum distilling apparatus	stainless steel	205
drier	1	350 kg/day	fluid bed dryer	enamelled	783
	1	100 kg/h	fluid bed dryer	stainless steel	195
	1	200 kg/h	fluid bed dryer	stainless steel	279
	23		fluid drier	stainless steel	400
	1	800 kg/h	spray drier	stainless steel	940
	2		tray drier		800
	4		tray drier	stainless steel	800
	22	12 m2	tray drier	stainless steel	1100
	1	2-3 m3	vacuum drier		1863
	14	0.25 m3	vacuum drier	stainless steel	205
	8	1 m3	vacuum drier	stainless steel	426
	1		vacuum drier	stainless steel	783
	2	3.5 t/d	vacuum drier	stainless steel	783
	2	1.9 m3	vacuum drier	stainless steel	1600
electrolyzer	4	3.5 m3	electrolyzer	carbonated steel / rubber	100
evaporator	1	3 m3	evaporator	enamelled	443
	3	3 m3/9 m2	evaporator	glass lined	443
	8		evaporator	stainless steel	120
	1	0.3 m3/h	evaporator	stainless steel	120
	2		evaporator	stainless steel	443

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
evaporator	1	200 kg/h	evaporator	stainless steel	443
(continued)	1	2.5 m2	evaporator	stainless steel	516
	2	5 m2	evaporator	stainless steel	1178
fan	2	1000 m3/h	fan	pvc	100
fermenter	3	2 m3	fermenter	stainless steel	200
	2	20 m3	fermenter	stainless steel	550
filter	1		bag filter		43
	1		bag filter	enamelled	32
	1	0.5 m2	bag filter	enamelled	32
	2		bag filter	stainless steel	43
	1	0.5 m2	basket filter	enamelled	32
	34		candle filter	stainless steel/ teflon	27
	1	0.5 m2	carbon filter	stainless steel	43
	22		dust filter		43
	1	2 m2	filter	stainless steel	212
	2	4 m2	filter	stainless steel	334
	1		plate filter	stainless steel	500
	1	300 l/h	Seitz filter	stainless steel	600
	5	0.5 m3/min	sterile filter	stainless steel	42
	3	5 m3/min	sterile filter	stainless steel	178
	2	30 m3/min	sterile filter	stainless steel	565
	32	3.5 m2	tray filter	stainless steel	214
	12	1.5 m2	vacuum filter	enamelled	300
	1	2 m2	vacuum filter	stainless steel	212
	1	10 m2	vacuum filter	stainless steel	1000
filter press	1	13 m2	filter press	polypropylene	441
	1	380 l/h	filter press	stainless steel	500
	2		filter press	stainless steel/ polypropylene	500
	1	20 m2	filter press	stainless steel/ polypropylene	564
filter washer	1	10 m3	filter washer		314
flash chamber	1	0.25 m3	flash chamber	stainless steel	75
granulator	2		granulator	stainless steel	50
	24	1000 kg/h	granuling machine	stainless steel	700
	16		milling, granuling machine		700
heat exchanger	8		heat exchanger		22
	8		heat exchanger	carbonated steel	30
	4	50 m2	heat exchanger	carbonated steel	605
	2		heat exchanger	stainless steel	22
	5	1 m2	heat exchanger	stainless steel	22
	2		heat exchanger	stainless steel	150
lift	4	500 kg	pneumatical weight lift	steel	100
Marcusson cover	7		Marcusson cover	glass lined/ stainless steel	75
mill	1		air reduction mill		500
	1	400 kg/h	mill	carbonated steel	50

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
mixer	1	0.1 m3	mixer	carbonated steel	35
	1	1.5 m3	mixer	stainless steel	186
pump	1	5 m3/h	centrifugal pump		49
	3	3 m3/h	centrifugal pump	stainless steel	47
	44	6 m3/h	centrifugal pump	stainless steel	51
	8	6 m3/h	centrifugal pump	teflon	51
	12	0-100 l/min	feeder pump	stainless steel	51
	8	0-100 l/min	feeder pump	teflon	51
	1	4 m3/h	oil pump		48
	8		oil vacuum pump		237
	24	6 m3/h	pneum. pump	teflon	100
	3	2 m3/h	pump		40
	1	4 m3/h	pump		48
	16		pump		51
	1	5 m3/h	pump	carbonated steel	49
	2	6 m3/h	pump	carbonated steel	70
	2	20 m3/h	pump	carbonated steel	95
	1	30 m3/h	pump	carbonated steel	113
	1	0.2 m3/h	pump	stainless steel	17
	4	1 m3/h	pump	stainless steel	33
	3	2 m3/h	pump	stainless steel	40
	7	3 m3/h	pump	stainless steel	47
	2	4 m3/h	pump	stainless steel	48
	2	1-100 l	pump	stainless steel	51
	61	6 m3/h	pump	stainless steel	51
	1		pump	stainless steel	54
	1	10 m3/h	pump	stainless steel	54
	13	20 m3/h	pump	stainless steel	95
	4	2.5 m3/min	pump	stainless steel	226
	10	6 m3/h	pump	teflon	51
	1	20 HP	vacuum pump		252
	12		water ringed pump		237
	27		water ringed vacuum pump		237
reactor	2		catalytic reactor	stainless steel	500
	1	5 m3	stirred reactor		997
	2	20 m3	stirred reactor		2318
	1	0.25 m3	stirred reactor	enamelled	154
	9	0.5 m3	stirred reactor	enamelled	222
	5	1 m3	stirred reactor	enamelled	320
	17	1.25 m3	stirred reactor	enamelled	360
	36	1.6 m3	stirred reactor	enamelled	410
	26	2 m3	stirred reactor	enamelled	462
	43	3 m3	stirred reactor	enamelled	593
	14	6 m3	stirred reactor	enamelled	840
	2	12 m3	stirred reactor	enamelled	1330
	2	2 m3	stirred reactor	glass lined	462
	6	3 m3	stirred reactor	glass lined	593
	8	5 m3	stirred reactor	glass lined	750
	1	6 m3	stirred reactor	glass lined	840
	2	7 m3	stirred reactor	glass lined	898

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
reactor	2	8 m3	stirred reactor	glass lined	964
(continued)	2	3 m3	stirred reactor	polypropylene	593
	5	50 l	stirred reactor	stainless steel	88
	1	1.25 m3	stirred reactor	stainless steel	479
	27	1.6 m3	stirred reactor	stainless steel	545
	11	2 m3	stirred reactor	stainless steel	614
	4		stirred reactor	stainless steel	789
	13	3 m3	stirred reactor	stainless steel	789
	1	4 m3	stirred reactor	stainless steel	887
	4	5 m3	stirred reactor	stainless steel	1000
	14	6 m3	stirred reactor	stainless steel	1117
	1	15 m3	stirred reactor	stainless steel	1990
	2	20 m3	stirred reactor	stainless steel	2318
receiver	16		cooled receiver		24
	28	0.16 m3	cooled receiver		43
	16	0.1 m3	cooled receiver	enamelled	26
	16	0.5 m3	cooled receiver	enamelled	82
	4		cooled receiver	stainless steel	24
	16	0.16 m3	cooled receiver	stainless steel	43
	35	0.25 m3	cooled receiver	stainless steel	75
	5	0.5 m3	cooled receiver	stainless steel	109
	212	0.63 m3	cooled receiver	stainless steel	123
	16		receiver		10
	1	3 m3	receiver	enamelled	192
	4	0.1 m3	receiver	stainless steel	35
	1	0.2 m3	receiver	stainless steel	51
	2	0.5 m3	receiver	stainless steel	109
	5	0.63 m3	receiver	stainless steel	110
	6	1 m3	receiver	stainless steel	130
	1	1.5 m3	receiver	stainless steel	150
	4	2 m3	receiver	stainless steel	167
scale	2	1500 kg	plattform scale		45
	1	2000 kg	plattform scale		50
	1	1000 kg	scale		35
	1	100 kg	scale	stainless steel	35
scrubber	1	5 m3	scrubber	carbonated steel / epox.	400
	1	3 m3	scrubber	polypropylene	350
	1	2 m3	scrubber	stainless steel	160
separator	2	0.25 m3	liquid/liquid separator	stainless steel	75
steam heating center	8		steam heating center		120
	14		steam heating center	steel	120
steam jet injector	9		steam jet injector		100
	2		vacuum steam jet. pay		50

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
tank	1	20 l	tank		51
	1	10 m3	tank		314
	4	20 m3	tank		476
	1	30 m3	tank		611
	2	0.63 m3	tank	carbonated steel / rubber	117
	2	1 m3	tank	carbonated steel / rubber	130
	1	32 m3	tank	carbonated steel / rubber	611
	2	5 l	tank	carbonated steel	24
	8	0.3 m3	tank	carbonated steel	80
	2	0.5 m3	tank	carbonated steel	109
	2	1 m3	tank	carbonated steel	130
	2	2 m3	tank	carbonated steel	167
	3	6.3 m3	tank	carbonated steel	280
	1	10 m3	tank	carbonated steel	314
	2	32 m3	tank	carbonated steel	611
	8	50 l	tank	enamelled	18
	8	0.1 m3	tank	enamelled	26
	4	0.25 m3	tank	enamelled	56
	62	0.5 m3	tank	enamelled	82
	32	20 m3	tank	enamelled	357
	1	0.8 m3	tank	glass lined	117
	1	6 m3	tank	glass lined	280
	1	10 m3	tank	glass lined	314
	1	30 m3	tank	glass lined	611
	2	0.5 m3	tank	polypropylene	109
	1	10 m3	tank	polypropylene	314
	1	50 l	tank	stainless steel	24
	2	0.1 m3	tank	stainless steel	35
	94	0.16 m3	tank	stainless steel	43
	4	0.2 m3	tank	stainless steel	51
	116	0.25 m3	tank	stainless steel	75
	10	0.5 m3	tank	stainless steel	109
	5	0.82 m3	tank	stainless steel	117
	3	1 m3	tank	stainless steel	130
	4	1 m3	tank	stainless steel	150
	1	1.5 m3	tank	stainless steel	150
	1	1-2 m3	tank	stainless steel	167
	7	2 m3	tank	stainless steel	167
	1	2-3 m3	tank	stainless steel	192
	6	3 m3	tank	stainless steel	192
	1	3.2 m3	tank	stainless steel	192
	5	4 m3	tank	stainless steel	224
	5	5 m3	tank	stainless steel	252
	1	5.3 m3	tank	stainless steel	252
	5	6.3 m3	tank	stainless steel	280
	4	10 m3	tank	stainless steel	314

Table 17 (continued): Equipment foreseen in the complex without research and development facilities

General description	Units	Capacity	Item description	Structural material	Unit cost ('000 ATS)
tank	1	12 m3	tank	stainless steel	346
(continued)	10	20 m3	tank	stainless steel	476
	1	24 m3	tank	stainless steel	524
	2	32 m3	tank	stainless steel	611
	2	40 m3	tank	stainless steel	687
	1	50 m3	tank	stainless steel	774
	1	0.25 m3	tank with jacket and stirrer	stainless steel	140
vacuum trap	8	2.5 m2	vacuum trap		39
	22	0.73 m2	vacuum trap	stainless steel	22
	1	1.4 m2	vacuum trap	stainless steel	30
vaporizer	1		vaporizer	stainless steel	443
ventilator	16		ventilator		100
vessel	2	1.2 m3	vessel	enamelled	360
	1	1 m3	vessel	stainless steel	130
	3	3 m3	vessel	stainless steel	789
washing tower	1		washing tower	carbonated steel	300

12.3. INSTRUMENTATION AND AUTOMATIZATION

Instrumentation of equipment used in chemical production in batch processes is as a rule closely related to the source of equipment itself. Established manufacturers of equipment, e.g. reactors, in many cases offer alternatives for instrumentation of their units, which may be selected according to requirements and financial background by the customers. Since it is too early at the present stage of the project to decide prescisely on the degree of instrumentation of the units, the evaluation in the present study is based on the assumption of installation of a comprehensive instrumentation of the production equipment. A survey on analytical instruments is given in chapter 12.4..

Automatization in a chemical manufacturing plant can take place at the following levels:

- unit of equipment
- process
- process building
- plant

The degree of automatization can reach the following levels:

- control of parameters only
- regulation of specific parameters
- control and regulation of a process
- control and regulation of a production
- organization of a plant

Due to the development in EDP automatization is applied more and more in chemical production. The degree of automatization of a plant is closely correlated to its dedication: The more uniform a production is, the more easily automatization can be established. With respect to the present project this means that in the case of single line products the degree of automatization could cover control and regulation of a production in a process building. With the multi purpose plants either regulation of specific parameters or control and regulation of a process may be reached controlling one or several equipment units.

Until recently a second rule applied indicating that full automatization is only justified with large scale processes. In the last years stored-program-control systems and other intelligent devices have become available on the market at very reasonable prices so that the bottleneck of optimum automatization nowadays is no more the required investment, but rather the requirement of qualified staff that is in a position to carry out a good deal of programming in the company.

Taking this into account it is recommended to foresee a flexible system of automatization for the plant, by which in a rather decentralized manner control and regulation systems of different degree of automatization are installed in the production units.

At the same time it is recommended to develop an automatization concept for the company, in which beyond production automatization it should be determined up to which degree computer based plant organization should be established at the SHAHID MODARRES Industrial Pharmaceutical Complex.

Since the success of application of EDP nowadays is no more a question of capital investment for hardware, but depends mostly on suited software and a well trained operating staff, it is recommended to start with training of staff as soon as possible, so that experienced personnel is available from beginning of the installation of the plant.

12.4. QUALITY CONTROL EQUIPMENT

The chapter "Laboratory Equipment" in the Annex "Quality Control and GMP File" is divided in subparts concerning each type of laboratory. For each laboratory (with the exception of the Microbiological Laboratory) the required equipment has been estimated on the one hand as equipment for use in special analytical procedures as described in the Pharmacopoeias and on the other hand as equipment commonly used in laboratories. The amount of required equipment has been estimated on the basis of proposed batch sizes and

the yearly output of the plant as well as estimated time consumption for one analysis running on the particular apparatus.

In the case of the in-process-control laboratories the laboratory equipment has been estimated for one laboratory. Special equipment for IPC-laboratories has been divided in two parts, one recommended for each laboratory and the other only necessary for particular laboratories. Although it is recommended to have an IPC laboratory at each production unit, e.g. an infrared spectrometer will not be necessary for each lab (but is recommended at least for those attached to the multipurpose production units).

An estimation of prices of special and common equipment is given in the Annex.

12.5. AUXILIARY AND SERVICE EQUIPMENT

There is a broad range of required auxiliary and service equipment in a industrial complex of the size of the present project. It is not feasible at the present stage of the project to present an exhaustive survey on all auxiliary and service equipment. Some of the most important areas, where this type of equipment is required, are listed as follows:

COMMUNICATION

- EDP: In regard to the different applications of a modern system it is recommended to install a network
- telephone and fax
- wireless facility interdepartmental
- alarm system internally and for external information

STORAGE AND TRANSPORTATION

- storage facilities, racks
- storage transport equipment, fork-lift trucks
- storage safety facilities

MAINTENANCE AND CIVIL ENGINEERING

- car mechanic workshop: buses and cars for personnel transportation; trucks for internal and external transports, special cars ; fire fighting engines, transporter cranes; bulldozers, ambulance
- gasoline filling station
- workshops for all types of metal working
- workshop for electric and electronic repair
- workshop for glass
- civil engineering services: supplied with all tools and equipments for joiner's work, plumber, painter, gardener, construction workers
- cleaning equipment for offices, production units and outside areas

SOCIAL SERVICES, SAFETY, SECURITY AND ENVIRONMENT

- fire fighting and security equipment
- medical equipment, sick-room, first aid
- kitchen and cafeteria
- laundry
- sports and leisure, radio, TV, library
- accommodations, lodgings, also for guests
- religious services

OFFICES

- office equipment, typewriters, office furniture

13. SUGGESTED LAY OUT OF THE COMPLEX

As far as the arrangements of the units of the complex is concerned a lot of work had been done already by the SHAHID MODARRES planning group. This lay - out concept could be used to a large extent, major changes being required by the introduction of the 4 sector concept. Instead of carrying out most of the productions in five production units, three of them multi purpose units, the concept foresees multi purpose production units in each sector. In addition to that single line production is foreseen, which however in most cases is carried out in combined units as follows:

Sector No.	Single Unit	Combined Unit*)	Multipurpose Unit
1	2		1
2	-	2	1
3**)	5	-	1
4***)	2	-	2
Total	**9**	**2**	**5**

The proposed arrangement of the plant is illustrated in a map, which is supplied with this report.

It is pointed out that the proposed concept is not binding in principle and that changes in the arrangement of the units would not effect the investment requirements to a large degree as far as import of material and equipment is concerned.

A specific situation is also given by the wish of the SHAHID MODARRES management to set up a remote solvent storage having a one year capacity. This requirement will have positive and promising effects on the non-shortage of solvents (due to import problems) and also safety of storages, because only limited quantities of solvents will be stored at the production sites, however this solution needs more investment and capital binding.

Long distances between the plant and the biological effluent treatment system have also as well positive as negative effects, which have been already discussed.

13.1. PRELIMINARY TECHNOLOGICAL DESIGNS OF THE UNITS

As mentioned earlier in this report a plant concept is proposed consisting of 4 sectors, each dedicated to a specific field of acivity of the company. In each of these sectors a set of different products is to be manufactured. This product mix determines the design of the units. A suited allocation of the different production processes to their production units is extremely important. For each product the decision has to be met to carry out production in single line units or to place the product together with other products into multi purpose plants.

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*) Two single lines are condensed into one unit.

**) Besides the units indicated, the Medicinal Plant Extraction and Biochemical and Genetic Engineering Centres are included.

***) Also Pilot Plant Research Centre is included.

For many years it has been a general ambition in pharmaceutical industry worldwide to install production units in a manner that will allow changes in the production profile according to the demands of the health sector or the international market without fundamental changes in construction of the unit and without productivity loss due to standstill. "Multipurpose production units" have been the answer to this ambition. Flexible technological buildings are set up frequently using prefabricated elements available in the civil engineering market.

The design of such halls is as uniform and flexible as possible, frequently a modular systems are applied. Technological equipment is selected to guarantee versatility, so that standard organic chemical key processes may be carried out.

UNIDO has successfully worked out this concept for technology transfer and implemented it in several cases. The present plant concept follows to a large degree this UNIDO concept.

The decision to foresee a product for production in a multi purpose plant was based first of all on production quantities. In addition to large volume products those products were considered for production in separated areas, which posed a risk of corrosion or explosion.

The preliminary technological design was worked out for all units and can be found in Volume 3 of this report.

13.2. REQUIRED AREAS

Since there is a lot of space available at the prospective plant site, there is no specific pressure concerning size of the production units and distance of these units from each other.

It was mentioned before that increasing space as a rule means increased cost of transport, but also increased security.

Table 18 shows the area requirements for each unit.

Table 18: Area requirements for each unit

Unit	Area [m²]
1.1.. 1.2.	1404
1.3.	1296
2.1.	1088
2.2.	1088
2.3.	1296
3.1.	2412
3.2.	648
3.3.	648
3.4.	648
3.5.	486
3.6.	648
3.7.	1728
3.8.	648
3.9.	446
4.1.	756
4.2.	648
4.3.	1728
4.4.	1404

It is pointed out that the areas given represent only indicative figures, which are based on the proposed type of production building.

14. BUILDINGS

14.1. TECHNICAL DESCRIPTION OF ONE PRODUCTION UNIT

The design of chemical production units is determined by technical requirements. Several acceptable options for arrangement of production units can be found. The two main types are differing in the flow of material: vertical arrangement, where the process starts at very high levels above ground and gravidity is bringing the flow of material down to the zero level, where the finished product is obtained and horizontal arrangement, where production takes place in two or three levels and the product is moved horizontally from one side of the unit to the other. Since frequently the arrangement of production units is closely correlated to the production technologies, the decision on a specific type of arrangement should be left to the implementing engineering company.

The present study is based on the generally accepted horizontal system with three main levels. Such levels might be :

- 0.00 m main level
- 3.50 - 4.00 m manipulating level
- 7.50 - 8.00 m helper level

with the 0.00 m and the 3.50 m levels as operating levels. The technological main equipment is placed at the 3.50 m level, dryers and centrifuges at the 0.00 m level. The condensers, feeder tanks etc. are installed at the 7.50 m level.

There should be a service corridor at the 3.50 m level, which is connected to the staircase. Emergency exits lead to an outside corridor, which serves as a runaway corridor. The pipes of the utilities should be installed at the tank storage side of the building. Pipelines are installed at floor level in a covered floor canal. All electrical installations have to be explosion proof. Cables branch off to switch casings attached directly to the hall.

Fixed pipe connections are installed between related equipment (stirred reactor, condenser, feeder tank, receiver). Also flexible connections for flow of material moving between units of equipment (stirred reactor-centrifuge etc.) are foreseen.

A very useful modular unit of this type of production building designed by a Hungarian company has been implemented in a UNIDO multi purpose plant project.

RAW MATERIAL SUPPLY

Measured and packed solid raw materials arrive at the production unit from the central store and are lifted to the manipulationg level by good lifts, placed at the outside or in the staircase of the building. From there they are transported to the processing sites on the service corridor by forklift trucks.

Liquid materials are directly pumped into the reactors or feeder tanks from the local liquid storage placed at the outside of the building. Liquids arriving in balloons or barrels are transferred to the processing site by a pneumatic drum pump. Liquids and solids from the centrifuges, which are placed at the zero level, can also be transported to the manipulating level in containers by pneumatic good lifts

UTILITY SUPPLY

Steam, gas and liquid utilities arrive on tubular bridges from the Energy Center. High temperature heating oil is produced using electrical heating equipment in a spearated room of the production hall and is circulated to the reactor by use of pumps. Cooling oil is prepared in the same place as heating oil.

DESIGN AND CONSTRUCTION MATERIALS

Only when the decision has been met on the technological design of the production buildings, architectural design can take place. Although it is possible to carry out civil engineering work of an industrial pharmaceutical complex without architectural design, it is advisable to provide a uniform architectural design concept for the whole plant.

If available, local civil engineers should carry out construction work. It is also recommended to use local materials as far as possible. The following short description may give an impression about standard construction materials used for industrial chemical production units built in a modular system: The frame of the units is made up by prefabricated reinforced concrete pillars with prefabricated main beam and ceiling. The dimensions of the pillars are suited to carry the weight of the manipulating and helper level. The foundations have to accomodate the frame. Local conditions of soil must be taken into consideration. The floor covering is placed on reinforced concrete. Usually metal doors and windows are installed. Insulation and painting depend on local conditions. A steel construction with two operating levels at 3.50 m and 7.50 m to which the equipment is attached is mounted in the building .

14.2. STORES

Due to increasing legal regulations concerning handling and storage of chemicals, the number of storehouse nowadays required in a chemical company has increased very much compared to the situation a few years ago. It is not enough to have a storage for solid materials, one for liquid materials and one for gases. For security reasons also acids have to be stored separated from bases, inflammable material separated from flammable material etc. The present study has made the attempt to come up to the requirements of the latest regulations, it is however pointed out that - as with many other aspects concerning environmental questions - it is advisable to observe permanently the development of the local Iranian situation concerning legislation on chemicals.

As a rule companies tend to keep their inventory of stored material as low as possible to avoid unneccessary capital binding. The prerequisite for low storage quantities is a perfect production planning, which allows precise forecasts on required quantities, and above all reliable suppliers delivering within short time. Considering the long distance between Iran and most of the international chemicals suppliers, it must be doubted, whether a storage management based on short time delivery could work properly. Therefore the wish of the Iranian experts to foresee a one year storage capacity is an expensive solution concerning initial investment and operating costs, but certainly understandable from the point of view of reliability of supply.

The request for one year storage capacity results in a considerable high amount of chemicals to be stored. Table 19 summarizes the quantities of solid, liquid and gaseous materials, which are required in each unit per year. In the following chapter a description is given for the one year storage facilities. This one year storage system allows to foresee only small storage units nearby the production facilities, which are indicated in Volume 3 of the present report.

Table 19: Quantities of starting materials required in each unit in [kg/year]

Unit	Starting materials (kg/year)		
	liquid	solid	gaseous
Unit 1.1.	2.027.550	475.350	0
Unit 1.2.	1.341.000	546.000	0
Unit 1.3.	1.885.207	386.623	1.727
Unit 2.1.	872.176	245.625	62.496
Unit 2.2.	8.694.803	912.250	0
Unit 2.3.	2.624.729	251.498	16.007
Unit 3.1.	4.895.100	1.394.400	29.900
Unit 3.2.	106.631	281.004	0
Unit 3.3.	761.000	142.900	0
Unit 3.4.	7.099.006	693.879	0
Unit 3.5.	0	1.000.000	0
Unit 3.6.	57.272	600	0
Unit 3.7.	2.731.912	521.122	67.005
Unit 4.1.	1.254.400	2.209.300	563.200
Unit 4.2.	1.686.570	245.087	0
Unit 4.3.	1.420.220	135.012	360
Unit 4.4.	366.105	25.712	1.317.769
sum	**37,823,680**	**9,466,362**	**2,058,464**

14.2.1. STORAGE OF SOLID MATERIALS

Solid material is to be stored on pallets. The average storage capacity of a pallet is 500 kg, the height of a pallet is 1 m. Considering the amount to be stored (9,500 tons) and an average volumetric weight of 1 ton/m^3 a total of 9,500 m^3 storage volume is required, which corresponds to 19,000 pallets. Two lines of pallets may be put on each other. Forklift trucks are used for transportation.

It has to be considered that there has to be a separate area for storage of incoming materials until inspection has taken place.

Inflammable solids should be stored separated from non flammable solids in a closed, one-storied building with reinforced concrete frame and brick walls. At the both ends of the building there are rooms to handle the incoming and outgoing products. The building is surrounded by a ramp having the same height as the loading area of trucks.

Method of storage: in steel drums, paper and jute sacks on pallets.
Dimensions of the building: Length: 86 m
Width: 20 m
Inside height: 4.2 m

Non flammable solids are stored in an identical manner in a separated building.

14.2.2. STORAGE OF LIQUID MATERIALS

Liquids will be stored in underground tanks and in horizontal or vertical cylindrical tanks. Due to request for one year storage capacity a tank farm will be installed for a considerable number of solvents to be stored in central tanks. These tanks will be arranged in groups of 6 tanks, each tank containing 100 m^3.

STORAGE OF FLAMMABLE LIQUIDS

underground tanks

Acetone	6 x 100 m^3	1 group	stainless steel
Dichloromethane	6 x 100 m^3	1 group	stainless steel
Ethanol	6 x 100 m^3	1 group	stainless steel
Ether	2 x 100 m^3		
Methanol	4 x 100 m^3	1 group	stainless steel
Methanol	6 x 100 m^3	1 group	stainless steel
Toluene	6 x 100 m^3	1 group	stainless steel

horizontal cylindrical tanks

Dichloromethane	2 x 63 m^3	stainless steel
Dichloroethane	2 x 63 m^3	stainless steel
Dioxane	1 x 63 m^3	stainless steel
Pyridine	1 x 63 m^3	stainless steel
Ethylacetate	1 x 63 m^3	stainless steel
Isopropanol	1 x 63 m^3	stainless steel
Isobutanol	1 x 63 m^3	stainless steel

STORAGE OF FLAMMABLE ACIDS

underground tanks

Acetic acid	4 x 100 m^3	stainless steel
Acetic anhydride	2 x 100 m^3	stainless steel
Ethyl chloroacetate	2 x 100 m^3	stainless steel
Formic acid	6 x 100 m^3	stainless steel
Castor oil	1 x 100 m^3	steel

STORAGE OF NONFLAMMABLE ACIDS

standing cylindrical tanks

Hydrobromic acid (48%)	1 x 63 m^3	poly propylene
Hydrochloric acid (32%)	5 x 63 m^3	poly propylene

horizontal cylindrical tanks

Nitric acid	1 x 100 m^3	stainless steel
Sulfuric acid	1 x 100 m^3	steel
Oleum	2 x 100 m^3	steel

STORAGE OF BASES

horizontal cylindrical tanks

Ammonium hydroxide	1 x 63 m^3	stainless steel
Pottassium hydroxide (50%)	2 x 100 m^3	stainless steel
Sodium hydroxide (40%)	2 x 100 m^3	stainless steel
Sodium hypochlorite (15%)	2 x 100 m^3	stainless steel
Hydrogen peroxide (30%)	1 x 63 m^3	aluminium

All other liquids should be stored in barrels (200 l each).

14.2.3. STORAGE OF GASEOUS MATERIALS

HYDROGEN CHLORIDE STORAGE

The gas cylinders should be stored in a shed like building, with light roof and asphalt covered floor. The gas cylinders are fixed in store cages in standing position. The cylinders must be protected from radiation, sunlight and mechanic damages.

Dimensions of the building: Length: 24 m
Width: 12 m
Inside height: 3 m

AMMONIA STORAGE

Ammonia is stored in the same manner as hydrogen chloride.

Dimensions of the building: Length: 12 m
Width: 12 m
Inside height: 3 m

ETHYLENE OXIDE STORAGE

Ethylen oxide is stored in a shed like building, with wire grating walls and concrete floor. The construction is furnished with a fire proof, light roof.

Method of storage: in specially shaped steel drums.
Dimensions of the building: Length: 24 m
Width: 12 m
Inside height: 3 m

14.2.4. SPECIAL STORAGES

STORAGE FOR METALLIC SODIUM AND SODIUM ALKOXIDE

Sodium and sodium alkoxide are stored in a separated building without heating having a concrete floor elevated to 0.5 m, with fire proof walls and well insulated roof. The building is furnished with steel doors and wire framed windows.

For transport of the materials explosion proof forklift trucks are used.

Method of storage: in soldered metal drums.
Dimensions of the building: Length: 24 m
Width: 12 m
Inside height: 3 m

STORAGE FOR CATALYSTS

Catalysts are also stored in a separated building with concrete floor elevated to 0.5 m, with fire proof walls and well insulated roof.

Method of storage: on steel construction frames
Dimensions of the building: Length: 12 m
Width: 6 m
Inside height: 3 m

STORAGE OF POISONOUS MATERIALS

Poisonous material should be stored in a separated building with concrete floor elevated to 0.5 m, with well insulated roof but without catch water drum.

Method of storage:

a. Solid poisons on steel construction frames in soldered metal drums.
b. Liquid poisons in well closed barrels with single line placing.

The rooms a. and b. are separated by reinforced concrete wall. The stores require special protection and control.
Dimensions of the building: Length: 24 m
Width: 12 m
Inside height: 3 m

14.2.5. END PRODUCT STORAGE

It must be taken into account that the end products are pharmaceutical chemicals which require careful storage and should be handled to follow the requirements of GMP, as outlined in the chapter on quality control.

It is proposed to set up a closed, four storied building with reinforced concrete frame and brick wall as end product storage. Goods lifts should be installed at both ends of the building. There should also be rooms at both ends of the building for incoming and outgoing products. The building is surrounded by a ramp having the same height as the loading area of trucks. For material transport in the building forklift trucks are used.

Method of storage: on pallets in suitable package
Dimensions of the building: Length: 86 m
Width: 20 m
Inside height of the levels: 3.0 m

14.3. CLIMATIZATION

Iran is a country exhibiting extreme temperatures: heat in summer and chill in winter. It is a question of considerable investment and operating cost to decide in which areas climatization or heating should be foreseen. The present study therefore confines its evaluation to those areas of the plant, where climatization is obligatory for proper performance of the plant.

The following rooms should be climatized to 20° - 25° C and a humidity of about 40 - 60% rH:

Warehouses for storage of the final products
Warehouses for storage of perishable products
Rooms, where the final product is handled
Laboratories
Offices
Messes

The following rooms should be cooled to 10° - 15°C without regulating humidity:

Storage rooms for highly inflammable solvents and/or chemicals (explosion proof!)

Refrigerating rooms should be foreseen for (2° - 6° C):

Storage of perishable compounds (milk!)

In production units where excessive heat may be produced cooling devices, e.g.fans, should be installed to guarantee an accepatable room temperature.

14.4. CLEAN CLASS REQUIREMENTS

Cleanliness nowadays is a basic requirement in chemical production. Usually companies are following their own instructions based on regulations of national and local authorities.

Far beyond such regulations, the pharmaceutical industry is perfectly regulated concerning clean working. Most regulations however refer to formulation operations. With the manufacture of pharmaceutical chemicals regulations are growing and GMP rules are being established. Until now however strict rules are given only for the handling of end products. Therefore only for those rooms, where the final product is handled - the last step of production and final product storage -, controlled conditions are necessary (refer to: Annex "Quality Control and GMP File": "The Scope of a Microbiological Laboratory in BPC Production").

14.5. STERILITY REQUIREMENTS

An analysis of the foreseen production programme revealed that there are no binding sterility requirements in production: In cases of compounds which are to be used for large volume parenterals control of batches to secure that these have a low germ count and are free of bacterial endotoxins will be sufficient to meet the requirements. Only those batches which comply with the sterility requirements shall be labeled to have injectable quality, all other substances shall be labeled to have oral quality.

15. TIME REQUIREMENTS FOR COMPLETION OF UNITS AND COMPLEX

It is not advisable at the present stage to set up the time plan for the implementation of the project before having decided on the modalities of contracting and global timing of project implementation. With such complex project it is advisable to implement not all sectors at once, but to choose an approach by which priorities are set and implementation is executed following these priorities. Such a step - wise approach would make organization of project much less complex and would allow to get the most promising units quickly into

operation. As far as project implementation in technical terms is concerned the following steps take place:

		time schedule
1. Signing of the contract		
2. Basic engineering		2 years
After approval of basic engineering:		
3. Detailed engineering		2 years
4. Purchase of equipment	parallel	2 years
After approval of detailed engineering:		
5. Erection of the buildings and installation of the equipment		2 years
6. Test runs of operation		6 month
7. Implementation of technology transfer in several steps		6 month
complete transfer of all 50 products		3 to 5 years

According to this schedule plant operation would start 7 years after signing the contract.

16. PERSONNEL

For the operation of such a big plant it will be necessary to build up a staff, which is well structured with different educational levels.

Fig. 7 shows the structure in principle while in table 20 more detailed information is given.

BOARD OF DIRECTORS

The board consists of 10 directors, the heads of the main departments, divisions, and is responsible for the strategies, corporate identity and organizational structure of the different divisions.

GENERAL MANAGER

He is the main representative of the company and responsible for the organizational goals.

Fig. 7: Organization chart

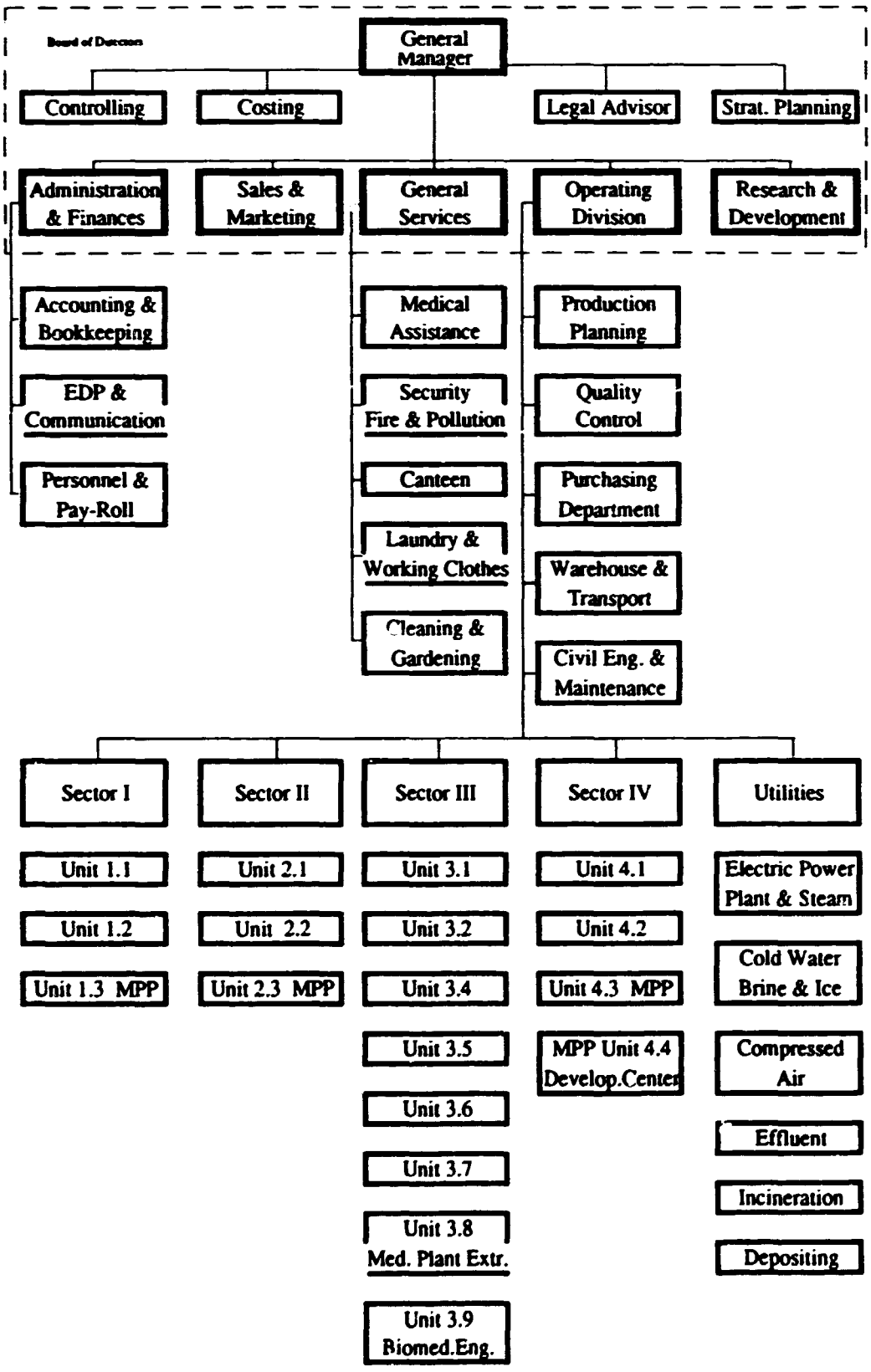

Table 20: Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
General Manager		1					
Assistant to General Manager		1					
Secretary			1	2			
Law & Patents	expert for local and foreign laws and patents right, responsible for contracts , patents and licensing						
Legal Advisor	multilingual	1					
Assistant to the Legal Adviser	multilingual		1				
Secretary	multilingual			2			
Controlling	budgeting, reporting, management information system and organizational procedures						
Senior Controller		1					
Junior Controller			1				
Secretary				2			
Costing							
Senior Cost Accountant		1					
Junior Cost Accountant			1				
Secretary				2			
Strategic Planning	long term planning of product mix, international contacts to licence holders						
Senior Planner	multilingual	1					
Junior Planner	multilingual		1				
Secretary				2			
Total of General Management		5	5	10	0	0	0
Head of Sales Dept.,		1					
Secretary			1				
Product Manager	4 sectors and export		5				
Secretary				5			
Total of Sales & Marketing		1	6	5	0	0	0

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Accounting & Bookkeeping							
Accounting Chief		1					
Senior Accountant			1				
Junior Accountant			1				
Assistant				4			
Secretary				1			
Personnel	hiring, coordination of personnel training						
Head of Personnel		1					
Assistant			2				
Secretary				4			
EDP & Communication							
Head of EDP & Communication		1					
System Analytic			2				
Programmer			3				
Operator				2			
Invoice							
Invoice Chief			1				
Assistant				4			
Total of Administration & Finances		3	10	15	0	0	0

Medical Services							
First Aid & Ambulance							
Chief Physician	medical doctor	1					
Physician	medical doctor, operating in shifts	4					
Ambulance Man	operating in shifts			5			
Hospital							
Nurse	operating in shifts			7			
Security, Fire & Pollution							
Head of Department	has to be an experienced chemist, takes care for all aspects of safety	1					
Assistant	deputy to the department head		2				
Secretary			1	1			
Security Group							
Head of the Group			1				
Assistant	operating in shifts			4			
Guards & Work protection force	operating in shifts				15	15	
Telephone Operator	operating in shifts			4			
Receptionist			2				

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Fire & Pollution Fighting Group							
Head of the Group		1					
Technical Assistant	operating in shifts		4				
Secretary				1			
Firefighter	operating in shifts				10	10	
Canteen	supplies meals 3 times a 3 day						
Head of Canteen			1				
Secretary				1			
Cook					6		
Cook-Assistant						12	
Kitchen Helper							18
Laundry							
Head of Laundry				1			
Helpers							4
Warehouse for Working Clothes							
Head of Warehouse				1			
Helpers							3
Cleaning & Gardening	cares fore cleaning of the administration buildings and the cultivation of the outdoor parts of the plant						
Head of Cleaning & Gardening			1				
Secretary				1			
Cleaning Labor						4	16
Gardeners					1		4
Total of General Services		7	12	26	32	41	45

Technical Director		1					
Assistant to the Techn. Director		1					
Secretary			1	1			
Central Production Planning							
Head of Central Prod. Planning	deputy to the technical director	1					
Assistants		1	1				
Secretary			1	2			
Quality Control							
QA Manager		1					
Secretary			1	1			

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Quality Assurance							
QC Manager		1					
Secretary			1	1			
Central Laboratory							
Head of Central Laboratory	deputy to the QC manager	1					
Secretary				1			
Technical Operator	experienced in HPLC, GC, IR			2			
Assistant				8	10		
Warehouse Laboratory							
Head of the Warehouse Lab			1				
Secretary				1			
Technical Operator	experienced in HPLC, GC, IR			1			
Assistant				4	4		
Microbiological Laboratory							
Head of Mircobiolog. Lab.		1					
Assistant				7	3		
Purchase Department							
Purchase Manager		1					
Assistants	multilingual, experienced in shipping and insurance		4				
Secretary				2			
Warehouse & Transport							
Head of Warehouse & Transport	in charge for Warehouse, internal transport		1				
Assistant			1				
Secretary				1			
Warehouses							
Head of Warehouses			1				
Secretary				1			
Stocker					3		7
Transport Group							
Head of Transport Group			1				
Driver					15		
Codriver							15

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Civil Engineering & Maintenance							
Head of Department	mechanical engineer	1					
Assistant	civil engineer, deputy to the department head	1					
Secretary				1			
Central Electric Workshop	not operating in shifts						
Electrician					2	2	
Central Electronic Workshop	not operating in shifts						
Electronician					2	2	
Central Mechanical Workshop	not operating in shifts						
Construction worker					4	2	
Painter & Varnisher					2	2	
Plumber					2	2	
Unskilled workers							8
Central Workshop for Glass Work							
Glass-Blower					2		
Car Repair							
Mechanics					3	3	
Subtotal of Production		11	14	34	52	13	30

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Head of Utilities		1					
Secretary				1			
Electric Energy Plant & Steam							
Operating Engineer			1				
Engineer in Charge				4			
Worker					6	4	6
Brine, Ice, Cold & Deionized Water							
Operating Engineer			1				
Engineer in Charge				4			
Worker					6	6	6
Compressed Air							
Operating Engineer				1			
Engineer in Charge					4		
Worker							3
Effluent							
Operating Engineer			1				
Engineer in Charge				4			
Worker						4	
Incineration							
Operating Engineer			1				
Engineer in Charge				4			
Worker						5	
Depositing	not operating in shifts						
Operating Engineer			1				
Engineer in Charge				1			
Worker							3
Subtotal of Production - Utility		1	5	19	16	19	18

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Sector Manager		1					
Secretary				1			
Production Planning & Logistic Group							
Head of Group	deputy to the sector manager	1					
Technical Assistant			1				
Secretary				1			
Maintenance & Repair Group							
Head of Group				1			
Ironworker	operating in shifts				4	2	
Mechanic	operating in shifts				4		
Electrician	operating in shifts				4		
Unit 1.1 Ibuprofen							
Operating Engineer			1				
Engineer in Charge				4			
Worker					10	10	6
Worker with special training					2		
Unit 1.2 Methyldopa							
Operating Engineer			1				
Engineer in Charge				4			
Worker					10	10	6
Worker with special training				1			
Unit 1.3 Multiple Product Plant							
Operating Engineer			1				
Engineer in Charge				5			
Worker					24	24	18
Worker with special training					4		
Subtotal of Production - Sector 1		2	4	17	62	46	30

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Sector Manager		1					
Secretary				1			
Production Planning & Logistic Group							
Head of Group	deputy to the sector manager	1					
Technical Assistant			1				
Secretary				1			
Maintenance & Repair Group							
Head of Group				1			
Ironworker	operating in shifts				4	2	
Mechanic	operating in shifts				4		
Electrician	operating in shifts				4		
Unit 2.1 Cetrimide (40 %) & Metronidazole							
Operating Engineer			1				
Engineer in Charge				4			
Worker					8	12	8
Worker with special training					2		
Unit 2.2 Sulfamethoxazole & Trimethoprim							
Operating Engineer			1				
Engineer in Charge				4			
Worker					8	8	4
Worker with special training					2		
Unit 2.3 Multiple Product Plant							
Operating Engineer			1				
Engineer in Charge				5			
Worker					24	24	18
Worker with special training					4		
Subtotal of Production - Sector 2		2	4	16	60	46	30

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Sector Manager		1					
Secretary				1			
Production Planning & Logistic Group							
Head of Group	deputy to the sector manager	1					
Technical Assistant			1				
Secretary				1			
Maintenance & Repair Group							
Head of Group				1			
Ironworker	operating in shifts				4	2	
Mechanic	operating in shifts				4		
Electrician	operating in shifts				4		
Unit 3.1 Ascorbic Acid							
Operating Engineer			1				
Engineer in Charge				5			
Worker					48	24	24
Worker with special training				12	2		
Unit 3.2 Calcium Caseinate							
Operating Engineer			1				
Engineer in Charge				4			
Worker					8	8	6
Worker with special training					2		
Unit 3.3 Nicotinamide							
Operating Engineer			1				
Engineer in Charge				2			
Worker					4	2	2
Worker with special training					2		
Unit 3.4 Magnesium & Zinc Stearate							
Operating Engineer			1				
Engineer in Charge				4			
Worker					8	4	8
Worker with special training					2		
Unit 3.5 Mannitol							
Operating Engineer			1				
Engineer in Charge				5			
Worker					8	12	12
Worker with special training					2		

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Unit 3.6 Isosorbide Dinitrate	operating only part of the year						
Operating Engineer			1				
Engineer in Charge				2			
Worker					2		2
Unit 3.7 Multiple Product Plant							
Operating Engineer			1				
Engineer in Charge				5			
Worker					24	24	18
Worker with special training					4		
Unit 3.8 Medical Plant Extraction	only partly in shift						
Unit 3.9 Biomedical engineering and generic development center							
Operating Engineer		1					
Engineer in Charge			2				
Botanist		2	4				
Microbiologist		2	4				
Analytical Chemist		2	4	2			
Laboratory Technician				6	8		
Worker					8	8	4
Worker with special training					4		
Subtotal of Production - Sector 3		9	22	50	148	84	76

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Sector Manager		1					
Secretary				1			
Production Planning & Logistic Group							
Head of Group	deputy to the sector manager	1					
Technical Assistant			1				
Secretary				1			
Maintenance & Repair Group							
Head of Group				1			
Ironworker	operating in shifts				4	2	
Mechanic	operating in shifts				4		
Electrician	operating in shifts				4		
Unit 4.1 Aluminium Hydroxide							
Operating Engineer			1				
Engineer in Charge				5			
Worker					12	8	18
Worker with special training					3		
Unit 4.2 Similitude							
Operating Engineer			1				
Engineer in Charge				4			
Worker					8	8	4
Worker with special training					2		
Unit 4.3 Multiple Product Plant							
Operating Engineer			1				
Engineer in Charge				5			
Worker					24	24	18
Worker with special training					4		
Unit 4.4 Multiple Purpose Plant Development Center							
Operating Engineer		1					
Engineer in Charge			4	4			
Worker					14	14	2
Worker with special training					4		
Subtotal of Production - Sector 4		3	8	21	83	56	42
Subtotal of Production		28	57	157	421	264	226

Table 20 (continued): Personnel requirements

Position	Job Description	Training					
		Staff			Labor		
		GR	UN	HS	sk	se	un
Head of R & D	coordinates R&D activities which is located in sector 3 & 4	1					
Assistant			2				
Secretary				2			
Documentation							
Head of Documentation	organizes documentation and library	1					
Assistant			2				
Secretary				2			
Subtotal of Central R & D		2	4	4	0	0	0
Total		46	94	217	453	305	271
Overall Headcount	1386						

STRATEGIC PLANNING, CONTROLLING, COSTING

These departments should be staff units attached to the general manager and members of the board of directors.

LEGAL ADVISOR

He is in organizational relationship to the general manager, member of the board, responsible for patents, licenses and contracts. He has to act in close cooperation with salesmen, marketing department and research and development.

ADMINISTRATION AND FINANCE

This department handles confident tasks as personnel, accounting and EDP (because of security aspects of data)

SALES AND MARKETING

Product and price policy linked with the strategic goals of the company are worked out here. In the very beginning the activities are concentrated on the domestic market, later foreign markets have to be made accessible.

GENERAL SERVICES

This department will take care of social, medical, security and safety aspects.

RESEARCH AND DEVELOPMENT

The research and development department will work on the implementation of the research concept of the company. Furthermore, as the main task during the start-up period of the company, it will provide a support to the technical department in all transfer of technology and scaling-up activities contributing with relevant know-how in particular.

Future activities, above all further development of new research targets will have to be worked out in close cooperation with sales and legal department.

With respect to the problems arising in production a trouble shooting team has to provide assistance to the technical director.

TECHNICAL DIVISION

The technical division is covering all organizational procedures of the plant, with the responsibilities planning, purchasing, producing, storing and maintenance of the plant. Quality control is reporting to the technical manager. The sector manager and the head of utilities are coordinated by production planning.

17. TECHNICAL ASSISTANCE AND TRAINING

17.1. TECHNICAL ASSISTANCE

Technical assistance is first of all required for the transfer of technologies, which should include training at the company site of the technology holder and presence of the technology supplier during the start up phase. Furthermore technical assistance should be established as a company feature including following steps:

1. Contracts with Iranian and in case given foreign research institutions for research and development in fields of interest of the company
2. Permanent advisory assistance for strategic long term planning of the company
3. Technical assistance in the training of the staff locally and abroad
4. Assistance in plant management including aspects of marketing and sales

It is strongly recommended to consider co-operations with foreign pharmaceutical companies. Such co-operations might not only take place as technical co-operations but could also include marketing and sales arrangements. It may be observed that in the international community of pharmaceutical companies there is a strong tendency towards joint activities. Within such co-operations technical assistance can be obtained easily.

17.2. TRAINING

From chapter 16. it can be seen that the company will require a diversified staff. Since SMDI is one of the first Iranian companies to step into the sector of pharmaceutical chemicals production there is no local Iranian market of personnel with required experience. Therefore extensive training programmes, many of them abroad, will be required. The training will cover all levels of staff and will have to deal with all relevant operations to be carried out by the staff. It is proposed to use UNIDO assistance to set up a

detailed training programme. Since it is impossible to foresee a training programme abroad for more than 1000 employees, it is recommended to set up training facilities within the plant and establish a local training programme.

18. FINANCIAL ANALYSIS

Based on the results of the technical evaluation a financial analysis was carried out using COMFAR. The detailed results of this analysis are given in the Annex. The following key data were obtained:

The total initial investment will be 332.169.900 US$.
The operating costs will be 55.802.700 US$.
The resulting depreciation is 33.474.670 US$.
This results in production costs including depreciation of 89.277.360 US$.
The total sales revenues will be 59.063.400 US$.

From these data it can be seen that the project requires some adjustment to be economically feasible. Recommendations to improve the perspective of the project are given in chapter 2. of the present report and in the Annex.

EXPLANATORY NOTES

GENERAL

A blank means that information is not given or is not applicable.
A slash between dates (e.g. 1991/1992) indicates a financial year.
The use of a hyphen between dates (e.g. 1991-1992) indicates the full period involved (e.g. beginning of 1991 until end of 1992).
A period (.) is used to indicate decimals.
A dash (-) is used to indicate amounts that are nil or negligible.
A comma (,) is used to distinguish thousands and millions.
Percentage rates, commissions, fees, etc. are per annum, unless otherwise indicated.
References to "tons" are to metric tons.
Totals may not add up precisely because of rounding off.

In addition to common abbreviations, symbols and terms, the following abbreviations have been used in this study:

TOT	Transfer of Technology
NCE	New chemical entity
OTC	Over the counter sold drugs
BPC	Bulk Pharmaceutical Chemicals equally used with the terms Bulk Pharmaceutical Compounds, Bulk Pharmaceuticals or Bulk Drugs, used as raw materials to produce formulated finished forms
QC	Quality Control
QA	Quality Assurance
n.a.	Not applicable
rec.INN	recommended International Non proprietary Name
USP XXII	Pharmacopoeia of the United States
NF XVII	The National Formulary (USA)
GMP	Good Manufacturing Process
IPC	In Process Control
SOP	Standard Operating Procedure
BP 88	British Pharmacopoeia
DAB	Deutsches Arzneibuch
BAN	British approved name
USAN	United States approved name
CA-Number	Chemical Abstract Number

US$	United States Dollar
USD	United States Dollar
ATS	Austrian Schilling (1 US$ = 11.5 ATS)
LIT	Italian Lira
DEM	German Mark
HFL	Dutch Gulden
SFR	Swiss Franken
FFR	French Franc

GBP	British Pound

Organizations

UNIDO	United Nations Industrial Development Organization
EEC	European Economic Community
WHO	World Health Organization
FDA	Food & Drug Administration (USA)

SHIFT WORK AND WORKING DAYS PER YEAR

Working days per year:	300 days
Working hours per day:	8 hours
Three shifts per day	3 shifts/day
Shifts per year	900 shifts/year

Effective working days per year: 205 days

Results in 4.4 workers per shift working place

Estimation of effective working days per year:

Days per year	365
Deduct Sundays	52
Deduct Saturdays	52
Training Leave	10
Holidays	12
Vacations	20
Average sick-leave	14

Abbreviations:

GR	Graduated
UN	Undergraduated
HS	High School
sk	skilled
se	semi-skilled
un	unskilled

Working-time model for operating division

In most of the Units the day-turn will be used for the major activities - e.g. starting of a production process, getting materials form the warehouses, depositing. Time during night will be used for keeping reactions running and certain types of maintenance work. Therefore it is intended to have less workers in the night-shift and more in the day-turn.

morning-shift	6 am to 2 pm	*ca* 500 workers
evening-shift	2 pm to 10 pm	*ca* 500 workers
night-shift	10 pm to 6 pm	*ca* 250 workers

SYMBOLS USED IN THE PROCESS FLOW - CHARTS

Fig. 8: Symbols used in the process flow - charts