



TOGETHER
for a sustainable future

OCCASION

This publication has been made available to the public on the occasion of the 50th anniversary of the United Nations Industrial Development Organisation.



TOGETHER
for a sustainable future

DISCLAIMER

This document has been produced without formal United Nations editing. The designations employed and the presentation of the material in this document do not imply the expression of any opinion whatsoever on the part of the Secretariat of the United Nations Industrial Development Organization (UNIDO) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries, or its economic system or degree of development. Designations such as “developed”, “industrialized” and “developing” are intended for statistical convenience and do not necessarily express a judgment about the stage reached by a particular country or area in the development process. Mention of firm names or commercial products does not constitute an endorsement by UNIDO.

FAIR USE POLICY

Any part of this publication may be quoted and referenced for educational and research purposes without additional permission from UNIDO. However, those who make use of quoting and referencing this publication are requested to follow the Fair Use Policy of giving due credit to UNIDO.

CONTACT

Please contact publications@unido.org for further information concerning UNIDO publications.

For more information about UNIDO, please visit us at www.unido.org



17090-E

Distr.
LIMITED
ID/WG.466/7(SPEC.)
22 April 1987
ENGLISH

United Nations Industrial Development Organization

Third Consultation on the
Pharmaceutical Industry

Madrid, Spain, 5-9 October 1987

MULTIPURPOSE PILOT PLANT
FOR THE PRODUCTION OF PHARMACEUTICAL CHEMICALS*

Background Paper

Prepared by

the UNIDO Secretariat

* This document has been reproduced without formal editing.

CONTENTS

	<u>Page</u>
I. Introduction	iv
1. UNIDO'S ACTIVITIES IN THE FIELD OF PRODUCTION OF PHARMACEUTICAL CHEMICALS - THE GENESIS OF THE MULTIPURPOSE PLANT CONCEPT	1
2. CHARACTERISTIC FEATURES OF A MULTI- PURPOSE PILOT PLANT	2
2.1 PRODUCTION RANGE AND FLEXIBILITY	2
2.2 CAPACITY AND SCALING-UP OF PRODUCTION	2
2.3 ADJUSTED SET OF TECHNOLOGIES	3
2.4 TRAINING FACILITIES	3
2.5 DEVELOPMENT ACTIVITIES WITH SCALING UP AND BACKWARD INTEGRATION OF TECHNOLOGIES ..	3
2.6 LINKAGE TO DOMESTIC FORMULATION INDUSTRY AND RESEARCH INSTITUTIONS	4
3. PURPOSE AND OBJECTIVES OF A MULTI-PURPOSE PLANT	5
3.1 ESTABLISHING PHARMACEUTICAL CHEMICAL SYNTHESIS INDUSTRY AND NEW PRODUCTION CAPACITIES FOR PHARMACEUTICAL CHEMICALS	5
3.2 CREATING TECHNOLOGICAL CAPABILITY FOR R&D IN PHARMACEUTICALS	5
3.3 A POLICY TOOL FOR DEVELOPMENT OF INDIGENOUS PHARMACEUTICAL INDUSTRY WITH FLEXIBILITY IN PRODUCTION CAPABILITIES	5
4. PREREQUISITES FOR SETTING UP A MULTI PURPOSE PILOT PLANT	6
4.1 TECHNOLOGICAL LEVEL OF THE COUNTRY'S PHARMACEUTICAL INDUSTRY	6
4.2 PRODUCTS AND TECHNOLOGIES	6
4.2.1 CRITERIA FOR CHOICE OF PRODUCTS	6

	<u>Page</u>
4.2.2 CRITERIA FOR CHOICE OF PRODUCTION TECHNOLOGIES	7
4.3 STARTING MATERIALS	8
4.4.1 BASIC CHEMICALS	3
4.4.2 INTERMEDIATES	8
4.4.3 NATURAL PRODUCTS	9
4.4 PLANT SITE AND PRODUCTION FACILITIES	9
4.5 EQUIPMENT	10
4.5.1 EQUIPMENT FOR SYNTHESIS	10
4.5.2 EQUIPMENT FOR DEVELOPMENT	10
4.5.3 ANALYTICAL EQUIPMENT	10
4.6 ENVIRONMENTAL ASPECTS	10
4.7 SKILLED MANPOWER	11
4.8 MANAGEMENT AND PRODUCTION ORGANIZATION	11
4.9 EXECUTING PARTY	12
4.10 INVESTMENT REQUIREMENTS	12
5. UNIDO'S EXPERIENCE AND ROLE IN MULTI-PURPOSE PLANT PROJECTS	13
5.1 THE CUBA PROJECT	13
5.2 THE IRAN PROJECT	14
5.3 ROLE IN MULTI PURPOSE PLANT PROJECTS	14

INTRODUCTION

The past two Consultations on the Pharmaceutical Industry have recognized that developing countries experience difficulties in obtaining suitable technology based on intermediates and/or raw materials directly available in the world market or locally produced for the manufacture of most of the pharmaceutical chemicals.

UNIDO has assisted those countries in the technology transfer through negotiations and technical assistance programme. In the experience of UNIDO the deployment of multipurpose plants for the production of pharmaceutical chemicals serves as a good strategy to enter flexible manufacture of a number of pharmaceutical chemicals, most important for creating facilities, transfer of technology, research and development, training of manpower and creation of production capacities.

Based on the above facts and arguments, an attempt has been made to present in this paper the concept of multipurpose plant for the production of pharmaceutical chemicals.

THE MULTIPURPOSE PLANT CONCEPT *

1. UNIDO'S ACTIVITIES IN THE FIELD OF PRODUCTION OF PHARMACEUTICAL CHEMICALS - THE GENESIS OF THE MULTIPURPOSE PLANT CONCEPT

Health care is an important factor in human societies. In this respect the pharmaceutical industry is one of the most sensitive areas among industrial activities.

UNIDO has endeavoured to assist developing countries in setting up and improving their pharmaceutical industries.

There are three sources of production of drugs, namely extraction and isolation of compounds from naturally occurring animal and vegetable sources, by biotechnological methods such as fermentation and by chemical synthesis. Pharmaceutical industry constitutes the following main subsectors: pharmaceutical formulation, pharmaceutical chemicals and biologicals. These subsectors are correlated to each other and it can be said that presently in most of the countries at least one or more of these activities are carried out.

A more detailed analysis concerning developing countries reveals that formulation industry has been successfully established in many countries whereas pharmaceutical chemicals industry is developed in a limited number of them.

The situation is rather unsatisfactory because formulation industry is dependent on the availability of pharmaceutical chemicals. At present in several countries complete dependence on imports of pharmaceutical chemicals has restricted the implementation of the national health care programmes.

One of the main reasons for the present situation of limited development of pharmaceutical chemicals industry in developing countries is certainly the dynamic character of the pharmaceutical industry itself with its rapid development and change of products. Other reasons include a limited market size, which does not justify entering into pharmaceutical chemicals production by setting up a single line plant, furthermore lack of local know how, infrastructure and finally investment aspects.

UNIDO initiated its activities in this specific field several years ago. At the Second Consultation on the Pharmaceutical Industry in Budapest (1983) the idea of starting local manufacture of pharmaceutical chemicals in a "multi purpose plant" has been discussed by UNIDO. In the meantime, apart from policy guidance approach, UNIDO has started project activities which have resulted in the erection of one multi purpose pilot plant in Cuba, which is now in operation. Another multi purpose plant project in Iran is under construction. Furthermore, preparatory studies relating to this topic are being carried out in several other countries which include Brazil, Algeria, Venezuela, Zimbabwe and Arab region.

* Contribution of Dr. C. Noe, Technical University Vienna, Austria, towards the preparation of this document is acknowledged.

Based on its experience UNIDO worked out a comprehensive multi purpose plant concept, and presents this applied concept in this paper. The strategy of this concept is to use a flexible and versatile approach in order to match the dynamic features of the pharmaceutical industry. The multipurpose plant would help both in development of R&D and production capabilities taking into account the market size, technology and intermediates availability problems and manpower development.

2. CHARACTERISTIC FEATURES OF A MULTI PURPOSE PILOT PLANT

Although the term "multi purpose plant" itself is well known, there are divergent opinions as to what it should mean. The multi purpose plant as presented by UNIDO is not just meant to be a production unit for pharmaceutical chemicals, but it represents rather a concept exhibiting some typical features for establishing local production of pharmaceutical chemicals in developing countries which plan to enter manufacture of active ingredients. The main characteristic features of the multi purpose plant concept are presented in this chapter.

2.1 PRODUCTION RANGE AND FLEXIBILITY

As the name indicates, the most obvious feature of a multi purpose plant is the fact that not one but several pharmaceutical chemicals can be manufactured by chemical synthesis in one plant.

The equipment of a multi purpose plant is chosen in a manner which allows production of a variety of different synthetic pharmaceutical chemicals without requiring additional investment for effecting a change in product mix.

The lay-out will allow a variety of unit operations and unit reactions to be carried out thus creating technological know-how in the country.

(In a standard case pharmaceuticals which are obtained by fermentation processes are not included in the multi purpose plant product range.)

2.2 CAPACITY AND SCALING-UP OF PRODUCTION

There are variations from product to product as regard the scale in which industrial production of pharmaceutical chemicals is economical. The scale in which production takes place in a multi purpose plant is however more or less determined by the requirements of the multi purpose plant concept, such as flexible lay out or scaling up facilities.

Compared to a single line plant the capacity of a multi purpose plant to produce one specific pharmaceutical chemical is rather limited. With respect to the fact that not one but several products are to be manufactured in the same plant, a production scale which is too big would create too many additional requirements concerning lay out, equipment and production organization.

For this reason it is foreseen to limit the maximum reactor size to 1 m^3 in the case of smaller multi purpose plants primarily geared to research and development activities and to a size of 3 m^3 for bigger multi purpose plants having more emphasis on production activities.

This limited scale of production is to be considered, when choice of products and technologies for their production is made.

2.3 ADJUSTED SET OF TECHNOLOGIES

A set of technologies for the production of pharmaceutical chemicals according to the requirements of the recipient country is available together with the installation facilities for a multi purpose plant. Choice of technologies and plant lay out are adjusted to each other to secure envisaged production output from the beginning of operation of the plant.

Technologies for the production of other pharmaceutical chemicals which may be either purchased or developed in the plant could be introduced.

2.4 TRAINING FACILITIES

The multi purpose plant concept with its mix of production and R&D activities provides an ideal opportunity for local training in the field of pharmaceutical chemical synthesis. Besides the training facilities in production, the plant serves to impart training in the areas of plant operation, administration, quality control and quality assurance.

2.5 DEVELOPMENT ACTIVITIES WITH SCALING UP AND BACKWARD INTEGRATION OF TECHNOLOGIES

It is often assumed that research in the field of pharmaceutical chemistry is consistent with development of new pharmaceutical chemicals. As a matter of fact this type of research is not foreseen within the multi purpose plant concept.

So far as a multi purpose plant is concerned, the development activities mean first of all developing know-how and capability to carry out synthesis reactions on an industrial scale. These activities will first of all result in achieving the capability to scale up reaction processes from laboratory scale to the production scale or at least to a scale which allows transfer to single-line production.

Therefore, the lay out of the equipment of a multi purpose plant will comprise units in a suitable series of different production scales to allow scaling-up of reactions to required levels. This is most important with respect to transfer and development of technologies.

Adaption of production technologies according to the specific situation in the country concerning raw materials, other chemicals, climate or other factors constitute another important factor in R&D in a multi purpose plant.

Within this aspect the so-called backward integration of technologies is of great importance, which means that approved production processes which start from a later step intermediate are expanded in such a way that production starts from a more basic raw material.

The impact of R&D activities may be summarized as follows:

Direct R&D activities: Process development for large scale production
Process improvement in connection with trouble shooting
Scaling up
Backward integration of technologies

Indirect R&D activities: Development of new technologies for known pharmaceutical chemicals
 Development of new pharmaceutical chemicals
 Synthetic transformation of selected natural products to be used as pharmaceutical chemicals
 Unpredictable impact

It may be expected that a well planned multi purpose plant project will successfully fulfill the direct R&D activities. The degree to which it will promote indirect R&D activities will certainly depend on the scientific and industrial standard of the recipient country.

2.6 LINEAGE TO DOMESTIC FORMULATION INDUSTRY AND RESEARCH INSTITUTIONS

A multi purpose plant should not only be linked to domestic formulation or to pharmaceutical research institutions, but it should in fact aim to be in itself the link between domestic formulation industry and research institutions.

In contrast to the situation concerning production of pharmaceutical chemicals, well developed formulation industry may invariably be found in developing countries. It is obvious that the linkage to such domestic formulation industry is of great importance, because the output of the multi purpose plant will be the raw materials for formulation industry. Therefore, it seems advisable to integrate formulation industry at an early stage into the planning of the product mix to be manufactured in the multi purpose plant. An even more promising approach is to set up the multi purpose plant within the frame of an existing pharmaceutical formulation organization.

As a matter of fact, basic pharmaceutical research is carried out in some developing countries. This research is mainly at university level and it usually aims at development of new chemical compounds with potential therapeutic activity. It is carried out on a small scale and frequently there is no direct connection with local pharmaceutical industry to make use of the results.

Considering these facts it may be stated that both formulation industry and basic pharmaceutical research are often reasonably established in some developing countries, sometimes both of a high standard. Unfortunately there is a gap between these two activities in the field of pharmaceutical chemicals. There are no facilities to carry out local production of pharmaceutical chemicals and as a consequence, there are no related industrial research and development activities. Existing local institutions which carry out basic pharmaceutical research and which might easily assist in such activities are not even in a position to transfer the results of their own research work to local industry.

It is exactly the multi purpose pilot plant concept that helps to fill this gap and to give the existing R&D potential an active part in industrial activities in the field of pharmaceuticals. Scaling up facilities found there are the connection between industrial production and basic pharmaceutical research and give an impetus for cooperation to both side.

3. PURPOSE AND OBJECTIVES OF A MULTI PURPOSE PLANT

3.1 ESTABLISHING PHARMACEUTICAL CHEMICAL SYNTHESIS INDUSTRY AND NEW PRODUCTION CAPACITIES FOR PHARMACEUTICAL CHEMICALS

Transfer of technology is a sensitive issue. The main aim of the multi purpose plant is to establish facilities for the chemical synthesis of pharmaceutical chemicals on a broad and flexible basis and providing a set of technologies together with R&D and training opportunities.

The obvious objective of the multi purpose plant is to create production capacity for manufacture of pharmaceutical chemicals. One of the features of the lay out of a multi purpose plant is to provide additional capacity for small scale production and R&D as to be a first step for production of pharmaceutical chemicals in the recipient country. Therefore, the plant itself will constitute a useful unit at any of the stages of development of local production of pharmaceutical chemicals.

3.2 CREATING TECHNOLOGICAL CAPABILITY FOR R&D IN PHARMACEUTICALS

One characteristic feature of the multi purpose plant is that a set of technologies is transferred which allows versatile operation of the plant from the beginning of its operation. Speaking of know-how there is in the first instance the know-how which is transferred together with these production technologies. Second, there is the know-how potential resulting from experience in the operation of a multi purpose plant. The fact that the plant has also a considerable R&D and training function will help in creation of this new type of know-how on a broad basis.

3.3 A POLICY TOOL FOR DEVELOPMENT OF INDIGENOUS PHARMACEUTICAL INDUSTRY WITH FLEXIBILITY IN PRODUCTION CAPABILITIES

Considering all the factors mentioned earlier, it can be seen that the multi purpose plant concept is an efficient policy tool for development of the pharmaceutical industry of the recipient country.

Any new production activity will influence the existing market to a certain degree. Sometimes the market forces may render new production uneconomic e.g. in cases of the reaction of the market being local decrease in product price or increase in raw material price. The advantage of the multi purpose plant compared to a single line plant is that it is a flexible production facility so that the plant is not dependent on only one product and not even totally dependent on the set of products transferred at the beginning of plant operation. It may be expected that after some time of operation a broad production range can be established in the plant, so that quick response can be given to reactions and requirements of the local market.

In many countries the health care system is an area of first priority with a lot of activities carried out in the government sector. Purchase of pharmaceuticals is often problematic, e.g. in countries with scarce foreign exchange resources. Local production facilities will reduce dependence on imports, by replacing international purchase by local production or at least by providing opportunity to buy an intermediate or a raw material instead of the finished pharmaceutical product whenever economically advisable.

4. PREREQUISITES FOR SETTING UP A MULTI PURPOSE PILOT PLANT

4.1 TECHNOLOGICAL LEVEL OF THE COUNTRY'S PHARMACEUTICAL INDUSTRY

The multi purpose plant concept concerns the basic branch of pharmaceutical industry which provides raw materials for the formulation industry. Therefore it seems advisable to initiate such activities only in countries with an existing formulation industry, which will use the products to be manufactured in the multi purpose plant.

Economic operation of any plant will depend on a sufficient size or the potential market. In the case of small countries it seems advisable to start multi purpose plant projects rather on a regional basis jointly with neighbouring countries than try them on a too limited scale. In any case an approach seems plausible in which the capacity of the first multi purpose plant to be set up in a country is not supposed to satisfy a major percentage of the total local demand of pharmaceutical chemicals. The capacity should be sufficient to allow economic operation of the plant, but the main aim of the multi purpose plant concept is to be a first step into a new area of pharmaceutical industry and to create know-how, R&D and training facilities as well as other follow up activities such as further plants for production of pharmaceutical chemicals.

Starting materials for production of pharmaceutical chemicals may be intermediates, basic chemicals or natural products. While as a rule existing local manufacture of intermediates may not be expected in developing countries, basic chemicals and natural products to be used as starting materials may be frequently available. Such a situation might create a welcome connection between local chemical and pharmaceutical industries. A careful analysis of the specific local situation in this respect seems advisable to make use of local sources to as great extent as possible.

4.2 PRODUCTS AND TECHNOLOGIES

4.2.1 CRITERIA FOR CHOICE OF PRODUCTS

The choice of products as well as production technologies to be applied in a multi purpose plant depend to a large degree upon several factors which in several cases are correlated to each other. The following are the main criteria which should be applied in drawing up a list of products to be manufactured:

- Requirement of the country's health system
- Requirements of the formulation industry
- Economy of production
- Availability of technologies
- Suitability of technologies for the multi purpose plant
- Patent situation
- "Technology transfer"-value of the technology

The most important factor for choice of a product is the factor of requirement of the country's health system. As a rule the assessment of this requirement will result in a first and probably too long a list of products to be manufactured in the multi purpose plant.

Further evaluation should start from this list and reduce it according to the parameters given above.

Some specific parameters specifically applicable to the multi purpose plant concept are the following:

A large number of pharmaceutical chemicals obtained from fermentation processes are of importance for the health systems of all countries and will appear in each list of products based on the requirement of the country. Even so it seems advisable not to consider such products but to restrict the use of the multi purpose plant to products of chemical synthesis, which do not require fermentation steps. Although there are chemical reaction steps in the synthesis of most of these products which might be carried out in a multi purpose plant in principle, a dependence on the fermentation intermediate will remain and future backward integration to basic starting materials cannot be carried out.

Another group of pharmaceutical chemicals not to be considered for manufacture in a multi purpose plant are low price products, such as acetylsalicylic acid or paracetamol etc. These products are usually manufactured in bulk quantities in large scale industrial processes. With such compounds it might happen that the raw material price for small scale production could have about the same price as the end product. Therefore it seems difficult to justify the transfer of such compounds within the first set of technologies in a multi purpose plant, unless it is required by a specific situation.

A third parameter of elimination which is typical for the multi purpose plant is the factor of low "technology transfer" value. The production of such compounds would not create significant know-how with respect of unit operations or unit reactions. With respect to the fact that some of such simple production technologies might be economically feasible, however such low value technologies might be considered as interesting targets for first attempts towards local know-how development.

4.2.2 CRITERIA FOR CHOICE OF PRODUCTION TECHNOLOGIES

The availability of a technology is prerequisite for a product to be chosen for transfer. Usually more than one production technology exists for the manufacture of a pharmaceutical chemical. Also degree of sophistication

and the value of such technologies show considerable variations. The choice of products and technologies for a multi purpose plant depends on several factors, some typical are the following:

- As a rule lay out of a multi purpose plant does not allow continuous processes, such as frequently used in single line production. Batch technologies are therefore applied.
- The typical multi purpose plant technology can be carried out in standardized equipment, which can also be used for manufacture of other compounds.
- The requirement of a multi purpose plant is not one but several technologies. As a rule it is not economical to finance a set of expensive technologies, also because of the limited production capacity of such a plant.
- The specific patent situation of the recipient country has to be considered.
- Concerning the cost of technologies there can be great variations due to the degree of sophistication of the specific technology and the market price and lifetime of the product. At present it may be estimated that an illustrative minimum price for a typical multi purpose plant technology would be about US\$ 30,000.- to 40,000.- per pharmaceutical chemical.

4.3 STARTING MATERIALS

4.4.1 BASIC CHEMICALS

Of course local availability of basic chemicals is an important factor in planning a multi purpose plant and the choice of its product mix, not only because the choice of production technologies and the economic evaluation of the project will be influenced by this situation, but also backward integration and the easy flow of material inputs will help to sustain an uninterrupted production cycle. On the other hand, a complete lack of local production of basic chemicals would render the setting up and operation of a multi purpose plant more difficult.

4.4.2 INTERMEDIATES

Synthesis of pharmaceutical chemicals frequently does not start only from basic chemicals but makes use of intermediates. These intermediates are available from the international market, same way as the pharmaceutical chemicals. As a rule it may not be expected that there is local production of specific intermediates for pharmaceutical chemicals in the recipient country.

One objective of the multi purpose plant concept is to create flexibility in local production capacities to meet a specific and well defined demand when it arises. Thus the question might arise whether it might be useful to replace an imported end product by an imported intermediate. The answer is positive, because first of all lower costs required for intermediate

imports will help to save foreign exchange. Secondly, international market provides more flexibility in acquiring alternative sources of most intermediate products which could also serve for alternative users. Thirdly an impact is given to back integration of technologies and the intermediates themselves might become interesting products for the local chemical industry to produce.

4.4.3 NATURAL PRODUCTS

In many developing countries, especially in tropical countries, a great variety of medicinal plants to be used for the production of pharmaceutical chemicals may be found. Frequently there are also some research and other activities in this field, as a rule however there are no facilities to carry out synthesis of larger quantities of pharmaceutical chemicals starting from isolated natural products. While plant extraction itself does not constitute a standard part of the multi purpose plant concept, chemical transformation of natural products certainly does fit into the concept. The multi purpose plant is in a position to enable local production of such compounds on a commercial scale. It may however not be expected that activities connected with local natural products might constitute a significant part of production in the first phase of a multi purpose plant project.

4.4 PLANT SITE AND PRODUCTION FACILITIES

Although a typical multi purpose plant carries out pilot plant and R&D activities, its appearance and prerequisites are clearly those of an industrial plant.

There is significant requirement for space (production facilities, laboratories, administration, storage, tank farm, effluent treatment, energy (electricity, steam) and water (process water, cooling water).

With regard to the production activities involving chemicals environmental measures (effluent, exhaust air and chemical waste treatment) will be of great importance.

Although in every case multi purpose plant will have a layout that will meet the requirements of the specific project, however, some indicative figures of the space requirements of a typical multi purpose plant are given:

Total reactor capacity:	30 m ³
Plant area:	10.000 m ²
Production area:	1.000 m ² (height of production area 9-10 m to allow required service floors)
Storage area:	600 m ²
Underground storage:	1.000 m ²
Service facilities:	500 m ² (administration, laboratories)
Utilities and effluent treatment:	500 m ²

Concerning the plant site it is recommendable to make the multi purpose plant adjacent to an existing formulation unit wherever feasible. In this case it may be expected that some of the infrastructural and administrative

requirements are already given in advance, so that investment may be saved. The erection of the multi purpose plant might provide a good opportunity to upgrade the standard of the existing plant infrastructure.

With respect to planning and erecting the plant, setting up the multi purpose plant as a separate unit in an industrial area would even be a preferable approach.

4.5 EQUIPMENT

The equipment of a multi purpose plant is determined by several characteristic features. Firstly, scaling up facilities must be given that means that the layout of the plant has to allow reactions in a series of different scales. Secondly, a great variety of unit operations and unit reactions should be feasible in the plant that means that careful choice has to be made with respect to versatility of equipment. Finally, research and development activities require reserve capacities and sufficient analytical equipment.

4.5.1 EQUIPMENT FOR SYNTHESIS

The typical layout of the equipment for chemical synthesis in a multi purpose plant will comprise reactors from a size of 100 L to a maximum size of about 3000 L (considering the required glass equipment the scale of synthesis will even start from 1 L). Appropriate choice has to be made concerning the material of the equipment. Steel and enamelled steel reactors are equally required to allow a broad range of reaction conditions. The rest of the equipment - above all: centrifuges, dryers, filters, pumps, condensers, tanks, vessels, receivers and balances - will be determined by the choice of processes and reactors.

4.5.2 EQUIPMENT FOR DEVELOPMENT

Equipment for research and development in a multi purpose plant to a great extent means just leaving reserve capacity in the normal equipment to carry out scaling up of new technologies and improving existing technologies. Beyond that, equipment for research and development also means that there has to be small scale glass equipment to carry out reactions in a small inexpensive scale either for trouble shooting or for technology development. Since investment required for equipment in this scale is rather limited special care should be taken with regard to obtaining a great versatility of unit operations.

4.5.3 ANALYTICAL EQUIPMENT

It has to be borne in mind that analytical instrumentation needed for quality control and technology development in a multi purpose plant requires considerable investment. Again careful choice has to be made to meet the high standard quality requirements of pharmaceutical industry.

4.6 ENVIRONMENTAL ASPECTS

Environmental aspects are of increasing importance in chemical and pharmaceutical industries. At times, Government regulations exist or may be

expected in the near future which will have a significant influence as well on plant site as on lay out and investment.

So far as environmental aspects of installation are concerned there are three main areas of concern: exhaust air, effluents and chemical waste.

As far as exhaust air is concerned installation of scrubbers connected to an efficient exhaust system will be required.

To deal with chemical wastes, installation of an incinerator is recommended or it is a must, if there is no general system for removal of chemical waste in the country.

Concerning effluent treatment it is without any doubt necessary to erect an effluent treatment plant. This plant will certainly require the greatest part of the funds used for environment control measures.

The extent to which investment for environmental purposes is required will to a great degree depend on Government regulations on this aspect. Therefore careful observation of all pertaining legislature is required at an early planning stage.

4.7 SKILLED MANPOWER

To operate a multi purpose plant there is a considerable requirement of skilled personnel for the following functions: plant director, production manager, finance and administration manager, R&D and quality control manager, mechanical engineer, production supervisors, technicians for R&D and quality control, maintenance technician, electrical technician, chemical operators, laboratory operators, maintenance personnel etc.

Availability of personnel having the required training will certainly depend on the general educational standard of the recipient country on the one hand and on the presence of related industries, such as formulation or chemical industries, on the other hand.

Together with planning of a multi purpose plant required training of personnel should start. It cannot be expected that all of this training can be carried out locally. Therefore arrangements should be made to carry out training abroad, if possible in the facilities of the technology suppliers or industrial units of similar nature.

Considering the variety of functions to be carried out, the multi purpose plant itself at a later stage may become an almost perfect versatile training facility to serve the requirements of local pharmaceutical and chemical industries.

4.8 MANAGEMENT AND PRODUCTION ORGANIZATION

It is obvious that a multi purpose plant such as any manufacturing unit requires a management and production organization. It has however to be pointed out that in the case of a multi purpose plant with its multiple production lines and changing production programme rather sophisticated production organization and flexible management are required.

Although the multi purpose plant may be considered to be only a pilot plant, there will be considerable costs for running the plant, which will require a corresponding production output. All aspects of production, such as financial planning, production planning, costing and pricing should be carried out, as if the unit were a purely manufacturing plant. Adequate quality assurance facilities should also be planned. It is recommendable to set up a production organization based on the use of computers, which has been proven to be a successful approach in small scale manufacturing units.

4.9 EXECUTING PARTY

It is obvious that the question of "who is going to make it" is of importance in every project. Depending on the country invariably three different situations are found concerning pharmaceutical industries: government sector pharmaceutical industry, private sector pharmaceutical industry and a mixed system in which both types are found. Concerning the executing party for a multi purpose plant it has to be borne in mind that it should be closely related to the local formulation industry. Therefore it seems as a rule advisable that the executing party to set up the multi purpose plant should be within the same sector as the formulation industry which will use its products.

As a matter of fact direct participation of the local formulation industry in such a multi purpose plant project is a desirable approach.

4.10 INVESTMENT REQUIREMENTS

It is not easy to give a definite answer concerning investment required to set up a multi purpose plant. An estimated amount of US\$ 1.000.000 (1 million) might be considered as a minimum investment to have available all the typical features of a multi purpose plant at a sufficient scale and to be in a position to reach the objectives of the concept. An optimum size plant with respect to the requirements of the presented concept having relatively larger production output would however require an estimated investment of about US\$ 5.000.000 (5 million).

The return on investment is the most important parameter in any production unit. Speaking of the multi purpose plant concept it is therefore very important to be clear from the beginning that the typical multi purpose plant is not merely a production unit but carries several additional functions, such as R&D or training activities. The extent of dedication of the plant to R&D activities on the one hand and production activities on the other hand should be clear already in the planning phase. While doing this the following limitations should be borne in mind:

R&D in a production by synthesis process as present in a multi purpose plant is very expensive. It is one of the basic ideas behind this. However, some minimum production activities are required to finance R&D. Therefore a pure pilot plant character without any economic production activity seems difficult to establish and an expensive operation in such a big scale.

On the other hand, there might be a position to use the multi purpose plant only as a production unit. Although such an approach would be feasible

in principle, the multi purpose plant should in this case however not be seen simplified as a magic box that manufactures economically any choice of pharmaceutical chemicals in one plant instead of only one product as in a single line plant. A required minimum scale of economic production will exclude manufacture of many pharmaceutical chemicals in this case.

The multi purpose plant as presented in the UNIDO concept exhibits a layout to enable both versatile production and R&D. In the UNIDO approach flexible layout of the plant will reduce the economic risk of the decision to manufacture one specific product. A decision to set up a merely production multi purpose plant would require a different approach to the project and a different layout of the plant.

Bearing these factors in mind it becomes clear why an early decision is already required at the stage of planning and in defining the partial dedication of the plant for both R&D and production activities.

5. UNIDO'S EXPERIENCE IN MULTI PURPOSE PLANT PROJECTS

Apart from studies carried out by UNIDO to support the multi purpose plant concept, there are two projects which have proceeded further. One of these projects has resulted already in an operating plant in Cuba and the other project is under construction in Iran. These projects reflect the outcome of both South-South and North-South cooperation.

5.1 THE CUBA PROJECT

Multipurpose pilot plant project has been implemented by UNIDO in Cuba. The pilot plant was commissioned and trial operations commenced in 1980. The contractor for the project is an Indian firm, which supplied equipment for process, utilities and laboratory. The contractor also supplied the know-how and technologies for 15 pharmaceutical chemicals. Based on the basic engineering prepared by the contractor, the Cuban counterpart worked out the detailed engineering. Two groups of Cuban technical personnel were trained in India in the fields of production, quality control, maintenance and engineering design. The technological processes for the production of 15 pharmaceutical chemicals were demonstrated to them with stipulated efficiencies and quality during their training. Installation materials were procured from India. Equipment such as storage tanks were fabricated in Cuba. Civil works and the installation of equipment were carried out by the Cuban counterpart based on the design approved by the contractor. Final installation, testing and commissioning were done under the supervision of the contractor.

The pilot plant has an annual production capacity of 242 tons of 15 pharmaceutical chemicals conforming to pharmacopoeial standards.

The pilot plant will facilitate the development and introduction of new technological processes and production techniques which will promote the growth and development of the indigenous pharmaceutical industry. The project is an example of South-South cooperation.

The products will be utilized by the Cuban pharmaceutical formulation industry. There is a potential for exports as well. The pilot plant provides facilities for training of personnel from the sub-region.

5.2 THE IRAN PROJECT

Another multi purpose pilot project is being implemented by UNIDO in the Islamic Republic of Iran. The contractor for this project is a Hungarian firm with subcontractors from Austrian firms which supply equipment for process, utilities and laboratory. The contractor also provides know-how and technologies for 13 pharmaceutical chemicals, basic and detailed engineering for process and utilities. Based on the layout prepared by the contractor, the Iranian counterpart will prepare detailed civil engineering drawings and will carry out civil works. Iranian technical personnel will be trained in Hungary and Austria in the fields of production, quality control, maintenance, engineering design and research and development. The pilot plant has an annual production capacity of 70 tons for 13 pharmaceutical chemicals of pharmacopoeial standard. A special feature of the pilot plant is the reserve capacity provided for Research and Development work. The pilot plant is located adjacent to a pharmaceutical formulation plant, which will use the products.

The pilot plant will facilitate the development and introduction of new technologies and production techniques, which will promote the growth and development of Iranian pharmaceutical industry which is well established in the formulation area.

This pilot plant is a typical case of South-North cooperation.

5.3 ROLE IN MULTI PURPOSE PLANT PROJECTS

In the present report an attempt was made to present the UNIDO multi purpose plant concept with its characteristic features, its purpose and objectives and the requirements to establish such a plant. It may be seen from this paper that a project to set up such a multi purpose pilot plant is a multi facet project containing many specific factors, which have to be considered, and requiring a high degree of coordination of activities.

UNIDO has expertise in this field regarding all aspects of such a project from basic considerations to operation of the plant. UNIDO is thus in a position to provide information and technical assistance in assessment, planning, setting up and running of such a plant and also ready to take part in coordination of such projects and participate in long term technical assistance. It is UNIDO's mandate to assist developing countries in taking this important step towards the development of their pharmaceutical industry with the view of improving the R&D as well as local production capabilities in this field.