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15036

Distr.
RESTRICTED

UNIDO/IO/R.183
16 September 1985

ENGLISH

UNITED NATIONS
INDUSTRIAL DEVELOPMENT ORGANIZATION

ESTABLISHMENT OF A DEVELOPMENT PLAN FOR THE PHARMACEUTICAL INDUSTRY

UC/ALG/85/062

ALGERIA

Technical report: Research and development of pharmaceuticals*

Prepared for the Government of the Democratic and People's Republic of Algeria by the United Nations Industrial Development Organization

Based on the work of Mr. Nitya Anand, expert in pharmaceutical research and development

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V.85-30907 (EX)

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I. SUMMARY

1. It was not possible to obtain a clear picture of the drug policy and development plans of the government for the pharmaceutical sector. The government should set up a Pharmaceutical Policy and Planning Committee to formulate national policies and plans dealing with all aspects of the pharmaceutical sector, and define short and long-term goals. The R & D institutions and production plants would then be in a better position to draw up their development plans within this framework.

2. The existing R & D facilities in Algeria are most inadequate to make any meaningful impact on the development and growth of the pharmaceutical industry to achieve self-reliance and reduce dependence on imports.

3. The scope and functions of the Laboratory for Development and Research should be expanded substantially to form a composite Research and Development Centre for Pharmaceuticals and Drugs which should include in its activities: (i) development of the whole range of formulations used in Algeria; (ii) development of technology for production of bulk drugs by chemical synthesis and isolation from medicinal plants; (iii) production of some high cost-low volume drugs involving one or two step processes; (iv) provide technical assistance to production plants; and (v) provide post-graduate training facilities leading to a Ph.D. degree for graduate students of Universities.

4. The Medea plant is a very large and modern complex for antibiotics production. A plant of this dimension and complexity is bound to face many problems which could be solved only if backed by a high level of research and development. As the Medea Plant is expected to start production soon, it is suggested that the R & D laboratories should be established at the plant site and should be operationalised with the highest priority. It should ultimately be expanded to a composite Biotechnology Research and Development Centre. Its main functions should be: (i) maintenance and improvement of strains; (ii) pilot plant production of antibiotics before their large scale production in the plant; (iii) laboratory scale work on synthesis of penicillins and cephalosporins and isolation of antibiotics; (iv) establish

capability in genetic engineering.

5. In the Medea plant it may be difficult to control the simultaneous production of all the antibiotics planned for production. It is suggested that while pilot plant experiments are being carried out with different antibiotics, production of only one antibiotic should be taken up at a time and all the problems connected with its production solved. The knowledge and experience gained and the confidence developed would be useful in controlling the production of the second antibiotics and so on.

6. Serious attention needs to be given to post-graduate teaching and research in the University for Scientific Research & Technology (USRT), the Institute of Pharmacy and other centres of higher learning to build up a cadre of well-trained scientists and technologists to staff R & D laboratories and production plants and to create a research culture and atmosphere.

7. A Research Advisory Committee should be formed for LDR consisting of representatives of LDR, production plants, Ministry of Health and marketing organisation to advise in formulation of its R & D plans.

8. It was observed that some useful research on pharmaceutical products is being carried out in some academic Laboratories such as the Department of Analytical Chemistry of the University of Algiers and Department of Mineral Chemistry and Pharmacology of the Institute of Pharmacy. It is suggested that a National Pharmaceutical Research Committee should be established to coordinate and support this research and to arrange for training of personnel within the country.

II. PHARMACEUTICAL POLICY AND PLANNING

The policies and plans of the pharmaceutical sector have many dimensions, including social, economic and strategic and the programmes of research and development institutions and of production plants have to respond to these policies. During visits to various institutions and discussions with different groups it was not possible to obtain any document or a clear exposition of government policies for this sector, on which plans for research, development and production could be based. It is necessary that the government should set up a Pharmaceutical Policy and Planning Committee to formulate national policy and plans dealing with all aspects of the pharmaceutical sector, with clearly defined objectives and short and long-term goals. This would facilitate drawing up of meaningful research and development plans.

III. RESEARCH AND DEVELOPMENT FOR PHARMACEUTICALS

The total consumption of pharmaceuticals in Algeria is estimated at US$ 220 million, of which less than 12% is formulated in the country. All the bulk drugs and most of the excipients are imported. The range of formulations produced in the country is rather small (about 70 out of a total of about 1800 in the market[1] and does not include formulations of many essential drugs such as: antiamoebics, antimalarials, antihelminths, cardiovasculars and antidiarrhoeals (except sulfaguanidine).

The pharmaceutical industry is a very highly research-based industry, with a high rate of obsolescence of both products and technologies. New innovations are well guarded by secrecy and patent coverage. Therefore, to build up self-reliance in this area and to gradually reduce dependence on imports, whether of technology or of products, it is necessary to establish a strong R & D capability. This capability would also be required for assimilation and upgrading of technology which may have to be imported.

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1) MEMENTO, Produits Pharmaceutiques, Pharmacie Central Algerienne, 1985

IV. EXISTING RESEARCH AND DEVELOPMENT

A. Laboratory for Development and Research (LDR)

This is at present the only development laboratory of SAIOAL. It was established in 1975 for development of formulations and for providing technical assistance to production units. It has four departments: Quality Control, Formulations, Pharmacotoxicology, Library & Medical Information. It is directed by Dr. Bensilman Mansouri, who is a Ph.D. in Pharmacology (Annex 1, Organisation structure). The total staff of the laboratory including the Director is 21; PH.D. 6; M.Sc. 2; Technicians 4; Helpers 9. An assessment of the laboratory is given below:-

Department of Quality Control

This laboratory carries out quality control and analytical tests of formulations developed by LDR as also of some which are referred to it by production plants. It has most of the essential modern equipment such as IR and UV spectrophotometers, GC and HPLC apparatus, atomic absorption photometer, Karl Fischer apparatus, polarimeter and the usual routine quality control equipment. This certainly was the best equipped and well-maintained laboratory of LDR, except for the fact that all the sophisticated instruments were kept in the main laboratory and exposed to laboratory fumes. A separate air-conditioned room should be provided for keeping the equipment and a fume hood for the atomic absorption photometer. The department has two Ph.Ds and one M.Sc. who are well trained in analytical chemistry and appeared to be carrying out their work quite efficiently.

Formulation Department

This department, though most important for fulfilling the objectives of LDR, was perhaps the most poorly equipped both in staff and instruments. It has only conventional equipment, mostly rather old, for development of tablets, syrups, creams and suppositories. The staff consists of one scientist and one technician. It has no facility for development of sustained release

tablets, capsules, parenterals, sterile powders or aerosols or for upscaling of formulations developed by it. The record-keeping system was not efficient. We were shown only one proper Feasibility Report, although technologies of 13 formulations developed since the inception of LDR (Annex 2) had been passed on to industry; six of these are being produced in the production plants. This department needs substantial expansion in terms of staff, equipment and space.

Pharmacotoxicology

This department is headed by the Director of the laboratory. It carries out acute toxicity studies (LD_{50}), a few pharmacological tests (anti-inflammatory and analgesic activity, rotarod test) and some haematological and biochemical tests. It is not carrying out any bioavailability studies, and also does not have any facility for histopathological work necessary for sub-acute and chronic toxicity studies. The animal facility is rather small; there are only rats and mice, which are kept under rather poor hygienic conditions.

Library and Medical Information

The Library is housed in one small room, and has practically no modern books, encyclopaedias and very few journals; it does not even have the latest pharmacopoeias. It has no space or arrangement for readers to sit and consult books and journals.

Critique

The laboratory has a good nucleus for formulation research, with a well-motivated staff and good analytical facilities. However, it is too small in size to be able to do any meaningful research and to have substantial impact on the industry; in fact, it is below the minimal viable size. The formulation department has only one scientist, which is not a satisfactory situation. It has no formal arrangement for consultation with industry. There is no arrangement for testing formulations for

bioavailability and for sub-acute toxicity which are essential for determining the quality and safety of new formulations. The department is not equipped to develop capsules, parenterals, sterile ointments, sterile powders and aerosols, which form a large proportion of modern pharmaceutical formulations. Thus substantial restructuring and expansion would be required if it has to serve even as a formulation development laboratory for the pharmaceutical industry. A plan for expansion of this laboratory is given later in this report.

B. Medea Plant

This is a large modern complex for production of antibiotics, consisting of nine fermenters, each of 130 m^2 capacity. When in full operation, which is expected in 1987, this plant is planned to produce annually: penicillin G 135 t; penn. V 29 t; tetracyclin 49 t; oxytetracyclin 15.4 t; streptomycin 33 t; semi-synthetic penicillins 61 t; and their formulations.

An antibiotic production plant of this size, and in the logistics of the surroundings in which it is being built, is bound to face a multiplicity of problems initially. It is surprising, and even a cause of worry, that an R&D laboratory for this plant has not yet been operationalised. A plant of this complexity, with a capital investment of US$ 220 million, should have been preceded by an R & D laboratory with a suitable sized pilot plant for trial production to control the quality of media and other inputs. An R & D laboratory for this plant should have at least 1% of the expected turnover as its annual developmental research expenditure.

1. Strategy for antibiotics production

The production of such a large number of antibiotics simultaneously will pose a multiplicity of technical and logistic problems initially. It is suggested that the production of different antibiotics may be planned one after the other, rather than simultaneously. When the production problems of one antibiotics are solved, it would provide useful experience to tackle the problems of the second, and in this way confidence would be created.

It was understood that the microbial strains and technology were supplied to the Medea plant in 1977; since then great advances have taken place and it is not unlikely that the technology supplied may have become outdated. The strain may have to be improved and technology modified. This would require much R & D work. For example, it was reported during discussion at the Medea Plant that the strain for production of penicillin G supplied by Squibb was at present giving a yield of 20,000 U, while the best world yield is about 60,000 U. This shows the difficulties of the situation. However, the yields reported for tetracyclin seemed to be in order.

The production of ampicillin from 6-APA was also discussed in detail. The method and the yield at each step seemed satisfactory. The scientists concerned appeared to have knowledge and awareness of the problems and confidence to solve them.

Apropos the above analysis, it is suggested that to begin with the Medea Plant should concentrate on the production of tetracyclins and ampicillin (from imported 6-APA), while only pilot plant trials of other antibiotics are undertaken. After the planned production of these two antibiotics is achieved, the production of other antibiotics could be started.

It was not possible to get full details of the original contract entered into between Medea Plant and the suppliers of technology. It would be useful to enter into a contract with a firm having experience in the production of antibiotics planned for production in this plant, for a period of two years from the beginning of production, with guarantee of yields. If this firm could be from a developing country it may be better, because their experience would be more relevant to the conditions prevailing in Algeria.

2. Genetic Engineering Group

The rapid advances in gene cloning and genetic engineering are going to have an important impact on antibiotics production techniques, and the

microbial strains and the technology of antibiotic production may be greatly modified. It would be useful to create a group for genetic engineering in this proposed Biotechnology R & D Centre to keep abreast of these advances and to develop capability to apply the new knowledge to modify production technology when required.

3. Vaccines and Sera production

It was gathered that plans have been finalised for a new plant for production of some conventional vaccines and sera, under the Ministry of Health. New developments in antigen characterisation and production and monospecific antibody production by gene cloning and hybridoma techniques are going to change completely the nature of these vaccines and sera in the near future. A few of these new vaccines have already become available. These developments should be taken into consideration in the production of vaccines and sera. As the R & D Centre at Medea would have a group for genetic engineering and pilot plant fermenters, it is suggested that contacts and consultation between the R & D Centre at Medea and Pasteur Institute (the latter would be involved in the production of vaccines and sera in the new plant) should be established and the possibility explored for production of these newer vaccines by genetic engineering right from the beginning.

V. AVAILABILITY OF SCIENTISTS AND TECHNOLOGISTS

A. Present situation

The shortage of well qualified and trained scientists and technologists is going to pose a very serious problem for the R & D laboratories and production plants. Further, no high level research can be carried out in isolation by the R & D laboratories unless the general level of education and scientific research in the universities and institutes of higher learning is kept high and a culture of research and academic excellence is built. The seriousness of the situation can be gauged from the facts that:

* production of semi-synthetic penicillins requires a high level of knowledge of organic synthetic reactions and experimental skills, while it was gathered that the Department of Organic Chemistry of USRT has very meagre facilities for practical work in organic synthesis and practically no post-graduate training programme;

* development of new formulations demands a high level of experimental training in modern galenical forms, while the Department of Galenicals in the Institute of Pharmacy has no laboratory course work for students.

* antibiotic production requires a high level of knowledge of industrial and applied microbiology, and it was gathered that these facilities are not available in any of the universities in Algeria.

So the question arises, where will the trained scientists and technologists come from? While some scientists can be sent abroad for training to meet the immediate requirements, this can not be done on a continuing basis. Immediate attention needs to be given to scientific and technical manpower development in the universities, polytechnics and Institute of Pharmacy. The level of teaching and laboratory work should be greatly raised and liberal funds provided for laboratory equipment, library, teaching aids and research projects. It would be difficult to suggest specific steps

that should be taken in this matter, but the problem is serious enough to warrant the establishment of a Commission for Higher Education to look into this problem and give recommendations.

Some of the specialisations in which well qualified scientists and technologists are required for R & D laboratories of the pharmaceutical industry are given below:

* Analytical Chemistry
* Organic Chemistry
* Chemical Engineering
* Pharmaceutical Sciences
* Pharmacognosy
* Biochemical Engineering
* Industrial Microbiology
* Pharmacology
* Toxicology/Pathology
* Microbiology

B. Central Laboratory for Instrumentation

Research in experimental sciences has become very much dependent on sophisticated instruments. And if research of good quality has to be carried out, ready access to these instruments should be provided. Modern sophisticated instruments are, however, very expensive and not every laboratory can afford to buy them and, what is even more important, maintain them in working condition. Some of the laboratories that we visited were handicapped in their research by the lack of these instruments. A few laboratories had very good equipment but a number of these were lying idle due to lack of repair facilities, and were dependent on the visits of engineers of the suppliers, which were often very delayed. It is, therefore, suggested that:

(a) A Central Instrumentation Laboratory be established to provide elemental analysis, spectroscopic analysis and other instrumentation analysis facilities on token payment. The laboratory could be situated in the USRT or in a R & D laboratory which could provide the necessary space and back-up facilities. The staff, equipment needed and its cost are given in Annex 3.

(b) Similarly, a Central Laboratory for Repair and Maintenance of Instruments should be established to help the different laboratories in the

repair and maintenance of costly equipment and instruments. The laboratory should have glassware repair and fabrication capability also. The staff and equipment required for this laboratory are given in Annex 4.

C. Research coordination

During our visits to the University and Institute of Pharmacy, it was observed that some of the laboratories were carrying out interesting research on problems relating to pharmaceuticals, and had good laboratory facilities and equipment. The Department of Analytical Chemistry of the University of Algiers had excellent analytical facilities, particularly for GLC, HPLC, GC-MS. This laboratory was involved in research projects pertaining to estimation of drugs in biological fluids and bioavailability studies. Similarly, the Department of Mineral Chemistry of the Institute of Pharmacy was studying polymorphism of drugs by X-ray crystallography and DTA and was very well equipped. It would be useful to coordinate the work of these laboratories with the R & D laboratories to make optimal use of facilities for training and for developmental projects. It is suggested that a National Pharmaceutical Research Committee be established having representatives of academic institutions, R & D laboratories and government science and planning departments to plan and coordinate the research and development of activities of various laboratories.

VI. PHARMACEUTICAL PRODUCTION

A. Existing production units

Pharmaceuticals production in Algeria is carried in three units: El Harrach, Pharmal and Biotic, and is confined to tablets, capsules, creams and suppositories, except for two injectables produced by Biotic. The units have conventional machinery, some of which is quite large and automated, though in some cases rather old. Of the three units, Pharmal plant is the most modern and automated. The three units together make sixty-four formulations of their own and six under licence from multinational companies. The total number of formulations in the market is about 1800 and the government has plans to cut it down to 800. The plants run in one shift only.

The general level of cleanliness and upkeep of the plants was much below that expected in pharmaceutical plants, and the observance of good manufacturing practices requires to be much improved. The plant at El Harrach is situated next to a main road and is exposed to dust. Some of the windows of the rooms of the plant opening on to the road were kept open and some panes were broken. There was spillage on the floor of the preparation rooms, in some cases the floors were muddy and had pot-holes. Most of the rooms were left open and exposed to the outside. The staff of the production department did not seem to have any idea of GMP and were found smoking or drinking tea inside the plant rooms. The rooms were full of packages of raw material; sometimes gunny bags containing sugar and kept on the floors. Storage space was very inadequate and crates of finished materials were lying piled up in the open exposed to the sun and rain.

Each unit had its own quality control laboratory, but none had an R & D laboratory. The quality control laboratories were reasonably well equipped, with small libraries of their own having some pharmacopoeias and some books on analysis, but in some cases they were rather old. Each quality control laboratory should have latest editions of B.P., U.S.P., Martindale's E.P. and European Pharmacopoeias in their libraries. The laboratories had well

trained staff who seemed to be doing their work efficiently. The analytical facilities in general seemed satisfactory, although somewhat inadequate to be able to analyse fully one sample of each batch, which is essential according to standard quality assurance practices.

As stated earlier, the volume of production of these plants accounts for only about 10% of the consumption of pharmaceuticals in Algeria; the number of products is only 70 out of a total of 1800 pharmaceutical formulations in the market and formulations of a number of essential groups of drugs are not produced, (loc. cit.). Although the objective of SAIDAL, as conveyed to us in a discussion with the DG of SAIDAL, was to substantially increase the production within the country and to gradually decrease the dependence on imports, none of the units seemed to have a clear perspective production plan or a policy on which expansion plans could be based. It could be on the basis of Volume of import and/or the essentiality of drugs for the large majority of the population. A suggested list of formulations which should be produced in the country is given in Annex 8. There would be no need to build new plants. At present if only the existing plants could be run in two shifts, production could be almost doubled. The upkeep of the present plants would need to be greatly improved and GMP strictly observed.

B. Central Control Laboratory

This laboratory is under the Ministry of Health and is situated in the premises of the Biotic Plant. We were informed that this laboratory has a total staff of about 30, and has conventional equipment for analysis of conventional formulations. It has no facility for bioavailability studies, for toxicity studies, for microbiological assays and sterility testing and limited capacity for pyrogen testing. The size of the laboratory is much too small, and the equipment very inadequate to be able to analyse and monitor the quality of all the raw materials, bulk drugs and formulations which are imported into the country, leave aside analysing some selected test samples of formulations produced in the country.

In addition to its role as a quality control laboratory, a drug control organisation has also to ensure the observance of good manufacturing practices so as to create confidence in the public in local products.

To fulfil the above functions, the laboratory would need to be greatly expanded, modern equipment added and additional facilities created for toxicity testing, bioavailability studies, sterility testing and microbiological assays. It may be necessary to shift the laboratory to a new site and to construct a well-designed modern building.

VII. PROPOSED R & D PLAN

A. Research and Development Centre for Pharmaceuticals

The existing research and development laboratory should be enlarged to convert it into a composite R & D centre for technology development for the pharmaceutical industry, both in respect of formulations and bulk drugs. This centre should be planned in its entirety though the establishment may be phased over a period of 5 years. It should have a modular structure so that the step by step increase in size does not create construction problems. The scope and function of different departments/sections of the Centre are given below and its organisation chart and space requirements in Annex 5. This Centre would require a built-up space of about 3000 sq. m. It is suggested that the El Harrach Pharmaceuticals Plant may be moved to a new site and the building thus vacated remodelled to house this Centre. Alternatively, LDR should move to a new site and this Centre established as a modern well-designed laboratory.

The Centre could also be affiliated to different universities in Algeria for Ph.D. and provide the necessary research facilities for students for this purpose.

1) Library and Documentation

* multidisciplinary holdings of major reference books, encyclopaedias and journals with back volumes (Annex 6 for proposed list);
* documentation and dissemination of information
* facility for translation from English to French and French to English.

2) Chemical Technology Department

For development of technology for bulk drugs by:

* chemical synthesis
* extraction of medicinal plants
* scale-up studies and production of a few drugs of high cost/low volume (Annex 7 for illustrative list).

3) Product Specification and Quality Control Department

* For development of product specifications of all products imported into the country and issuing these for circulation
* Quality control
* Implementation of quality assurance and GMP.

4) Galenicals Department

* For development of a whole range of formulations:
  - tablets and capsules
  - syrups and suspensions
  - creams and sterile ointments
  - parenterals and sterile powders
  - aerosols
  - scale-up studies

5) Analytical Department

- elemental analysis
- IR, UV, GLC & HPLC
- polarimetry

6) Biology Department

* microbiological assays and microbiological contamination tests
* sterility and pyrogen testing
* acute and sub-acute toxicity studies
* bioavailability studies on animals and humans
* animal house for mice, rats, rabbits and dogs.

7) Pilot Plant

* for carrying out synthetic reactions up to 50-100 kg scale
* for extraction of plant materials up to 100 litres capacity
* production of drugs involving one or two step reactions.

8) Project Evaluation and Industrial Liaison Department

* monitor projects
* prepare feasibility reports
* liaise with industry

A list of major chemical technology and pilot plant equipment that this Centre would need is given in Annex 9.

B. Biotechnology Research & Development Centre

During our discussions in Algiers or our visit to the Medea Plant it was not possible to get a clear picture of the R & D plans as a back-up for the antibiotics production in the plant. Some laboratories have been built for the purpose of strain maintenance but they were still not occupied or equipped. Some experimental fermenters have been installed on the floors of the main plants. This, however, appeared a very disjointed effort and not much emphasis or attention was being given to R & D. All this scattered activity should be brought under one roof and a composite Biotechnology Research & Development Centre should be established to carry out coordinated developmental work on antibiotics planned for production in the plant and for other fermentation products. The scope and functions of this Centre are given below and Annex 10 gives the proposed organisation chart and space required. A list of major equipment required for this Centre is given in Annex 11. Some of this equipment may be lying in different laboratories of the plant or may have been ordered. All these should be brought under one scientific chief in one building.

1) Microbiology Department

* strain maintenance and improvement by classical methods and genetic manipulation
* selection of strains for new fermentation processes
* improvements of the processes for import substitution, process economy
* development of new techniques like immobilisation of whole cells or enzymes.

2) Pilot Plant

* establishing the technology and pilot plant trials of antibiotics planned for production in fermenters of 10-5000 litres; standardising raw material requirements
* upscaling of processes developed in laboratory
* development of new fermentation processes such as for glucose from starch
* solving plant problems
* training of personnel for the plant.

3) Chemical Synthesis Department

* improvements of chemical processes associated with the main product streams for yields, efficiency and economy
* synthesis of semi-synthetic penicillins
* synthesis of cephalosporins
* chemical modification of known and new antibiotics.

4) Genetic Engineering

* to establish capability for gene cloning, hybridoma development and genetic manipulation.

5) Library and Documentation

Holding of all major books, reviews and journals on antibiotics and related subjects.

VIII. PHASING OF THE R & D PROGRAMME

A. 1986-87

1. Laboratory for Research and Development

	Sc. staff	Space
* Expansion of the Formulation Department to include a section on parenterals	3	75 sq. m.
* Creation of facility in Pharmacology Department for: - bioavailability studies - sub-acute toxicity studies - microbiological and sterility testing	2	75 sq. m.
* Provision of an air-conditioned room for instruments in the Analytical Dept.	-	50 sq. m.
* Establishment of an Animal House with proper hygiene conditions; appointment of a Veterinarian as its Incharge, addition of rabbits to the colony.	1	50 sq. m.
* Expansion of Library substantially (Annex 6 gives list of books and journals).	1	100 sq. m.

2. Establishment of a Research Advisory Committee for the LDR, Production units, Marketing Dept., and MOH to identify products for R & D and production.

3. Biotechnology R & D Centre

Consolidation of all the R & D units at Medea plant in one building and setting up of a composite Biotechnology R & D Centre with the scope and function described above and recruitment of additional staff. This Centre should start functioning immediately.

4. Deputation for study visit/training

	No.	Period
* Director LDR to visit R & D Centres abroad	-	3 months
* Pharmacologist, for bioavailability studies	1	6 months
* Toxicologist	1	12 months
* Microbiologists, for strain selection and improvement	2	24 months
* Pharmacist, for production of parenterals	1	12 months
* Pharmacist for sustained release preparations	1	12 months
* Biochemical Engineer/Industrial Microbiologist for pilot plant operation	2	24 months

Suggested institutions for training

* Sarabhai Research Centre, Vadodara, India
* Indian Drugs & Pharmaceuticals Ltd., Research Centre, Hyderabad, India
* Antibiotics Research Centre, Rishikesh, India
* Central Drug Research Institute, Lucknow, India.

5. Finalise plans for setting up of R & D Centre for Pharmaceuticals.

B. 1988-90

1. The expansion of LDR should have been completed to form a composite R & D Centre for Pharmaceuticals & Drugs with the scope and functions given earlier. All the staff should be in position and equipment installed during this period, except for the pilot plant. A suggested list of formulations and drugs for technology development during the period 1986-90 is given in Annexes 7 & 8; some low volume products could be manufactured in this Centre.

2. Expansion of the R & D activity at the Biotechnology R & D Centre by creating a group for genetic engineering.

3. Deputation of the following staff for training:

	No.	Period
* Chemical engineers for pilot plant operation	1	6 months
* Pharmacist for production of aerosols	1	12 months
* Veterinarian for Animal House maintenance	1	6 months
* Pharmacists, for production of sustained release forms	1	6 months
* Microbiologists, for genetic engineering techniques	2	24 months
* Biochemical engineers for pilot plant for fermentation	2	12 months
* Organic chemists for chemical synthesis	2	24 months

C. 1991-2000

If the plans suggested above are implemented, the scenario during this period would be of greatly increased industrial production of pharmaceuticals, beginning with production of bulk drugs, increased interaction between R & D institutions and industry and this will set in motion a self-generating system.

The rest of the staff suggested in the organisation charts should be recruited and, depending on the state of developments, some more scientists could be sent for training, senior scientists for 8-12 week visits and junior scientists for 6-12 months. Provision should be made for about 80 man-months.

During this period steps should be taken to invite an expert in pilot plant operations for 6 months for the R & D Centre for Pharmaceuticals.

ANNEX I

Existing Organisation and Staff of Laboratory for Development and Research

Director : Dr. B. Mansouri, Ph.D. (Pharmacology)

Department of Quality Control:

Head : Mme Iguertsira Leila, Ph.D. (Organic Chemistry)
Dr. Ferkioui, Ph.D. (Analytical Chemistry)
Dr. Achab Said, Ph.D. (Organic Chemistry)
Chemist - 1 M.Sc. (Chemistry)
Technician - 1
Helpers - 3

Department of Formulations:

Head : Dr. Ouali, Ph.D. (Pharmaceutical Sciences)
Technician - 1
Helpers - 2

Department of Pharmacology and Toxicology:

Head : Dr. Bakhti, Ph.D. (Pharmacology)
Pharmacist - 1
Technician - 1
Helpers - 3

Library and Medical Documentation

Librarian : - 1 M.Sc. (Documentation)
Helper : - 1

ANNEX II

Medicaments for which technology has been developed by LDR

CREAMS	-	AUREOMYCINE	
	-	NYSTATINE	
	-	MYCOCIDE	
	-	NEOMYCINE	
	-	NEOMYCINE HYDROCORTISONE	
	-	NEOMYCINE TRIAMCINOLONE	
SUPPOSITORIES	-	ASPIRINE PHENOBARBITAL	BB
	-	" "	ENF
	-	" "	AD
	-	GLYCERINE	BB
	-	"	ENF
	-	"	AD
	-	THEOPHYLLINE	ENF
	-	"	AD
	-	THEOPHYLLINE BUTOBARBITAL	BB
	-	" "	ENF
	-	" "	AD
SYRUPS	-	SULFOLYPTOL	
	-	PROMETHAZINE	
	-	PECTORAL	BB
	-	"	ENF
	-	"	AD

ANNEX III

I. Instruments for Central Laboratory for Instrumentation

		No.	US$ (x 10^3)
1.	High Resolution Mass Spectrometer with chemical ionisation, field desorption capability	1	400
2.	100 & 200 Mz NMR Spectrometer with liquid helium liquification and liquid nitrogen plants. Antianalyser for (C,H,N,O)	2	500
3.	Elemental Autoanalyser for (C,H,N,O)	2	20
4.	High performance liquid chromatographs (analytical and preparative)	2	100
5.	Gas liquid Chromatograph	1	40
6.	Fourier IR Spectrophotometer	1	150
7.	Infra Cord	1	20
8.	Recording UV Spectrophotometer	2	30
9.	ORD/CD Spectrometer	1	30
10.	Spectropolarimeter	1	30
11.	Spectrophotoflorimeter	1	150
12.	Miscellaneous		100

II. Staff

1.	Ph.D. (Physics, Electronics or Analytical Chemistry)	2
2.	M.Sc. (Physics, Electronics or Analytical Chemistry)	8
3.	B.Sc. (Physics & Chemistry or Electronics)	10
4.	Helpers	4

ANNEX IV

I. Major Equipment:	Estimated price US$
1. Oscilloscope, portable 100 MHz, 2 mV/div with integrated counter/timer/DMM Tektronix Model 2236	10,000
2. Tektronix TM 500 modular instruments a) TM 515 power module main frame b) DC 503 A universal counter/timer c) FG 504, 40 MHz function generator d) SC 504, 80 MHz oscilloscope with two probes type P 6062 B e) TG 501 TimeMark Generator	10,000
3. Data analyzer - Tektronix Model 308 ADDRESS: TEKTRONIX INC. P.O. Box 1700, Beaverton, Oregon 97075, USA	5,000
4. Multimeter - Digital, hand held $4\frac{1}{2}$ digit with integrated frequency counter ADDRESS: John Fluke Mfg. Co. Inc. P.O. Box C 9090 Evareatt, WA, 98206, USA	1,000
5. Multimeter, Digital, hand held HIL 2102 or equivalent ADDRESS: Hindustan Instruments Limited, 603, Vishal Bhawan, 95 Nehru Place, New Delhi - 110019.	200
6. Multimeter - Analog AVO Model 8 X Mark III or equivalent ADDRESS: Motwani Private Limited, 127, Mahatma Gandi Marg, P.B. No. 1312, Bombay - 400023.	200

7.	Digital LCR meter HP 4261 A or equivalent	2,500
8.	Logic comparator with reference boards, HP 10529 A or equivalent	)
9.	Logic probe HP 545 or equivalent	) 1,000
10.	Current tracer HP 547 A or equivalent	)
11.	Logic pulser HP 546 A or equivalent	)
	ADDRESS: for 7, 8, 9, 10, 11 Hewlett Packard Company, 3495 Deer Creek Road, Palo Alto, CA 94304, USA.	
12.	Mini lathe with accessories	2,000
13.	Miscellaneous tools and spare parts	5,000

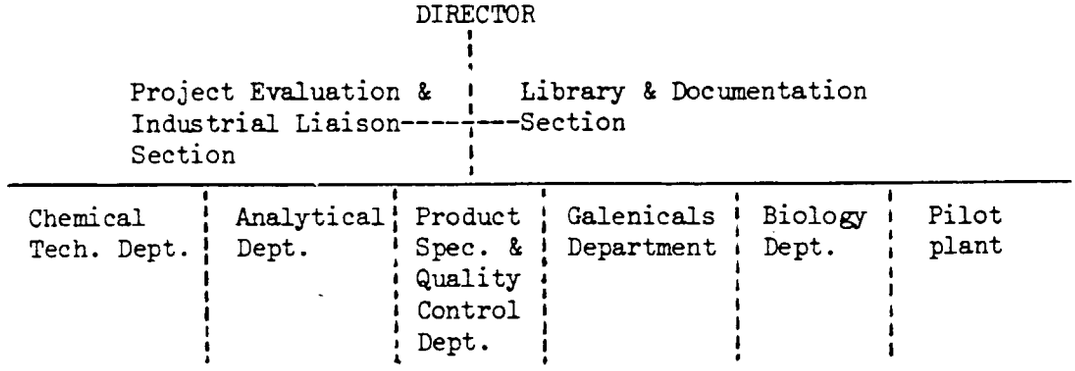
II. Staff:

1.	Ph.D. (Physics, Electronics)	...	1
2.	M.Sc. (Physics, Electronics)	...	4
3.	M.Sc.B.Tech. (Electrical)	...	2
4.	B.Sc.	...	4
5.	Glass technologist	...	2
6.	Helpers	...	4

Annex V

Research and Development Centre for Pharmaceuticals

Organisation Chart



Directors Office - 100 sq. m.

a. Library & Documentation:

Staff	No.	Area
M.Sc./B.Sc. (Lib. Science)	2	300 sq. m.
M.Sc. (Org. Chemistry)	1	
M. Pharm.	1	
English translator	1	
Helpers	4	

b. Chemical Technology Dept.:

Ph.D. (Organic Chemistry)	2	500 sq. m.
M.Sc. (Organic Chemistry)	4	
Technician	4	
Helpers	2	

c. Analytical Department:

Ph.D. (Anal. Chemistry)	1	300 sq. m.
M.Sc. (Anal. Chemistry)	2	
Technician	4	
Helpers	2	

d. Product Specification & Quality Control Dept.:

Ph.D. (Pharm.)	2	300 sq. m.
M. Pharm.	2	
Technician	2	
Helpers	2	

e. Galenicals Department:

Ph.D. (Pharm.)	2	500 sq. m.
M. Pharm.	2	
Technician	4	
Helpers	2	

f. Biology Department:

Ph.D. (Pharmacology)	1	1000 sq. m. (including Animal House)
Ph.D. (Toxicology) or D.M.	1	
M.Sc. (Microbiology)	2	
M. Pharm. or M.Sc. (Biochemistry)	2	
Veterinarian	1	
Technician	4	
Helpers	4	

g. Pilot Plant:

Chem. Engineer	2	500 sq. m.
M.Sc. (Organic Chemistry)	2	
Technician	4	
Helpers	2	

h. Project Evaluation & Industrial Liaison Section:

M.Sc. (Organic Chemistry) or M. Pharm.	2	50 sq. m.
Technician	1	

i. Stores:

Store Officer	1	150 sq. m.
Purchase Officer	1	
Technician	2	
Helpers	2	

This building would have a built area of about 4000 sq. m. and at the present cost of construction in India*, it would cost about $ 700,000.00. The total staff envisaged for 1991 would be about:

Scientist	40
Technician	25
Helpers	20
Store keeper	2

A list of the chemical technology and pilot plant equipment is given in Annex 9.

* Construction cost is to be corrected on the basis of existing rates in Algeria.

ANNEX VI

Periodicals, dictionaries, encyclopaedias and handbooks - A select list

PART A

PERIODICALS:

1. Accounts of Chemical Research
2. Acta Pharmaceutica Jugoslavica
3. Acta Pharmaceutica Suecica
4. Advances in Chemistry Series
5. Advances in Immunology
6. Advances in Pharmacology and Chemotherapy
7. American Journal of Medical Technology
8. American Journal of Pharmaceutical Education
9. American Journal of Public Health
10. American Laboratory
11. American Pharmacy
12. American Scientist
13. Analytical Chemistry
14. Analytica Chimica Acta
15. Analyst
16. Annals of Biomedical Engineering
17. Annales D Immunologie
18. Annales Pharmaceutiques Francaises
19. Antibiotica et Chemotherapia
20. Antimicrobial Agents and Chemotherapy
21. Archiv Der Pharmazie
22. Arzneimittel-Forschung/Drug Research
23. Bulletin of the World Health Organization
24. Biotechnology
25. Biotechnology and Bioengineering
26. Biotechnology Letters
27. British Medical Journal
28. Canadian Journal of Pharmaceutical Sciences
29. Chemical & Engineering News
30. Chemistry and Industry

31. Chemical and Pharmaceutical Bulletin
32. Chemtech
33. Drug Development and Industrial Pharmacy
34. Drugs of the Future
35. Drugs of Today
36. Drugs
37. Drugs made in Germany
38. Immunobiology
39. Immunochemistry
40. Immunological Reviews
41. Industrial and Engineering Chemistry
42. Industrial and Engineering Chemistry Analytical Edition
43. International Journal of Pharmaceutics
44. Journal of the American Chemical Society
45. Journal of the American Medical Technologists
46. Journal of the American Pharmaceutical Association
47. Journal of Antibiotics
48. Journal of Antimicrobial Chemotherapy
49. Journal of the Association of Official Analytical Chemists
50. Journal of the Chemical Society
51. Journal of the Chemical Society-Chemical Communications
52. Journal of the Chemical Technology and Biotechnology
53. Journal of Fermentation Technology
54. Journal of Medicinal Chemistry
55. Journal of Pharmacy and Pharmacology
56. Journal of Pharmaceutical Sciences
57. Methods of Biochemical Analysis
58. Nature
59. New Scientist
60. Pharmaceutica Acta Helvetiae
61. Pharmazeutische Industrie
62. Pharmacy International
63. Pharmazeutische Praxis
64. Pharmaceutische Weekbladscientific Edition
65. Pharmaceutical J.
66. Pharmazie

67. Revue de Medecine
68. Science
69. Tetrahedron
70. Tetrahedron Letters
71. Trends in Pharmacological Sciences
72. W.H.O. Technical Report Series
73. Zeitschrft für Chemie
74. Biological Abstracts
75. Chemical Abstracts

PART B

DICTIONARIES, ENCYCLOPAEDIAS AND HANDBOOKS:

1. Chambers Dictionary of Science and Technology, ed. by T.C. Collocott & A.B. Dobson, 1982, Published by W & R Chambers, Edinburgh.

2. Concise Science Dictionary, Published by Oxford University Press.

3. Dictionary of Scientific and Technical Terms, ed. by D.N. Lapedes, Published by McGraw-Hill, New York.

4. Encyclopaedia of Chemistry, Published by Romhold, New York.

5. Handbook of Chemistry and Physics, Ed. C.D. Hodgman & others, Published by C.D. Hodgman, R.C. Westard, C.M. Selby Cleve & Rev. Ed. by C.J. Kingzett.

6. Chemical Encyclopaedia ed. by R.K. Strong, Published by Bailbere, London.

7. World Chemical Directory, Atlas Publishing Company, 425 West 25th Street, New York.

8. Comprehensive Organic Chemistry: The Synthesis and Reactions of Organic Compounds, Ed. by J.F. Stoddart, Published by Pergamon, Oxford.

9. Nomenclature of Organic Compounds, ed. by J.H. Fletcher, O.C. Dermer & R.B. Fox, Published by American Chemical Society, Washington.

10. Dictionary of Organic Compounds (5th Ed.), Published by Chapman & Hall, 733 Third Avenue, New York.

11. Elsevier's Encyclopaedia of Organic Chemistry, ed. by F. Radt with the assistance of A. Georg and Dora Stern. Published by Elsevier, Amsterdam.

12. Abbreviations in Medicine by E.B. Steen, Published by Bailliere Tindall, London.

13. Merck Index of Chemicals and Drugs: An Encyclopaedia of Chemicals, Drugs and Biologicals, Published by Merck & Co. Inc. Rahway, N.J., U.S.A.

14. Medical and Pharmaceutical Dictionary English-German by Werner E. Bunjes, Published by Georg Thieme, Stuttgart.

15. Dictionary of Drugs by Fisher & G.A. Christie, Published by Granada, London.

16. Pharmacology and Chemical Syncnyms - A Colletion of Names of Drugs and Other Compounds, Excerpta Medica Foundation - Amsterdam.

17. Pharmacology and Chemical Synonyms & Compiled E.E.J. Marler (7th ed.) Excerpta Medica - Amsterdam.

18. American Drug Index by C.O. Wilson, Published by Lippincott.

19. Handbook of Materia Medica Toxicology & Pharmacology by F.R. Davison, Published by Mosby, St. Louis.

20. Side effects of Drugs - Annuals, Excerpta Medica Foundation, Amsterdam.

21. Drug of Choice by Medell, Walter, Published by CV.

22. Progress in Drug Research by Ernst Jucker (No. I-XXV), C.V. Mosby Company, St. Louis.

23. Current Drug Handbook by M.W. Falcone & H.R. Patterson & E.A. Gustafson, Published by W.B. Saunders.

24. Annual Drug Data Report, ed. by J.R. Prous & D. Vedrilla, D. Ledicer.

25. Chronicles of Drug Discovery by J.S. Bindra & D. Ledicer.

26. Non-Prescription Drugs by A.L. Wanpo, Published by Blackwell, Oxford.

27. Basic Principles for Pharmacopeial Tests, by Reiness, F. (1956), Published by Ejnar Munkasgaard, Copenhagen.

28. Pharmaceutical Arithmetic by M.L. Schroff & G.P. Srivastava (1937), Published by B.H.U., Varanasi, India.

29. Pharmaceutical Formulas by P. McEwan (1944), Published by Chemist & Druggist, London.

30. USAN and USP Dictionary of Drug Names by Mary C. Griffiths, Published by U.S. Pharmacopoeial Convention Inc., Rockville.

31. Instrumental Data for Drug Analysis (1982) by T. Mills & others, Published by Elsevier, New York.

32. Profiles in Drugs Syntheses, Vol. I & V (1982), V.N. Gogte, Published by Gokul Pub., Bombay, India.

33. Handbook of Antibiotics Compounds by Jamos, Berdy (Vol. 1-7), Published by C.R.C. Press.

34. Encyclopaedia of Antibiotics by J.S. Glasby, Published by Wiley, London.

35. Medicine and Poisons Guide (1980) by C.E. Hay & M.E. Pearce, Published by Pharmaceutical Press, UK.

36. Practice of Pharmacy by J.P. Remington, 1947, 1961, in 1980, Remington's Pharmaceutical Sciences, Published by Mack Pub. Co., Easton.

37. Pharmaceutical Sciences, Remington's, Published by Mack Pub. Company, Easton, Pennsylvania.

38. Current Therapy, H.F. Conn (All Annual Volumes), Published by Saunders, Philadelphia.

39. Modern Drug Encyclopaedia and Therapeutic Index (17th Ed. 1981) by A.J. Lewis, Published by Yorke Medical Books, 666 Fifth Avenue, New York.

40. American Medical Association - Drug Evaluation (latest 4th edition), Published by American Medical Association, Columbus, Chicago.

41. Encyclopaedia of Chemical Processing and Design by J.J. McKetta & W.A. Commingham, Published by Marcel Dekker, New York.

42. Encyclopaedia of Chemical Technology (3rd Ed.), Kirk-Othmer, Vol. 1-22 (1978-1983), Published by Wiley-Interscience, New York.

43. Pharmacopoeia Francaise

44. Pharmacopoeia of United States

45. British Pharmacopoeia

46. International Pharmacopoeia, W.H.O., Geneva

47. Pharmacopoeia of Japan (Japanese Ministry of Health and Welfare)

48. United States Dispensatory (Lippincott)

49. National Formulary of U.S.

50. British Pharmaceutical Codex

51. Organic Chemistry of Drug Synthesis, Vol. 1 & 2, by D. Lednicer & L.A. Mitscher.

ANNEX VII

List of bulk drugs for technology development/production in R & D Centre

1. p-Acetamol (from phenol or nitrobenzene)
2. Benzyl benzoate
3. Chloramphenicol (from l-base)
4. Ethambutol (from D-aminobutanol)
5. Metronidazole/tinidazol (from 2-methyl-4(5) nitro-imidazole)
6. Methyl salicylate
7. Piperazine citrate
8. Propranol
9. Phthaloyl/Succinoyl phthalazole
10. Sorbitrate

ANNEX VIII

Formulations for which technology should be developed

1. Aluminium hydroxide gel
2. Aspirin + Vitamin C.
3. Chloroquine
4. Erythromycin
5. Ferrous fumarate
6. Furazolidone
7. Gentamycin
8. Glafamine
9. Mebendazole
10. Methyl dopa
11. Metronidazole
12. Miconazole
13. Niclosamide
14. Nitrofuroxazide
15. Piperazine citrate
16. Pyrantel
17. Rehydration salt
18. Rifampcin
19. Rifampicin + INH
20. Sorbitrate
21. Succinyl/Phthalyl sulfathiazole

ANNEX IX

Some major equipment for R & D Centre for Pharmaceuticals

I. For Pilot Plant Laboratory: Equipment	No.	Approx. price (US$)
1. Stainless steel (SS) reactor 50 lit.	1	6,000.00
2. S.S. reactor 100 lit.	1	8,000.00
3. Glass lined reactor 50 ltr.	1	8,000.00
4. Glass lined reactor 100 lit.	1	10,000.00
5. Fluid bed drier 50 kg.	1	5,000.00
6. S.S. centrifuge 24"	1	8,000.00
7. All-glass reactors-cum-distillation unit 10 lit.	2	1,000.00
8. All-glass reactors-cum distillation unit 25 lit.	2	1,500.00
9. All-glass reactors-cum-distillation unit 50 lit.	1	1,000.00
10. Vacuum pumps industrial	4	4,000.00
11. High pressure autoclaves - 1 lit. & 10 lit.		5,000.00
12. Solvent recovery unit	1	20,000.00
13. Filter: Nutsche Sparkler Rotavacuum	1) 1) 1)	2,500.00
14. Centrifuge - Basket type Sparkler	1) 1)	4,000.00
15. Crystallisers - 250 lit.	2	2,000.00
16. Soxhlit extraction with distillation unit 250 lit.	1	5,000.00
17. Climbing film cyclone evaporator	1	2,500.00
II. Services for Pilot Plant Laboratory:		
1. Boiler 200 kg/hour	1	20,000.00
2. DM water unit	1	1,500.00
3. Chilled water 5 TR		10,000.00
4. Chilled brine 2.5 TR		20,000.00
5. Compressed air line 5000 LPM		1,000.00
6. Vacuum line		15,000.00

III. For Chemical Technology Laboratory: Equipment	No	Approx. price (US$)
1. Heating mantles for 100 ml to 1000 ml flasks	12	2,500.00
2. Mechanical stirrers	6	2,000.00
3. Magnetic stirrers	6	3,000.00
4. Melting point apparatus	2	1,000.00
5. Water baths	12	2,000.00
6. Balances, semimicro and analytical	4	5,000.00
7. Flash evaporators	4	4,000.00
8. TLC unit	1	2,000.00
9. Flash chromatography apparatus	1	2,000.00
10. Laboratory centrifuge	1	1,000.00
11. Glass distillation unit	2	2,000.00
12. Hydrogenation pressure-low pressure	1	2,000.00
13. High pressure hydrogenation pressure on lit. capacity	1	5,000.00
14. High pressure steel bombs 100 & 250 ml	2	2,000.00
15. Ovens	2	2,000.00
16. Vacuum pumps	4	2,000.00
17. Laboratory glassware - miscellaneous		20,000.00

IV. For Pharmacology Laboratory:		
1. 4 channel polygraph with preamplifiers and transducers	Grass Equipment Co. Quincy, Mass. USA	20,000.00
2. Electronic stimulators - 2	" "	10,000.00
3. 2-unit isolated organ bath	Biosciences, Sheerness, Kent, UK	1,500.00
4. Respiration pump	" "	2,000.00
5. Columbus activity monitor	Columbus Instrument Co., Colombus, Ohio, USA	15,000.00
6. Rota rod	UGO Basille, 21025, Comerio, Varese, Italy	2,500.00
7. Electroconvulsometer	" "	2,300.00

8. Analgesiometer	UGO Basille, 21025, Comerio, Varese, Italy	1,000.00
9. Paw Plethysmography	" "	1,200.00
10. Operation table shadowless lamp and other related equipment	Biosciences	5,000.00
11. PH meter, flame photometer, spectrophotometer, etc.	A. Thomas Philadelphia, USA	15,000.00
12. Electronic thermometer with thermistor probes	" "	
13. Binocular microscope	" "	3,000.00
14. E.K.G. machine	" "	2,500.00
15. Desktop computer	" "	5,000.00
16. Dissolution simulator and absorption simulator with artificial gastric and intestinal barrier kits for bioavailability studies	Sartorius GmbH, Weender Landstrasse 94-108, P.O. Box 19, D-3400 Gottingen West Germany	10,000.00
17. Pipette centrifuge "Analysette"-21 for particle size analysis (0.01-5 μm)	Alfred Fritsch & Co., 6580 IDAR-OBERSTEIN 1 Hauptstrasse 542, West Germany.	7,000.00

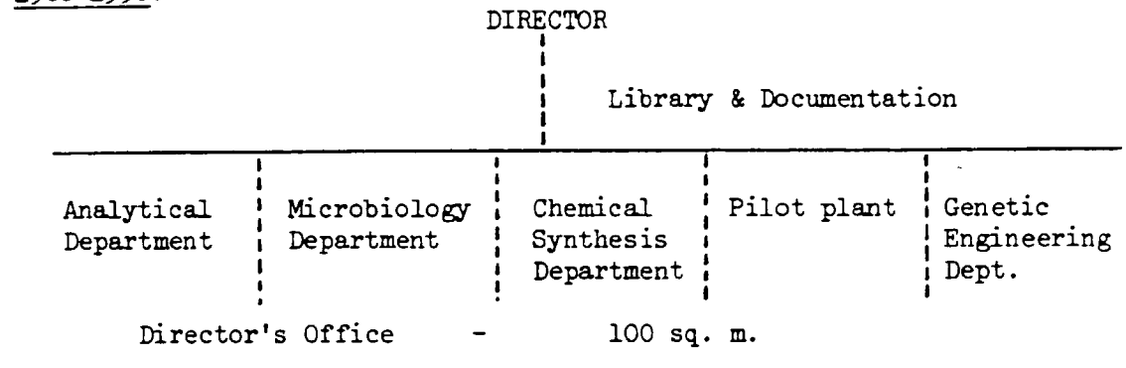
ANNEX X

Biotechnology R & D Centre (Medea)

4000 sq. m.

ORGANISATION CHART

1986-1990:



Director's Office - 100 sq. m.

1. Library & Documentation:

Staff	No.		Space
M.Sc./B.Sc. (Library Sci.)	2	Reading Room	200 sq. m.
English Translator	1	Stock room	
Technicians	2	Librarians	
Helpers	2	Office	

2. Microbiology Department:

Ph.D. (Mycology or Botany)	1	Culture Room	1500 sq. m.
Ph.D./M.Sc. (Microbiology)	4	Incubation Room	
Technicians	4	Shaker Rooms	
Helpers	4	Cold Room	
		Laboratories	
		Media Preparation	
		Laboratory	
		Washing room	

3. Chemical Synthesis Department:

Ph.D. (Organic Chemistry)	2	Develop. Lab.	500 sq. m.
M.Sc. (Organic Chemistry)	4	Lab. for Hazardous reactions	
Technicians	2	Catalytic	
Helpers	2	Hydrog. Lab.	
		Chromatography	

4. Pilot Plant:

Staff	No.		Space
Ph.D. (Industrial Microb.)	2	Fermentation Lab. with 10-1000 Lit. fermenters	1000 sq. m.
M.Sc./Ph.D. (Biochem. Eng.)	2		
M.Sc. (Microbiology)	2		
M.Sc. (Organic Chemistry)	1	Media making & Sterilising Lab.	
Technicians	4		
Helpers	4	Chemical Isolation Lab.	

5. Store:

Store keeper	2	Stock rooms	200 sq. m.
Technicians	4	Issue room	
Helpers	2	Office	

1991-

6. Genetic Engineering Department:

Ph.D. (Micro. Genetics)	2	P3 Lab.	500 sq. m.
M.Sc. (Microbiology)	2	Ultra Centrifuge Lab.	
Technicians	4		
Helpers	2	Electrophoresis	

ANNEX XI

Equipment for Biotechnology R & D Centre

It was informed that an R & D Laboratory has been planned for the Medea Plant for the maintenance of stock cultures and strains. It was not possible to get details of the plan and layout of the laboratories nor of the equipment. A list of some laboratory equipment that had been ordered was provided, but this equipment appeared suitable for a Quality Control Laboratory and not for the presently proposed R & D Centre. The R & D Centre should start functioning, with full pilot plant facility, before production commences on the plant. The pilot plant should have facilities for downstream processes for all the products planned for production in the plant. The geometry and material of construction of pilot plant equipment, particularly the fermenters, should be similar to those used in the main plant for ease of scale up studies.

A list of major pilot plant equipment with estimated cost is given below:

	Equipment	No.	Estimated Unit price (approx.)
1.	100^{L} S.S. inoculator	4	$ 8,000
2.	500^{L} S.S. seed vessel	3	$ 15,000
3.	5000^{L} S.S. fermenter	2	$100,000
4.	Plate and frame S.S. filter press pilot plant model	1	$ 15,000
5.	Rotary vacuum S.S. filter-pilot plant model	1	$ 50,000
6.	Counter current liquid-liquid extractor - S.S.	1	$ 40,000
7.	Rubber-lined resin columns M.S.	10	$ 1,000
8.	Jacketed glass lined reaction Kettler: 250 lit.	2	$
9.	Holding tanks, rubber and glass lined ($1M^3$)	4	
10.	Vacuum trey drier	1	$ 5,000
11.	Spray drier-pilot plant model	1	$ 15,000

ANNEX XII

Laboratories visited and persons met

1. Laboratory of Development & Research, El Harrach

   Dr. B. Mansouri, Director
   Mme Iguertsia Leila, Head, Quality Control Department
   Dr. Ouali, Head, Formulations Department
   Dr. Achab Said
   Dr. Ferkioui
   Mr. Bakhti
   Mme Belanara
   Mme Rudjala, Incharge, Documentation

2. Department of Analytical Chemistry of the University of Algiers

   Prof. Guermouche, Chairman of the Department
   Dr. Chelghoum
   Dr. Nadjem

3. Quality Control Laboratory of the Biotic Plant

   Mme Meghriche, Head, Quality Control Laboratory

4. Commissariat for Scientific Research and Technology

   Mlle Lai Soudi
   Mr. Benzaghow

5. Medea Plant

   Mr. Taileb Abdel Kader, Director of Industrial Project
   Mr. Aksous, Pharmaceutical Technologist
   Mr. Abchiche, Process Engineer
   Mr. Bouchakour, Head, Penicillin Production Plant

6. Meeting at Biotic Plant

   Mr. Belkebir, D.G. SAIDAL
   Mr. Whaley, Res. Rep. UNDP

7. Institute of Pharmacy, University of Algiers

   Prof. Reggabi, Director
   Prof. Reghis, Director Adjoint
   Dr. A. Tazairt, Dept. of Mineral Pharmaceutical Chemistry
   Dr. B. Mohammed, Department of Pharmacology
   Prof. Denine Rachid, Department of Pharmacy

8. El Harrach Plant & Quality Control Laboratory

   MI Douafia Honeef, Director, Pharmacist
   Mme Abderahmane, Head of the Quality Control Laboratory
   Mme Dernaoui, Pharmacist, Production