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DESIGN, CONSTRUCTION, DEVELOPMENT AND MANAGEMENT OF NIGEB
COMMENTS AND RECOMMENDATIONS ON A PRE-PROPOSAL AND
RESULTS OF DISCUSSIONS WITH THE STUDY TEAM
OF THE EGYPTIAN ACADEMY'S FOCAL POINT

EGYPT

Report

Prepared for the Government of Egypt
under UNDP-financed TSS-2 facility

V.94 23581

The report was co-ordinated by the ISED/CHEM, Area Programmes Division based on the work of Zoltan Csizer, M.D. Ph.D., Senior Interregional Adviser.

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INTRODUCTION

A request for consultancy services in the field of genetic engineering was received through the United Nations Development Programme (UNDP) from the Ministry of Scientific Research, Arab Republic of Egypt on 22 November 1994. Two international consultants were requested to provide advice in two different domains, namely in design and construction of the National Institute of Genetic Engineering and Biotechnology (NIGEB) and in the organization development and administration of the same.

The name and CV of the consultant was subsequently submitted for covering both domains. His candidature was approved. The consultancy services financed by TSS-2 programme was carried out from 27 February to 10 March 1994.

The consultant's work was organized and managed by Prof. Dr. Hamdy Abdel-Aziz Moursy, Vice-President of the Academy of Scientific Research and Technology (ASRT). The consultant would like to express his greatful appreciation for his guidance and advice throughout his work.

The main contribution of the Egyptian counterpart to the consultant's work were:

1 - The Pre-Proposal prepared by the assigned study team headed by Prof. Hamdy Moursy, supervisor of the Egyptian Focal Point for Genetic Engineering and Biotechnology, ASRT;

2 - The in-depth discussions with the scientific sub-groups (on agriculture, industry, human health, environment and construction of facilities) branching from the above mentioned study team; and

3 - The in-detail situation-analysis and discussions with Prof. Hamdy Moursy.

The consultant is also indebted to Prof. Dr. A. M. Hamouda, President of the Mubarak International Science Park (MISP) to arrange his visit to the Mubarak City for Scientific Research (MCSR).

1 SUMMARY OF GROUP DISCUSSIONS AND RECOMMENDATIONS

1.1 INDUSTRY GROUP

As an introductory note to the summary of the discussions with the Industry Group, the consultant has to mention that the meeting concluded with full concensus in the matters discussed. It has been agreed that the projects should result in products or services that directly can be used by industry. It should also be emphasized that the Indutry Group should serve the interest of both public and private industries. It has, however, been stressed that any production activity in NIGEB should not be commenced unless a qua lity assurance system is established.

1.1.1 PRIORITIES

1.1.1.1) Upgrading/improving production strains of different microorganisms used in fermentation of chemical and pharmaceutical industries in Egypt

The genom of only a very few microorganisms has been fully described (E. coli, S. typimurium). The genetic mapping of B.subtilis has not yet been completed. The same is true for S. cerevisiae. Since the genom of the eukaryotes is about 100 times bigger than that of the prokaryotes, the genetic mapping of fungal strains will take a longer period of time.

Due to the lack of our knowledge on the genom of the most important industrial microbes (with the exception of B. subtilis and S. cerevisiae), all major fermentation companies are **using traditional strain improvement methods** such as mutagen techniques and mutant selection. The induced mutagenesis followed by selection of mutants have resulted in a dramatic increase of the antibiotic production capacity of the different strains used in the industrial scale fermentation (e.g. penicillin fermentation).

Commercial laboratories gained high reputation in improving and marketing production strains (Panlabs Inc.).

The strain improvement from technological point of view is a complex task. The most important aspects of this work to be taken into consideration are as follows:

- Optimal physiological state of the parent strain (exponential growth phase of bacteria or germinating cells of fungi);

- Optimal mutagenic dose (the best chemical mutagen is NTG, however it is carcinogenic, therefore it should be handled with extreme care),

- Optimal selection medium; and

- Optimization of culture parameters of the mutant strain.

For strain improvement **modern techniques such as protoplast fusion can also be applied** even though this technique improves only the secondary characteristics of the strain (less foaming, easier filtration, etc.).

The strain improvement work will provide an excellent training opportunity in all aspects of industrial microbiology/biotechnology such as:

- Maintenance of strains;

- Stability of strains;

- Optimization of culture parameters;

- Optimization/improving of the media composition;

- Induced mutagenesis;

- Selection of mutants;

- Designing of selection media (taking into account of the catabolic repression);

- Comparative studies on the characteristics of parent strains and mutants;

- Studies on solid surface and submerged fermentation cultures;

- Determination of product yields;

etc.

The strain improvement work should be coordinated with the activities of the National Culture Collection, Ain-Shams University, Faculty of Agriculture (MIRCEN).

The strain improvement work would give a very good opportunity to provide services to domestic private and public industry, therefore while it would contribute to the financial sustainability of MCSR-NIGEB, it would make the Egyptian fermentation industry more competitive.

Note: As soon as the priority projects are approved, the respective group should immediately start to elaborate a detailed project plan with all details, e.g. identifying specific microbes of industrial importance, the main objectives of research plan, the time frames of project implementation, and all requirements of the project in terms of trained staff, equipment and consumables, etc in order to enable the Management of NIGEB to make the final decision on financing and start up of the project.

1.1.1.2) Developing/improving down-stream processing in the biotechnology industries with particular reference to the membrane filtration techniques

The last decade has brought an unprecedented change in the down-stream processing of fermentation. The utilization of membrane filtration techniques has changed the industry. This technique combines in most cases the eariier desalting and centrifugating steps.

Membranes are currently used for clarification, sterile filtration, concentration, separation, purification, etc.

Since the membrane technology is developing very fast, the application of membranes growing with high pace and changing of the technology of many industrial subsectors, it seems to be extremely important that MCSR-NIGEB promotes the widest application of this technology.

By the introduction of ceramic membranes, the filters based on this composite materials can take a very high work load for a long period of time With the introduction of spiral laminated membranes, the maintenance problems faced with the holofiber membranes have been significantly reduced. Both of these advancements have resulted in a better cost-effectiveness of this technology.

Since membranes used not only in down-stream processing but in production of clean air and water for fermentation and in general laboratory use they applied as HEPA filters for biosafety cabinets and for filtration of media, for production of reverse osmosis water, etc. **the development/training of specialists in downsteam processing familiarized in membrane technology has to be a top priority.**

The expertise and experience in membrane technology will be a good business opportunity for MCSR-NIGEB as offering consultancy service in process improvement for other institutions and companies.

1.1.1.3) Other priorities that might be considered for further discussion

- Fermentation pilot plant facilities in MCSR-NIGEB. According to most authors biotechnology means fermentation. The achievements of the genetic engineering e.g. recombinant DNA techniques in microbiology, hybridoma techniques are applied in fermentation. Fermentation is used not only in the industrial biotechnology but in the human and veterinary health areas as well as in the environmental programmes. Even the agriculture is using fermentation while preparing inoculants. The Industry Group but all other Groups confirmed to the consultant that a fermentation laboratory will be established in MCSR-NIGEB. According to the consultant's views, however, a fermentation laboratory differs from a fermentation pilot plant. The former only tests the product of the research, in other words a new

product prototype, while the latter presents it in a palatable/ applicable form to the clients, e.g. to the industry. Since the costs of a fermetation pilot plant would amount to approximately US $ 700,000 (for further information please see 1.1.2.2) and the activities at NIGEB would not require such a facility at the start up, it was the consultant's recommendation that it should only be established in the second or third year of operation (as part of the second or third equipment "package"). **(NOTE: if such a pilot plant would be established the Industry Group should be it's focal point and this group should be responsible and accountible for its mamagenent);**

Note: Since if established, this would be the first modern/ sophisticated fermentation pilot plant in Egypt, the Management of NIGEB or the study group would require advice on all relevant technical details on such facilities (e.g.catalogues, construction drawings, technological layouts, equipment specifications, etc). To obtain such a professional advice a consultancy service financed most probably by TSS-2 programme, that can be used for technical support services at project level, is recommended.

- Development and production of culture media and their components (e.g. yeast extract, peptones based on soybean, yeast, etc) for domestic use;

- Development and production of fine chemicals/biochemicals/enzymes for domestic use. **NOTE: before entering such a venture of preparation of any biological product a quality assurance/quality control unit should be put into operation. For further information please see 1.2.1.1).**

1.1.2 EQUIPMENT REQUIREMENTS

Notes: - The following prices are based on actual purchase prices and price estimates in Canada, in May 1992.

- Please also note that the list of equipment given here only an illustration and therefore it is not necessarily covering the requirment of a given laboratory e.g. NIGEB.

- Finally please note that some important items are missing becausc the laboratory, which anonymously provided the following illustrative list, did not use them in 1992. Such pieces of equipment are e.g. electroporation equipment, particle gun, cell disintegrators. Some other items have been left out because the consultant felt that their prices might be prohibitive, e.g. flow cytometry equipment (the price of the latter might be in the range of US $ 500,000 - 1,000,000). Similarly a larger size pilot fermenter of 1,000 litres and electron-microscope have not been included in the list.

1.1.2.1) Main equipment list for genetic engineering laboratory

		US$
1	DNA synthesizer	73,000
1	PCR (vacuum oven, etc.)	73,000
1	gels system	18,000
1	eppendorf centrifuge	4,000
1	water bath	1,000
1	biosafety hood	7,000
1	balances	7,000
1	spectrophotometer	11,000
1	scintillation counter (radiation)	146,000
1	freezer - 70 C	58,000
1	fridge	1,000
1	photography equipment	29,000
1	radiation laboratory	73,000
1	gamma counter	73,000
1	centrifuge with rotors	22,000
1	DNA sequentiator	73,000
	computers	15,000
	Total	**685,878**

1.1.2.2) Main equipment list for fermentation pilot plant

			US$
1	mamalian fermenter	20 L	58,000
3	bacterial fermenter	20 L	110,000
1	mamalian fermenter	100L	183,000
1	bacterial fermenter	100L	110,000
2	incubator		10,000
2	incubator shaker		9,000
1	cold room		11,000
1	freezer		1,000
1	fridge		1,000
1	microscope		15,000
1	spectrophotometer		11,000
1	glucose analyser		7,000
1	osmolality detector		6,000
1	alpha laval continuous centrifuge		88,000
2	storage vessels		15,000
	analytical / regular balances		7,000
1	hot air oven		7,000
1	coulter counter		29,000
1	water bath		1,000
1	biosafety hood		7,000
	Total		**686,609**

Small size (1 - 2 litres) bench top fermenters should not necessarily be part of the Fermentation Pilot Plant. These fermenters, to be used for microbial, plant and animal cell fermentations, could be part of the equipment of the relevant Groups.

Note: A misconcept, namely the problem of foam control during the fermentation has to be clarified. The consultant has to emphasize that foaming should be prevented, because the foam if once generated cannot really be controlled, moreover it would immediately disturb the aeration of the culture.

1.1.2.3) Main equipment list for downstream processing laboratory

		US$
1	bio pilot chromatographic system and columns	73,000
1	ultra centrifuge	58,000
1	sorval centrifuge	7,000
	rotors for centrifuge	7,000
1	ultrafiltration unit	9,000
1	minitan ultra filtration unit	2,000
1	autoclave	44,000
1	freeze drier	37,000
1	tank SS.	7,000
1	spectrophotometer	11,000
1	SDS/page/western	18,000
1	elisa reader	9,000
1	elisa washer	11,000
1	eppendorf centrifuge	4,000
1	water bath	1,000
1	biosafety hood	7,000
	balances	7,000
	miscellaneous: glass ware,accessories,cold room, computer, etc.	146,000
	Total	**466,748**
	GRAND TOTAL	**1,839,235**

1.1.3 HUMAN RESOURCE REQUIREMENTS

Notes: - The human resource requirements have been given for the Industry Group only as an illustration. The reason is that the fermentation equipment cannot be run in one work shift. One fermentation cycle can, particularly when fungi are grown/ cultured, take as long as one week - ten days, which consequently means 3-shift work schedule inluding Fridays. In case such fermentation runs are going on the fermentors have to be kept under continuous supervision. At least two persons should carry out this work, 1 professional and 1 technician.

- For the other Groups the human resource requirements have to be kept at the minimum level. in the first year of operation a head should be assigned for each group and each priority programme should be staffed with a senior scientist (team leader), 2 - 3 junior scientists and 2 - 3 technicians.

Head : Chemical engineer/Industrial microbiologist/Biotechnologist

Team leader 1: Industrial microbiologist - Strain maintenance and improvement laboratory

Team leader 2: Chemical engineer/ Process engineer/ Industrial microbiologist - Fermentation pilot plant

Team leader 3: Preparative biochemist/ Process engineer - Downstream processing laboratory

Each team should have 2 - 3 postgraduates (industrial microbiologist/ chemical engineer/ process engineer/ preparative biochemist/ industrial pharmacist/ biotechnologist/ instrumental analyst) and 2 - 3 technicians , except the fermentation pilot plant that should have 3 - 4 postgraduates (they should be specialized in bacterial, plant - fungal - or animal cell fermentation) and 4 - 6 technicians to be able to cover 3 shifts adequately.

Total requirements: 11 - 14 professionals

8 - 12 technicians

1 typist/secretary, 1 driver and additional general staff

Note: It is highly recommended that as soon as the priority projects are approved, detailed training programmes, to be carried out in selected institutions of high reputation and excellence in overseas, should be formulated. For funding these training programmes bilateral or multilateral funds could be secured. For possible UNIDO contribution requests should be channeled through UNDP Office, Cairo.

1.2 HUMAN HEALTH GROUP

As the result of a long discussion the consultant's recommendations have been accepted by the Group. The main debate was over the possibility to start production of fine chemicals and biochemicals/ biologicals, e.g restriction enzymes, polymerases, etc. in NIGEB. The consultant felt that this would be a very expensive proposal. According to him, no production activity should be started as long as a quality assurance system is not in place. After this small or medium scale manufacturing activities may start in a phase wise manner taking into consideration the actual production costs inclusive overheads. Before the Management of NIGEB decides to enter this venture a small market study establishing an estimate for domestic demand should be carried out.

1.2.1 PRIORITIES

1.2.1.1) Establish a national quality assurance system for diagnostics in Egypt

The medical diagnostic reagents have become more sophisticated. Instead of one or two reagents it is quite usual that one might need a whole series of reagents for a certain specific test to be carried out and these reagents are available on the market as kits. Many cases a specialized instrument or instruments are needed to perform the test. The leading companies are very often selling diagnostic kits together with the required specialized equipment. For promotion the readers and other instruments are provided free-of-charge, however, they are eventually included in the price of the diagnostic kits. This type of promotion facilitates the market penetration of the vendors, since as long as the instrument works, the client is bound to buy the same product.

In Egypt, the National Quality Control Authority for Biological Products, such as medical diagnostic kits has not yet developed a testing facility for quality control of imported diagnostics. The MCSR-NIGEB could be designated to carry out this activity.

If established, this laboratory should obtain international certification.

The laboratory should also try to facilitate the purchase of diagnostics for domestic needs via a certified vendor system. If a vendor will give written guarantee to supply of quality products of internationally accepted consistency, a purchase contract could be made for reasonable negotiated prices for a certain period of time. Such contract would have several advantages:

- timely supply,
- guaranteed quality and consistency of quality,
- reduced prices,

- additional services such as trouble shooting by the vendor.

The laboratory will establish a national quality assurance system for medical diagnostics in this area by providing:

- standard operating procedures for testing (SOPs),
- test performance records (TRs)
- calibration of equipment,
- certification of equipment,
- validation of equipment,
- verification of testing procedures,
- validation of testing procedures,
- validation of personnel (round robin test, proficiency),
- quality control of diagnostic materials,
- laboratory auditing,
- Good Laboratory Practices (GLP),
- Good Measurement Practice (GMP),
  (Note: Do not miss with the "other" GMP that stands for Good Manufacturing Practices)
- Good Analytical Practice (GAP),
- Good Control Laboratory Practice (GCLP),
- Protocols for Specific Purposes (PSP), etc.

In order to analyse the reasons of error, the traceability is one of the most important elements that the Quality Assurance System should establish. One of the elements to this is to review the performance characteristics (figures of merit) of each technique, test to be used. The most important performance characteristics are as follows:

- Limit of detection,
- Sensitivity,
- Accuracy,
- Cost,
- Linear range,
- Limit of quantitation,
- Precision: repeatability,
  within laboratory repeatability,
  reproducibility,
- Ruggedness,
- Specificity,
- Selectivity, and
- Bias

It is not the consultant's responsibility that he should give a more detailed review of the importance of quality assurance at this place. He only wants to emphasize that quality assurance is not quality control, it is not a synonyin for it. Quality assurance is a management system (equipped with sophisticated computerized systems) which aims at providing services and supplying goods that would meet ail of the expectations of the customers.

Note: The quality assurance activities can be offered as regular services against certain reasonable charges/fees which will contribute to the financial sustainability of NIGEB.

1.2.1.2) Promotion of polymerase chain reaction (PCR) application

The importance of PCR reaction in the modern biotechnology (molecular biology) is well established. MCSR-NIGEB should, therefore, promote its wide application.

The field of application could be determined later on but it is believed that PCR could play an important role in all three areas of Health Group (infectious diseases, malignancies and genetic disorders). Its application in the research of infectious diseases e.g. schistosomiasis, hepatitis (A,B,C,E, delta), tuberculosis and of malignancies (p53) should be promoted.

Since the PCR is an extremely sensitive test, the evaluation of the results should be made with care. The quality assurance of the test procedures have, therefore, of great importance.

It is suggested that PCR reagents could, if feasible, be purchase in larger quantities within the purchase contract with a certified vendor for the use of primer prepared at MCSR-NIGEB.This scenario should be discussed while negotiating a purchase contract, hence the vendor could give useful advice.

1.2.1.3) Promotion of the use of transgenic animals in the medical research

The use of transgenic animals has become a very important new technique of highly promising perspectives in the health research.

One of the possible applications of transgenic animals could be in the research of the possible interactions among schistosomiasis and the different types of hepatitis in the development of hepato-cellular carcinoma. If we take into consideration that most of the anti-schistosomiasis drugs have either carcinogenic or mitogenic effects, the effects of these drugs in the pathogenesis of these diseases should also be investigated.

Note: For establishing a modern animal facility that meets the international requirements, consultancy services would be required to provide detailed specifications.NIGEB or the National Focal Point on Genetic Engineeering and Biotechnology of ASRT could request such consultancy services from UNDP. TSS-2 may be used for such technical support services at project level.

1.2.1.4) Other areas of interest that might be considered as priorities for further discussion

In the area of malignancies the consultant's expertise and working experience can only cover some specific areas of tumor immunology and the production and administration of certain immunomodulants. Likewise, in the area of hereditary disorders he only dealt with the diagnosis and replacement treatment of some rare agammaglobulinaemias and other immunoglobulin de ficiencies.

Therefore, and based on the discussions with the members of the Health Group, he accepts that the following areas could be regarded as priorities:

- Research on malignancies based on molecular biological tools such as p53 with particular reference to breast carcinoma;

- Research on bone marrow transplantation as second priority in the treatment of leukemias (PCR could possibly be applied);

- Since prenatal diagnosis and termination of pregnancy are legal in Egypt, promotion for screening of carrier detection and prenatal diagnosis of the most prevalent genetic diseases has at national level of high priority.

NOTE: It has been recommended that MCSR - NIGEB should establish a network of closely cooperating units in all relevant institutions working in the same area in Egypt. This way a coordination of research could be achieved. The Focal Point for Genetic Engineering and Biotechnology at ASRT can play a role in this respect.

1.3 AGRICULTURE GROUP - PLANT PRODUCTION

1.3.1 PRIORITIES

The Agriculture Group's contribution is the best planned and presented in the Pre-Proposal. The booklet of the Agricultural Genetic Engineering Research Institute (AGERI) has given an excellent example for the presentation. The proposed research priorities for MCSR - NIGEB therefore fully accepted by the consultant.

It should be noted that the Agriculture Group of MCSR - NIGEB should work in very close coordination with AGERI.

It is recommended that the experiences gained in establishing and developing AGERI should be taken into account at the planning and execution phases of MCSR - NIGEB. It should be further mentioned that the research pertaining to agriculture is of top priority (priority No.1). The topics of research needed to be

carried out are plenty and cannot be covered by one or even two centres like AGERI.

1.4 AGRICULTURE GROUP - ANIMAL PRODUCTION AND FISHERIES

The consultant most probably had his longest discussion with this Group. At the same time he felt that in this area there is a very wide gap between the results of the current international research and the reality in Egypt. In this domain, therefore, the infrastructure in Egypt has to be strengthened in order to make able the sub-sector to successfully absorb new technologies to be developed by NIGEB.

1.4.1 PRIORITIES

1.4.1.1) Promotion of artificial insemination

It is well understood that the scope of the activity of MCSR-NIGEB will cover only genetic engineering and biotechnology. The term biotechnology here refers to "modern" biotechnology.

In developing countries, even if they are, such as Egypt, highly advanced in many areas, the capability has not often been developed to readily absorb/ adopt/ use the new technological achievements. This type of inability can be caused by several factors, it is mostly due to the lack of infrastucture, but it could have its reasons in cultural, climatic or educational differences as well.

Artificial insemination can by now regarded as the most successful traditional technique to improve production. In cattles, the average annual yields for milk grew from 2,000 kg (1945) to 4,700 kg (1975). In poultry, broilers reach 2 kg bodyweight in 5 weeks and this figure shows an annual 4 % increase, while the percentage of breast meet is also steadily increasing.

In Egypt the percentage of artificial insemination in cattle is estimated about 40 %. The MCSR-NIGEB should actively facilitate the overall use of this technique in the animal production. **This activity should not obviously be regarded as a research project,** but NIGEB, if the institute aims at establishing itself as a national institute of excellence, should promote by information, education, etc the widest use of well established routine techniques through the relevant Groups.

It has not been mentioned but the consultant would draw the attention to the fact that in paragraphs 1.1.1.1 and 1.2.1.1 the establishment of a strain/cell maintenance/ improvement laboratory and a national quality assurance system, respectively are also outside the scope of activities of the MCSR - NIGEB. The consultant , however, strongly recommends to establish these units as prerequisites for the commencement of the research activities in a proper way according to the international standards.

1.4.1.2) Construction of genetic linage maps for farm animals

The genetic mapping should have a top position in the priority list, since this would establish the base for further research such as gene transfer and embryo transfer. The Group should start with one animal species only. The consultant cannot give advice on what species should be selected but the choice should definitely be based on scientific, technical and economic considerations.

1.4.1.3) Construction of primers/probes for diagnosis of the most relevant veterinary diseases

Several veterinary diseases are endemic in Egypt. The local isolates are in many cases have specific characteristic. The development of diagnostics for these would have of great economic relevance.

1.5 ENVIRONMENT GROUP

The programme of the Environment Group has been very vaguely elaborated. This can be due to the fact that this area is a very complex one and actually ot os closely integrated with the other 4 domains.

1.5.1 PRIORITIES

The Environment Group has to face very complex problems and those would need a multidisciplinal approach to tackle. Therefore, the members of the Group felt that they should start only with one project.

This project would be **the control and reduction of pollutants that endanger the aquatic life in the North Egyptian freshwater lakes.** The lakes are being polluted by industrial, agricultural and municipal wastes. As a result of toxic wastes and substances being dumped and washed into the lakes, the production of fish has significantly decreased, and has left the local population without the main staple food and cash source.

It should be noted, however, that in any environmental type of project one should deal with the problem in its complexity. Therefore, after identifying the pollutants, their amounts and sources (inventory of waste materials), on the one hand cleaner technologies generating less amounts of wastes should be developed (waste reduction), and on the other hand the reduced amounts of wastes should be properly treated

(elimination, recycling, etc) Since the application/use of certain products can generate wastes, the use of these substances should be optimized, e.g. pesticides.

Genetic engineering and biotechnological techniques can be used in **developing cleaner technologies and products** which should be one of the main goals of the Environment Group. A few example for these clean products are **biofertilizers, biopesticides, biosurfactants, etc.**

The priority project should develop a specific strategy to address the particular environmental problem of the North Egyptian lakes by developing biotechnological/ microbiological tools such as bioindicators for biomonitoring of the concentration of toxic substances in the lake water.

As a second step special microbes could be developed and used for the biological treatment of the wastewaters generated by the industry. By promotion of biofertilizers and biopesticides in agriculture should decrease the use of chemically and environmetally hazardous and toxic agrochemicals. The municipal wastes should also be collected properly and the feasibility of their use for biogas production should be investigated.

Note: It should be stressed that the environmental issues are priority issues at global level. Therefore attracting funds from bilateral and/or multilateral sources seems to be a good opportunity for such programmes. Among the multilateral funds available, the consultant would mention the Global Environmental Facility (GEF) as a possible source of financing this programme.

2 THE FACILITY

The consultant visited the provisional facility and the new construction of NIGEB at the Mubarak City for Scientific Research on 3 March 1994. The visits were arranged by Prof. Dr. A. M. Hamouda, President of the Mubarak International Science Park (MISP).

The provisional facility, which has been made available by the Ministry of Industry, is a large rectangular building located in one of the industrial suburbs of Alexandria. It has 4 floors with ample space. It has electricity and water but its use for a genetic engineering and biotechnology laboratory would require a significant remodelling. This would be not only a painfully costly process but it would take a considerable period of time. Since currently the "would be" staff of NIGEB is assigned in different institutes and university departments, the consultant feels that their work should not preferebly be disturbed by two movings, the first to the provisional facility and the second to the Mubarak City for Scientific Research.

The provisional facility, however, would give a good opportunity for the start of some other components of the (MCSR) e.g. Informatics Research Institute, Scientific and Technical Capabilities Development Center, Engineering Industries Development Centre. According to the consultant's view these institutes/ development centres would require only moderate remodelling and therefore their start up seems to be feasible.

The new facility of the MCSR located at New Burg El Arab, about 40 km westward from Alexandria. The construction has a pyramidal shape and it is based on a modular system of 2.70 m x 2.70 m. The Engineering Consultants designed the building is Prof. Dr. Emam Shalabi, the contractor for the construction works is Hassan Alam Company. The construction at the time of the consultant's visit reached its third level, the concrete skeleton of the basement and ground floorhas mainly been completed.

2.1 FACILITY REQUIREMENTS

It should be noted that the biosafety standards of MCSR - NIGEB should meet the internationally accepted standards.

It has been a concensus of all Groups that the laboratory facilities should meet the requirements of containment level 2, hence the biohazard risks are moderate at the levels of individuals and limited at the level of community. These are, at least, as follows:

> **Note: It has been prepared in line with the Laboratory Biosafety Guidelines of the Medical Research Council of Canada and the Laboratory Centre for Disease Control, Health Protection Branch, Health and Welfare Canada 1990.**

The requirements in brackets (...) are only recommended.

2.1.1 LABORATORY LOCATION

Separated from public areas by door

Laboratory doors should be labelled with biohazard sign

Access limited to authorized personnel

Office areas can be located within the laboratory next to access or egress door

Office areas must be outside the biocontainment facility

Facility must be kept locked when not in use (consistent with local fire and safety regulations)

2.1.2 LABORATORY CONTAINMENT PERIMETER

A. WALLS

Structural masonry (reinforced)

Non-load-bearing masonry (reinforced) (steal frame reinforced)

Concrete

B. CEILINGS

Steel frame gypsum partition or ceiling acoustic tile

C. COATINGS AND SEALANTS

Seamless gas- and chemical-resistant wall and ceiling coatings

Chemical- and gas-resistant, non-hardening sealants

Containment seals for mechanical and electric service openings

D. DOORS

Doors to public areas lockable

Doors self-closing

Door openings should be of sizes to allow passage of all anticipated equipment

Doors to have required fire ratings and be located as for fire safety standards

All exits marked and illuminated

Egress to fire exits set out so that it is not necessary to travel through any high hazard areas on exit route or to conform to applicable codes

E. WINDOWS

Windows if openable protected by fly screens

F. FLOORS

Slip-resistant flooring

Seamless, rolled or resilient tile flooring

(Seamless, gas- and chemical resistant epoxy coating with cove base)

2.1.3 AIR HANDLING

A. ROOM AIR SUPPLY

Directional inward, non-recirculated airflow

(Interlocked with exhaust ventilation to prevent pressurization)

(Equipped with manual damper to permit sealing for decontamination procedures)

B. EXHAUST VENTILATION

(Interlocked with air supply to prevent pressurization)

(Equipped with manual damper to permit sealing for decontamination)

Exhaust from laboratory at a minimum of ten room volumes per hour

(Air vertically discharged to the outside, clear of buildings or air supply intakes, at 12 metres/second)

Recirculated HEPA-filtered air permitted

Ventilation sufficient to remove vapours of flammable liquids and dangerous chemicals before they reach hazardous concentrations

C. BIOLOGICAL SAFETY CABINETS

Class I

Class II

Cabinet air can be recirculated in laboratory if HEPA-filtered

Requirements for biological safety cabinets in all level laboratories (prevent backflow, permit decontamination, away from travel zones, min. 30 cm clearance)

Requirements for HEPA filters in levels 2 - 4 biocontainments laboratories (close to hazard area, leakproof, allow decontamination, magnehelic gauges)

2.1.4 DECONTAMINATION, STERILIZATION AND WASTE DISPOSAL SYSTEM

A. DECONTAMINATION

Laboratory floors, walls and ceilings to be treated with disinfectant-resistant, cleanable coatings

Laboratory with all furnishings and surface materials disinfectant-resistant and cleanable

B. STERILIZATION

Autoclave in the facility (in the laboratory)

Exposed steam pipes covered with insulating material

C. WASTE DISPOSAL SYSTEM - LIQUIDS

Drainage traps filled with disinfectant specified by lab operator

Radioactive liquide waste disposal should be done in line with the international regulations

WASTE DISPOSAL SYSTEM - SOLIDS

Provide space for stands supporting bags for collection of biomedical waste

Provide space for a lockable, closed storage facility for biomedical waste which has to leave the laboratory for autoclaving or **incineration**

Radioactive solid waste disposal should done according to the international regulations

2.1.5 PERSONAL HYGIENE AND SAFETY FACILITIES

Handwashing facilities in laboratory

(Handwashing facilities in laboratory with foot-operated taps)

Eye/face wash facilities

Provide storage space for laboratory clothing in lab or adjacent changing area

Provide space for laundry adjacent to exit door for used laboratory clothing to be autoclaved prior to laundering

2.1.6 BUILDING SERVICES

A. PLUMBING AND DRAINAGE

All exposed hot and cold water pipes are to be covered with insulating material and protected from movement

B. COMPRESSED AIR AND GAS

(All supply lines HEPA-filtered or equivalent as backflow protection)

(All vacuum lines HEPA-filtered or equivalent)

(Compressed gas cylinder storage outside laboratory)

C. ELECTRICAL

(Building security systems integrated with laboratory safety and monitoring systems)

All circuit-breaker switches and controls to be labelled

Electrical system is to be equipped with standby generator for emergency support of essential equipment.

Laboratory to be equipped with fire alarm system

2.1.7 EMERGENCY AND MONITORING PROVISIONS

A. AIR HANDLING

Directional inward non-recirculated airflow

Biological safety cabinets equipped with magnehelic gauges to monitor all HEPA filters

Provision of access for decontamination of HEPA filters

B. FIRE PREVENTION AND CONTAINMENT

Equipped with fire alarms

Equipped with fire extinguishers

Doors to have appropriate fire ratings

All fire exits marked and illuminated

Equipped with suitable storage cabinets or explosion-proof refrigerators which are clearly labelled for flammable liquids

Storage for flammable liquids to be located outside biocontainment area

C. PERSONNEL EMERGENCY EQUIPMENT

Eye/face wash facilities in laboratory

Emergency lighting

D. BACKUP SERVICE

Equipped with standby generator for support of essential equipment

2.1.8 COMMISSIONING

Testing of biological safety cabinets meets required specifications after installation

Testing of autoclaves to meet specified standards after installation by use of biological indicators

Verification of alarm systems for electric failure

Verification of fire alarm systems

Testing of directional airflow demonstrated by field tests with visual smoke

2.2 FACILITY MANAGEMENT

The Facility Management as a separate organizational entity seems to be missing in the NIGEB. Reviewing the drawings of the facility, the consultant could not find office and workshop areas allocated in the building for this group.

2.2.1 MAIN RESPONSIBILITIES

The responsibilities of the Facility Management should be as follows:

- Building management and safety services;

- Maintenance and repair of building, equipment and utilities;

- Maintenance of building perimeter including roads, fences, etc.

- Gardening;

- Provision and management of essential supplies e.g. electricity, water, etc.

- Environmental issues e.g. management of chemical and biological hazardous wastes, handling of garbage;

- Disposal of radioactive waste;

- Incineration;

- Management of animal farm and green houses;

- Management of new projects; etc.

2.2.2 SPECIFIC TASKS RELATED TO THE INSTALLATION OF THE FERMENTATION PILOT PLANT

The Fermentation Pilot Plant requires many utilities that would not be required in the laboratories engaged with genetic engineering programmes or laboratories of more general use.

The Fermentation Pilot Plant should have at least a few (4 - 6) identical fermenters of 10 - 20 litres and at least one fermenter of 100 litres and another one of 1,000 litres. The latter should be purchased only at the time when actually would be needed. This size of fermenter would definitively be needed in any work on industrial enzymes, fermentation of antibiotics, amino acids, inoculants for agricultural use, or in any project of biological waste treatment.

Even if these fermenters will not be purchase at the same time but rather in a phase-wise manner the infrastructure, services and supplies should be established at the construction phase of the building. For the Fermentation Pilot Plant at least the following utilities and supplies should be provided:

- Electricity

- HVAC: Heating

  Ventilation

  Air Conditioning

- Water: Cold

  Hot

Deionized

Distilled and/or Reverse Osmosis Water

- Gas
- Compressed Air and Vacuum
- Sterile Filtered Air
- Exhaust Air Incineration
- Drainage
- Sprinklers (Fire Prevention)
- Medical Gasses: Nitrogen

  Oxygen

- Biosafety Cabinet

The conduits and piping of all these services and utilities should be arranged in such a way that they would be easily accessible for maintenance and repair. It is therefore suggested that a separate room adjacent to the Fermentation Pilot Plant should house all switchboards, connections to the main supply lines, motors and pumps, etc. that would require maintenance. This way the work of the fermenters, in other words the fermentation cultures will not be disturbed/ interrupted by the service personnel of the Facility Management.

2.2.3 GENERAL SERVICES REQUIRED FOR THE FACILITY

Some other general services that would be required are not mentioned in the Pre-Proposal. These are the security services (reception, guards) and the procurement services (purchase, importation, transport, mail).

It is recommended that an incinerator should be installed for the facility. The incinerator should comply with the current international standards.

Disposal of radioactive wastes should be carried out in line with the internation regulations. The procedures for the safe handling and use of radioactive materials should be established, and all personnel working in the radiation laboratory should be specifically trained in the safety procedures.

An emergency response procedures manual should also be established as a response guide for emergency situations such as fire, hazardous spill, service interruptions, etc.

2.2.4 REQUIREMENTS OF LABORATORY MATERIALS, EQUIPMENT AND TECHNIQUES IN GENERAL

The materials, equipment and techniques which are, in general, used in laboratories are of a very wide range. Currently the most commonly used materials and equipment are made available of highly specialized materials (composites, etc) for specific purposes. In genetic engineering and biotechnology one works with very sensitive live systems that may be effected by picogramm amounts of materials leached out from commonly used laboratory ware such as plastic containers. Therefore, the purchase of the laboratory supplies requires a very special experience and knowledge. To facilitate the procurement of these items, in general use, the consultant offers a checklist as follows:

2.2.4.1) Materials in the laboratory

glass

flexible tubing

corks, stoppers and enclosures

O-rings

2.2.4.2) Measurement

length: ruler, caliper, micrometer

volume:volumetric flasks, graduated cylinders, pipettes, burettes

weight and mass: balances, analytical and top-loading balances

temperature: expansion-based thermometers (linear, volumetric), pressure expansion thermometers, thermocouples, resistance thermometers

2.2.4.3) Joints, stopcocks and glass tubing

joints and connections: standard taper joints, ball-and-socket joints, o-ring joints, hybrids and alternative joints

stopcocks and valves: glass and teflon stopcocks, rotary valves

maintenance: greases, teflon

glass tubing

2.2.4.4) Cleaning glassware

soap and water

ultrasonic cleaners

organic solvents

base bath

acids and oxidizers

chromic acid

hydrofluoric acid

2.2.4.5) Compressed gases

compressed gas tanks: nitrogen, oxygen

pressure regulator

2.2.4.6) High and low temperature

high temperature: hot water, steam, open flames, thermal radiation, hot air

low temperature: room temperature tap water, ice, ice with salts, dry ice, liquid nitrogen, liquid (cryogenic) gas tanks

2.2.4.7) Vacuum systems

pumps: mechanical pump oils, diffusion pumps, dissusion pump oils

traps: cold, separation and liquid traps

vacuum gauges

2.2.4.8) Gas-oxygen torch

2.3 COMMENTS ON BUILDING DRAWINGS

Without a rank of importance the consultant's comments on the building drawings are as follows:

2.3.1 GENERAL COMMENTS

- Elevator cannot be used in case of fire. The closed tube-shaped structures as fire escapes cannot be accepted because in case of fire these tubes could be filled up with smoke, and the oxygen content of the air could also be decreased. Fire escapes should be open metal structures/ stairs outside of the building sloping down from the pyramidal structure.

- More than one elevator would be required (at least 3 or 4).

- The cafeteria has 3-floor height, that would be waste of space.

- There has been no are designated to the Facility Management offices and workshops. An area of considerable size should be made available for Facility Management for:

offices e.g. to prepare drawings, for computers;

workshops e.g. electrical switchboards, steam generation, stand-by electric generator, deionized water, etc; and

maintenance and repair workshops.

- A ramp for shipments would be required.

- The central/main air intake is not clearly shown in the drawings.

2.3.2 SPECIFIC COMMENTS

- The Fermentation Pilot Plant should be placed one of the larger corner laboratory of the basement. One of the adjacent rooms should be served to house the computer monitor and control system of the Pilot Plant. The other adjacent room should be the service area for the Pilot Plant. All service conduits, pipes, switchboards, motors, pumps, etc should be located here. With this arrangement the clean area is not disturbed either by control/ monitoring activities or servicing.

- The surface final finishes should be seamless at least certain selected clean and/or hazardous laboratories, where general cleaning, fumigation could be foreseen frequently or regularly. During fumigation the laboratories should be sealed.

2.3.3 PLANT AND ANIMAL FARMING

- The NIGEB requires an area of farm land for agricultural research and an animal farm for animal research. The size and location of these farms and their requirements in terms of facilities, equipment and personnel should be identified. Their location should preferably be in the vicinity of MCSR-NIGEB.

3 VIEWS ON ITEMS OF THE STUDY STILL UNDER DISCUSSION

3.1 GOALS

It is the consultant's view that while pursuing the establishment of NIGEB as a national centre of excellence, its main goal should be applied research. The research should result in product ideas and prototypes of products, which in turn should consequently be developed to become products prepared and tested at pilot scale. Likewise, one can aim at research and development (R & D) in the services sector.

Five areas have been selected as priority for R & D as follows:

- Agriculture - Plant Production,
- Agriculture - Animal Production and Fisheries,
- Human Health,
- Industry, and
- Environment.

In addition to these selected domains, any important and relevant area could and should eventually be developed in NIGEB if there is a newly emerging specific demand.

3.2 FUNCTIONS

NIGEB should, at least, have the following functions:

- Planning
- Research (basic and applied)
- Development (up to pilot scale)
- Quality assurance (quality monitoring and control)
- Management
- Human resources (training)

- Performance appraisal
- Coordination (internal, external and international)
- Administration (finance)

3.3 ACTIVITIES

The substantive units of NIGEB should, in general, perform the following activities:

- Analysis
- Assessment
- Review
- Decision making
- Research
- Development
- Quality control
- Quality monitoring
- Quality assurance
- Information
- Training
- Technology transfer
- Publication
- Management
- Public relations
- Performance appraisal

At project level the consultant recommends to start up activities at NIGEB in a phase wise manner.

In Phase I, the Agriculture Group - Plant Production and the Environment Group are recommended to commence their respective top priority projects (each Group one project only) in the first year after commissioning of the building.

In Phase II, in the second to fifth year after commissioning of the building, the other Groups would also start but only with one project each.

The commencement of Phase III should be decided by NIGEB's Management. At this Phase, depending on the performance of the Groups and their achievements at project level, the activities can be expanded for the rest of the priority projects.

The consultant has recommended that the Agriculture-Plant Production and Environment Groups should be moved into the new facilities of NIGEB and start their respective activities, because according to his opinion, these are the areas where, within a short period of time, successful achievements can be expected. In these areas the human resources are highly developed in Egypt (agriculture) and the coverage by intellectual property rights is moderate (environment).

In spite of the global economic slow down and the scarcity of funding, these Groups, but particularly the Environment Group, have the best chances to attract donor funds, grants, bilateral or multilateral technical cooperation.

To commence with Groups and projects of better opportunity would provide the Management a lead time of 1 year to organize MCSR - NIGEB.

It should be noted that the technologies used mainly by the Human Health and Industry Groups are very strictly controlled at international level by regulations and intellectual property rights. According to the consultant's opinion these regulations are more strict than those of the Animal and Plant Health Inspection Services (APHIS).

In addition to the above, the economy of scale, as one of the most important factors to reach financial sustainability and achieve sustainable development, should also be taken into serious consideration.

3.4 STRUCTURE

The tentative structure of NIGEB given in the Pre-Proposal is acceptable by the consultant.

When designing the structure of NIGEB, the right-sizing, one of the main principles of management, should be followed. This means that in the organigram, the chain of command should be clearly shown among the multiple layers of managers. Each manager/ senior staff should have preferably 3 but not more than 5 direct reports. The organigram and consequently the distribution of the personnel should neither be top or bottom heavy.

The functional laboratories to be established as priority should be as follows:

- **Recombinant DNA laboratory with viral, bacterial (including strain improvement with traditional methods), plant and animal sections;**
- **Molecular cloning;**
- **Nucleic acid, gene/genome sequencing;**
- **Cell and tissue culture laboratory with plant and animal sections;**
- **Microbial biotechnology with fermentation pilot plant;**
- **Downstream processing laboratory;**
- **Immunology (ELISA);**
- **Hybridoma laboratory;**
- **PCR laboratory;**
- **Radioactive isotope laboratory;**
- **Human genetics laboratory with outpatient clinics;**
- **Small controlled environment laboratory for plant cultivation;**
- **Small experimental animal laboratory;**
- **Support units:**
  - **Quality assurance, quality control laboratory;**
  - **Media preparation;**
  - **Photography;**
  - **Bioinformatics;**
  - **Library;**
  - **Meeting rooms;**
  - **Training facilities;**
- **Experimental units outside the facilities:**
  - **Pilot farm land;**
  - **Pilot animal farm;**
- **Outside support facility: Incinerator.**

3.5 MANAGEMENT

Knowing science and having personal working experience in R & D might be very advantageous for a manager. However, the most important criterion for managers is that they should firstly be managers, that is they should have managerial capabilities. These, in the consultant's view, are at least as follows:

- Personal identification with NIGEB's goals;
- Understand the importance and role that all of its functional elements play;
- Put high emphasis on training;
- Promote team work;
- Accept quality as priority criterion for performace appraisal;
- Able to make decisions;
- Impartial in discussions and debates, and facilitate them;
- Accept criticism;
- Accept weaknesses and errors; and
- Promote a common vision.

The Management with the senior research staff should discuss, review and set/ re-set the priorities for R & D activities/ projects each year.

One of the top priority resposibilities of the Managment should be the training. Internal and external training courses in Egypt and overseas should be planned, organized and carried out at all level of personnel. The monitoring of the training should be done individually at the time of the annual performance appraisal.

The management should be flexible to offer NIGEB's services to both public and private institutions, enterprices, etc. The fees/ charges obtained by this service activity may significantly contribute to the financial sustainability of NIGEB.

3.6 FACILITIES

All of the consultant's comments have been given in paragraph 2.

3.7 EQUIPMENT

Most of the consultant's comments have been given in 1.1.2, 2.2.2 and 2.2.4.

The consultant would like to make at this place two further recommendations;

- A Bioinformatics Unit should be established networking, if possible, with international databanks. A good example of such a unit is operational in AGERI.

  The Bioinformatics Unit should very closely cooperate with the Management Information Services (MIS), that would be the major tool for Administration (procurement, inventories, book-keeping, etc).

- The purchase of equipment should be carried out in phases/ packages in line with the start up of the group activities. In other words the funds earmarked for equipment will be spent in 3 phases. In this way not only experience will be gained in purchasing a very large number, relatively low price items in one package, but ample amounts of funds would remain available for corrections/ modifications. Furthermore, while the funds allocated for equipment earn interest in the bank, NIGEB would have the opportunity to buy the newest equipment models and new equipment items in the market in Phase II and III.