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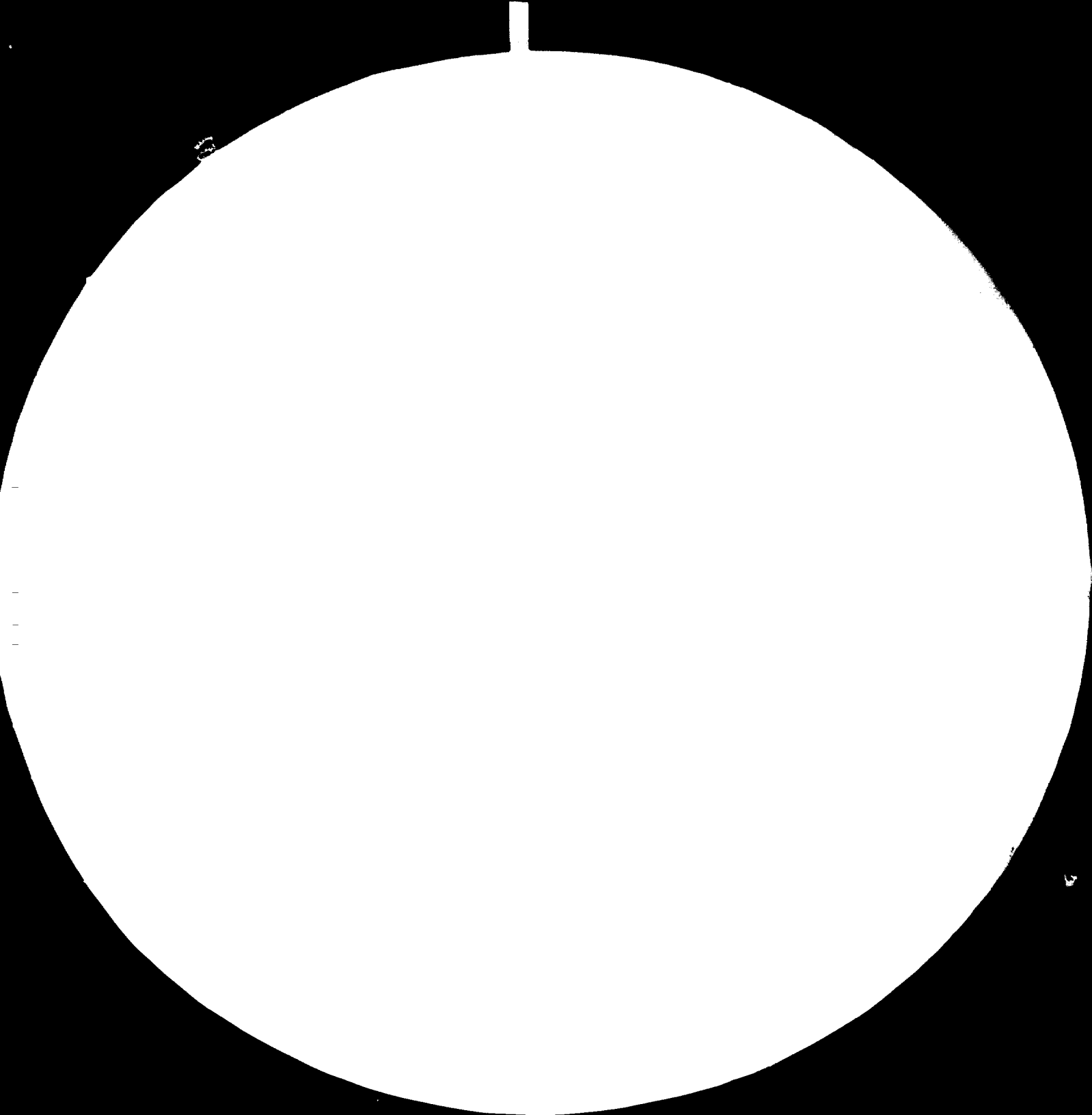

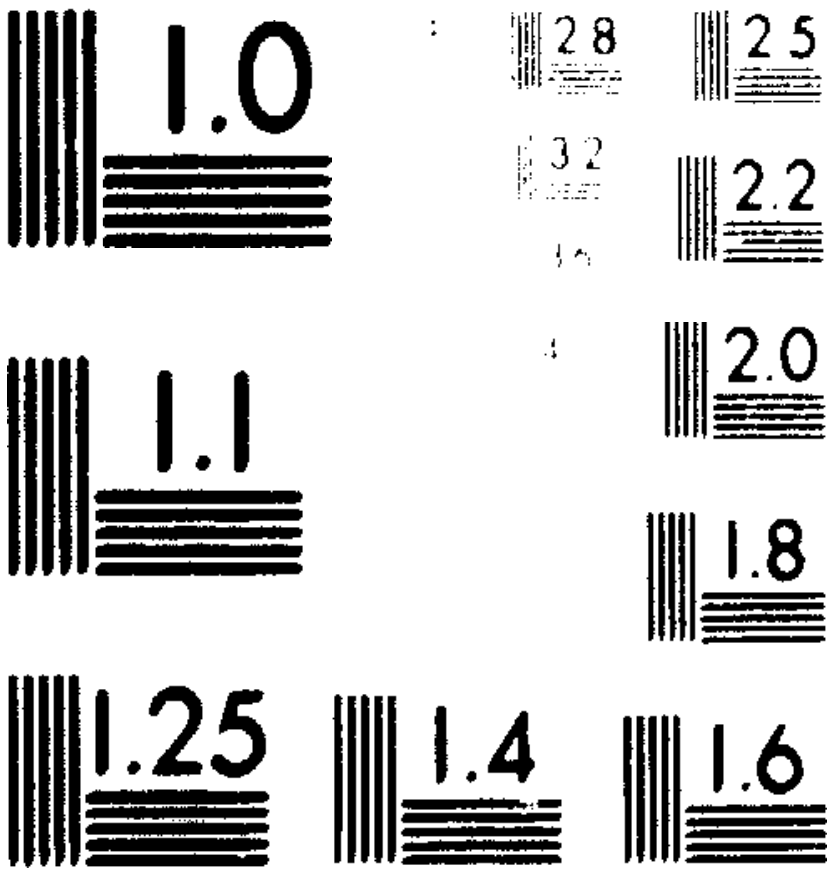

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GENETIC ENGINEERING AND BIOTECHNOLOGY IN EGYPT

prepared by
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Contents

I. INTRODUCTION

1. Over the last decade or so there has been great interest in biotechnology brought about by many factors. In the first instance this technology based largely on fermentation using microorganisms is now in principle applicable to a range of products and processes, including many aspects of energy, (including oil), industry (including chemical, pharmaceutical, food processing); medicine and agriculture. The extraordinary power of modern biotechnology is derived from the interaction between fermentation technology, genetic engineering and enzyme engineering. There has been remarkable progress in the theory and practice of all of these technologies, none more so than the revolutionary changes in genetic engineering, which now provides methods for transferring genes and, therefore, biochemical and chemical properties from one organism to entirely different kinds of organisms, including not only bacteria but also fungi, plant cells and animal cells. It has been argued that the new biotechnology will have an effect on society over the next twenty to fifty years similar to that which we are beginning to experience through microelectronics. Such a prediction is impossible to sustain rigorously but the dimensions of the effect of biotechnology can be gauged from the following examples:

(a) It is being applied to increase the efficiency of tertiary oil recovery (Enhanced Oil Recovery - E.O.R.) with promising early results.

(b) It has already led to a new strategy for the production of vaccines, both for human and animals - these vaccines will be safer and more potent. Effective vaccines are expected to be made for the first time against leprosy and the new strategy is likely to be especially valuable in dealing with those diseases which show antigenic shift and/or drift, for example, influenza and perhaps trypanosomiasis. Although none of these vaccines is available yet on the market, the first animal vaccine produced by this method, which is likely to be against foot and mouth disease, is expected within a few

years, to be followed soon by the first human vaccine probably against hepatitis B. There are prospects of vaccines against malaria, schistosomiasis and other parasitic diseases.

(c) Biotechnology is being applied to increase the efficiency of production of industrial alcohol from starch for use as fuel either as a substitute for petroleum or as an extender (gasohol), and as a feedstock for the chemical industry. Major efforts are under way in Brazil and the United States of America.

(d) It is being applied in a related programme to produce high fructose syrup, a sweetener which is being used as a cheap substitute for cane sugar and beet sugar.

(e) Biotechnology has been used to construct bacteria which will degrade the powerful and dangerous herbicide 2,4,5 T (Agent Orange). In principle the same approach can be used to generate bacteria and plants which degrade other "non-degradable" herbicides and pesticides which may then have a wider application and acceptability.

(f) Biotechnology has been used to generate food protein in the form of Single Cell Protein (SCP) from natural gas. The ICI process uses methanol as the chemical feedstock, and genetic engineering has been applied recently to increase its efficiency.

(g) The production of additives especially amino-acids for both human and animal feed is being carried out by biotechnology on a greatly increased scale in Japan.

(h) The fine chemical and pharmaceutical industry is beginning to incorporate novel biochemical (enzymatic) steps in otherwise chemical processes. One well established example is the use of penicillin acylase in the production of semi-synthetic penicillins.

(i) In medicine the impact of biotechnology is expected to be very great. Already bacteria have been constructed which synthesize human insulin, human growth hormone and human interferons, none of which has been available in sufficient quantities even for experimental purposes until the technology of genetic engineering was developed. Interferon is being studied for its potential as an antiviral agent and cancer drug. In addition it is expected that the following human proteins, amongst many others, will become available in large amounts for general use, if they are found to be acceptable:

- asparaginase (for some types of leukaemia);
- clotting factors (for haemophilia);
- oligopeptide opioids, such as the endorphins (as painkiller and anaesthetics);
- many enzymes, for example, hexosaminidases, hypoxanthine-guanine-phosphoribosyl-transferase for enzyme replacement therapy;
- serum albumin as an extender of serum and serum substitutes.

2. The range of applications of biotechnology is therefore very wide extending from the energy and chemical industries to food production, and health. It implies a gradual shift from chemistry to biochemistry and microbiology reducing energy consumption (biochemistry generally proceeds under milder conditions than chemistry), and changing the quality of pollutants which will be more easily biodegraded, recycled, or used for secondary and tertiary purposes. It has a logic which is applicable to sophisticated processes, for example, the production of antibiotics or the reduction of biowax formation in oil pipelines and other installations or the prenatal diagnosis of genetic disease, and to village level processes such as biogas production or the more effective use of herbicides and pesticides.

3. <u>In essence there is a new logic in the design of biotechnological processes</u>

This logic can be summarized as follows:

- Identify a desirable biological product or process.

- Identify organisms which make this product or carry out this process singly or together.
- Use genetic engineering to increase the efficiency of the system. In general the system will involve fermentation by bacteria or fungi, but some systems will entail algae and plants as the technology develops.

4. The scale, method and source of investment

The new logic of biotechnology has been recognised by governments and private interests worldwide. Several nations have undertaken to increase funding for research and development especially in the key area of genetic engineering. The scale of expenditure is large. For example, the following table shows the planned government expenditure per person per year in genetic engineering R and D in several countries:

Japan	$ 2.1
Canada	$ 1.2
United States of America	$ 0.6
Federal Republic of Germany	$ 0.5
The United Kingdom of Great Britain and Northern Ireland	$ 0.1

France will spend F 25 billion over five years, and India 20-30 million dollars over eight years.

5. In the private sector there have been two kinds of activity. On the one hand a large number of small companies have been established specialising in various aspects of contract and venture research. About 300 have been founded worldwide, and some are well established, for example, Cetus which was set up before the genetic engineering phase, Genentech, the first genetic engineering company proper, and Biogen. On the other hand many large oil, chemical, pharmaceutical, food processing, and agribusiness companies have established in-house research units to apply the new biotechnology. Exxon has been reported to be

establishing a new research centre at a cost of 200 million dollars. Eli Lily, ICI, Schering Plough, Kabi, Wellcome, Novo, Hansens, Gist Brocades and Rhone Poulenc are companies known to have invested in the technology. Fourteen Japanese companies including Mitsubishi, Sumimoto, Asahi, Takeda and Mitsui have joined to form a biotechnology research association and will spend at least 110 million dollars over the next ten years. Some companies are sponsoring major developments at universities such as Hoechst, which is spending 50 million dollars to establish a research unit at Massachusetts General Hospital Boston under Dr. Howard Goodman, a pioneer of genetic engineering.

6. The response of the developing countries

It has been recognized that the new biotechnology poses major problems and offers substantial opportunities for the developing countries. Problems will be caused by the impact of the application of biotechnology in the developed countries. For example, if industrial alcohol is produced on a very large scale in the United States, Canada and Australia from maize and other food grains, the price of food will be directly affected by the price of fuel, and food supluses will be diverted to fuel. Oil imports by these countries and others e.g. Brazil, will be reduced. As other examples, novel drugs, antibiotics, vaccines, pesticides and herbicides will be developed and will be exported to the developing countries, and there will be large changes in trading patterns in commodities such as cane sugar, beet sugar and molasses.

7. To counterbalance and adapt to these adverse changes the developing countries must consider adopting and adapting the new biotechnology to meet their own requirements.

8. The record of developing countries in the new biotechnology and UNIDO

Several developing countries are undertaking major programmes in biotechnology. India has already been mentioned. A Biotechnology Board has been established there under the close personal interest of the Prime Minister, Mrs. Indira Gandhi. Efforts are under way to induce

skilled Indian scientists to return from abroad, and plans are being developed for a new institute. A delegation from UNIDO visited India in January 1982 to discuss the general theme of the new biotechnology with Indian scientists, policy-makers and administrators. Similar delegations have visited about 20 countries including Argentina, Brazil, China, the Federal Republic of Germany, France, Ireland, Italy, Kuwait, Mexico, Saudi Arabia, the Union of Soviet Socialist Republics, the United Kingdom, the United Republic of Tanzania, the United States and Yugoslavia. A delegation visited Egypt on 31 August - 2 September 1981.

9. The purposes of these visits were firstly to gather information and opinions about biotechnology and the developing countries; secondly to catalyse an exchange of views between developing countries themselves and with developed countries; thirdly to promote co-operation between developing countries in acquiring and applying the new technology.

10. Most developing countries including all of those visited have a traditional biotechnology sector e.g. fermentation of molasses to produce ethanol, production of beers and wines and some have projects involving elements of the new biotechnology e.g. single cell protein production, gasohol production. Many were acutely aware of the need to develop this sector and there was much interest in acquiring the technology of genetic engineering. It was widely recognised that this must be acquired soon in view of the fact that much of the knowledge and many of the personnel in this field are rapidly becoming associated with major medical, industrial and agricultural projects. Genetic engineering is being "privatised".

Assessment of genetic engineering and the new biotechnology in Egypt

11. In 1981 Dr. A.I. Bukhari, expert adviser, together with a staff member of UNIDO visited Cairo to discuss genetic engineering and biotechnology with Egyptian scientists. They visited Dr. Fayez at the Academy of Scientific Research and Technology (ASRT) and Dr. Kamel at the National Research Centre (NRC). The ASRT established a Genetic Engineering Committee of which the Chairman is Dr. A. El Bindary and this report has been prepared in consultation with that Committee and Dr. A. El Bindary.

12. The brief for the mission is included as Annex I and details of meetings are in Annex II. The mission lasted from 3-16 May 1982. It is appropriate here to thank the Egyptian scientists and policy-makers who facilitated the mission in every way and who made it so pleasurable and interesting, displaying the hospitality and courtesy for which their country is well known.

13. Much of the technical background to this report is substantiated in a series of general reports produced by UNIDO as follows:

UNIDO/IS.254	The Establishment of an International Centre for Genetic Engineering and Biotechnology (ICGEB)
UNIDO/IS.259	Exchange of Views with Experts on the Implications of Advances in Genetic Engineering for Developing Countries Vienna, Austria, 4-6 February 1982
UNIDO/IS.261	The Potential Impact of Microbiology on Developing Countries
UNIDO/IS.269	The Impact of Genetic Engineering
UNIDO/IS.270/ Rev. 1	Elements of Some National Policies
UNIDO/IS.272	Commercialization of Genetic Engineering Technologies: Some Considerations

II. BIOTECHNOLOGY AND GENETIC ENGINEERING AND THEIR APPLICATION IN BOTH PRIVATE AND PUBLIC SECTORS IN EGYPT

Public and Private Sectors of the Egyptian Economy and Biotechnology

14. Most large Egyptian-owned industrial enterprises related to biotechnology are owned and run by government agencies. No private industries were visited and it was stated that there were few if any likely to be involved in biotechnology. Therefore most developments in biotechnology in Egypt must occur in the public sector.

15. It is possible that foreign organizations may become increasingly involved as, for example, the Institute Française de Petrole (IFP) has in a joint research project on carbon fixation by Spirillum. This is being conducted with the Petroleum Institute of the Academy of Scientific Research and Technology (ASRT). However, there was no suggestion that foreign corporations will contribute significantly to the development of Egyptian biotechnology except by way of licensing or construction and commissioning of industrial plant on contract.

Biotechnology Now in Egypt

16. The Egyptian national industrial sector has a number of industrial groups using biotechnological processes. These include the Organic Chemical Industries Company which is part of the Sugar and Distillery Company. It uses molasses and rice-bran as a feedstock to produce ethanol, acetic acid, acetone and butanol by fermentations at Hawamdia about 50 km south of Cairo. It also produces ethylacetate and butylacetate by secondary chemical processes. The country is self-sufficient in these six primary organic solvents. By-products from this industry include yeast, and CO_2 used in the softdrinks industry. This company is part of an integrated system for processing sugar cane of which 6.5 million tons are produced per year. This represents cropping 2.2 million acres. The

molasses, which is a by-product of sugar-refining amounts to about 300,000 tons per year of which about 50 per cent is exported and 50 per cent is used in fermentation and as fodder. The company employs 27,000 persons. If other fermentation systems for production of bulk chemicals, for example, citric acid (Aspergillus niger), lactic acid (Lactobacillus spp) etc. are judged to be economical in the Egyptian context, this company has the basic experience needed to undertake them. There are no plans to undertake new developments. The company has benefited from close association with the National Research Centre for example in debugging the acetone-butanol fermentation in the early stages but it does not have an independent research capacity and has no plans to develop one. Its laboratory facilities are poor.

17. The El Nasr Company manufactures the basic antibiotics, penicillin and tetracylcine and the enzymes α-amylase (used in desizing cotton) and proteases (used in tanning). These are produced by fermentation. Egypt used to import 600 tons of α-amylase and 6000 tons of protease per year but is now apparently self-sufficient or nearly so. It was not possible to visit El Nasr. Antibiotics are apparently still imported on a large scale.

18. The experience gained in establishing and running the fermentation plants of these two companies, and some others not referred to, provides an invaluable base for future developments in biotechnology. The acetone-butanol fermentation is reputed to be one of only four operating in the world and may be a valuable model for other developing countries.

19. Egypt has a brewing industry (Stella beer with a plant in Giza) and a wine-making industry.

20. The Egyptian Organization for Biological Products and Vaccines (EOBPV) directed by Dr. Imram Zagloul produces a range of vaccines including TAB (typhoid/paratyphoid), cholera, B.C.G., diphtheria, tetanus and pertussis. It is a World Health Organization (WHO) reference centre for polio vaccine and now imports concentrated polio vaccine which is diluted in Cairo before distribution to many countries in the region. This cuts costs by 80 per cent. This centre is awaiting final approval

for manufacturing polio vaccine. It has an excellent research capacity. Dr. Rifky has made substantial contributions to the study of Rift Valley Fever and Rabies viruses. It is building a new complex to include a high-level containment diagnostic laboratory. This is being designed on contract by Porton Down in the United Kingdom and will have one P4 and three p3 level laboratories.

21. The EOBPV is one of the most technically skilled elements of the biotechnology industry in Egypt.

22. Food processing is a growing industry. There is a large soft drinks industry with much manufacturing or compounding on licence. Cheese is an important commodity. Fruit juices are canned and jams are manufactured. There is a leather industry. These industries must or may use enzymes but apart from the proteases supplied by El Nasr to the leather industry no other information was obtained.

23. General Comment

In general the size of the biotechnology sector in Egypt is small and is concentrated at the low and medium level end of the technology scale. There is considerable opportunity for development to reduce high cost imports and to develop export markets.

III. PROGRAMMES OF RESEARCH AND DEVELOPMENT IN BIOTECHNOLOGY AND GENETIC ENGINEERING IN ORGANIZATIONS AND INSTITUTIONS AND THEIR APPLICABILITY TO INDUSTRIES IN THIS AREA

Genetic Engineering in Egypt

24. There is probably no research in genetic engineering using recombinant DNA in Egypt. None was observed or reported in Cairo and none reported in Alexandria. Two scientists both in the Department of Genetics at the Faculty of Agriculture Ain-Shams University have had some limited experience and facilities at every level in this field and in the related field of microbial genetics are the most serious obstacles to be overcome in the transfer of the new biotechnology in Egypt.

25. The deficiencies cannot be explained except as a result of neglect and mismanagement of teaching and research in microbial genetics, nucleic acid enzymology, molecular genetics and related fields over the past fifteen to twenty years. During much of that period, up to say 1979, it is important to note that these fields were largely in the realm of pure science - only microbial genetics could be applied in the production of mutants more efficient in the production of antibiotics, amino acids, enzymes etc. and this may have influenced policy-makers in a country where priority must be attached to applied science. It was during this period that the Japanese fermentation industry became so powerful based on a combination of applied microbiology, microbial genetics and fermentation technology. Even these subjects have not prospered in Egypt. In fact as will be observed later research in biotechnology is not supported in a way that presages success.

Current Research and Development in Areas of Biotechnology not Involving Genetic Engineering

26. There is a programme of research and development in biotechnology in government research centres such as the NRC, ARC and EOBPV and some relevant work is also being conducted in the universities. This will be discussed by sector noting areas of relevant research which is being conducted.

The Agricultural Sector: Livestock

27. The largest effect of the new biotechnology on the livestock industry is expected to stem from developments in three areas:

(a) Vaccines;

(b) Antibiotics;

(c) Growth Enhancers, e.g. bovine growth hormone.

The Animal Health Institute has a programme in the area of vaccines and there is co-operation with the EOBPV especially in the case of these diseases which affect both livestock and human populations. Rift Valley Fever Virus is an example of this and particularly because this disease was not known as a major problem in Egypt until the epidemic of 1977. The vaccine programme should be developed strongly in association with a new Genetic Engineering Institute preparing vaccines against diseases which have a high priority in Egypt and other related developing countries, but which have a low priority in the developed countries, and choosing carefully one or two which cannot be successfully prepared by traditional methods for inclusion in a genetic engineering programme. Under (b) Antibiotics, the development of this field in Egypt will be related to the capacity for the manufacture of synthetic and semi-synthetic antibiotics in general. Under (c) Growth Enhancers, there should not be a large Egyptian programme until results are available from the trials abroad.

The Agricultural Sector: Plants

28. The new biotechnology as referred to agricultural plants does not usually include the area of plant breeding by classical genetic methods. In fact the new biotechnology seeks to circumvent classical plant genetics - one major objective is to introduce new genes into valuable plant strains without genetic crossing. Three methods have been considered. In the first, cells of two species are grown in tissue culture, they are converted to protoplasts and combined in a single culture medium; fusion between protoplasts is promoted, and whole plants regenerated

from the hybrid protoplasts. In the second, pure DNA (gene) from one species is added to protoplasts of another which absorb the DNA, incorporate it into the chromosomes by illegitimate recombination, and are then regenerated into hybrid plants. In the third, plant DNA viruses (e.g. Cauliflower Mosaic Virus) or bacteria (e.g. Agrobacterium tumefacieus) are adapted by genetic engineering to act as vectors transferring genes from one plant species into another.

29. The work represented by any of these methods is at an early stage of development in the United States, Europe, Japan and elsewhere. Work of this kind in Egypt has not been described. It should only be undertaken after careful assessment of the probability of success. There are two important guidelines:

(a) Concentrate on the development of methods of tissue culture for its own sake, that is:

(i) As a method for mass propagation of valuable species which are difficult or expensive to propagate otherwise, e.g. oil palms (as has been done in the United Kingdom by Unilever), date palms (developing work already under way at Ain Shams University);

(ii) As a method or rapid strain improvement by clon tion;

(iii) As a method for preparing disease free stocks.

(b) In gene transfer experiments only undertake projects involving the expression of single genes. For example it is more likely to be possible to produce tomato plants which synthesize chicken ovalbumin, the product of a single gene, than to produce tomato plants which express the nitrogen fixation genes of bacteria which in nature form a symbiotic relationship with a legume. In this latter case an attempt is being considered to engineer the expression in a tomato of at least ten to twenty bacterial genes which normally function in a highly specialized organ, the root nodule, consuming large quantities of photosynthate in the process.

Under these guidelines a variety of valuable projects can be considered applying genetic engineering to plants under the following headings as examples:

(i) Transfer of single genes for disease resistance.

(ii) Transfer of single genes for metal resistance.

(iii) Transfer of single genes (or groups of genes composed in bacterial intermediates) for resistance to herbicides.

(iv) Transfer of single genes coding for proteins which enhance the nutrient value of the crop.

The Agricultural Sector: Pesticides/Insecticides

30. One important strategy under this heading which has been made more attractive by the development of genetic engineering is the search for bacterial and viral pesticides, particularly insecticides. About 100 species of bacteria are known which are insecticidal and three of them (B. thuringiensis, B. moritai and B. popilliae) are produced and used commercially. In some of the other cases the insecticidal effect is too weak to be useful, or the bacteria cannot be grown successfully on a large scale. In such cases the insectical activity can in principle be amplified by genetic engineering technology.

31. Venoms provide another example of the same general kind - that is they may contain powerful biological antagonists in minute quantities and if so these could be produced in very large amounts by genetic engineering.

The Oil Industry

32. The General Petroleum Corporation of Egypt has overall responsibility for national research related to oil within the Egyptian oil industry. There is in addition the Petroleum Institute of the ASRT and this is collaborating with the Institut Français de Petrole in a single cell protein using Spirillum. Biotechnology is being related to five areas of the petroleum industry:

(a) Production of Single Cell Protein from methane/methanol or CO_2. This is especially important as a method of making full use of natural gas which is often "flared-off". In the ICI process, Methylophilus methylotrophus is used with methanol as feedstock.

The Egyptian authorities are fully aware of the waste entailed in "flaring-off" and are developing fertilizer production, and domestic gas systems to reduce it. A new law is being promulgated to forbid "Flaring-off". While present levels of natural gas can probably be used productively, it will be advantageous to look carefully at SCP production as an additional "sink". Since natural gas can be converted more or less directly to food protein this must be considered carefully for its potential in relieving the Egyptian food problem.

(b) Enhanced Oil Recovery. Oil recovery can be divided into three phases. In the primary process the oil is expelled by "natural" pressures. In the secondary process further oil is extracted after pumping in water or other materials. These two processes are expected to allow recovery of only about 30 per cent of originally estimated reserves. If the remainder is to be recovered, Enhanced Oil Recovery (EOR) technology of the tertiary process must be resorted to.

Biotechnology and genetic engineering offer a new approach to EOR. Bacteria can in principle contribute to EOR in several ways:

(i) through partial degradation of the high molecular weight components of crude oil so decreasing and increasing flow;

(ii) through producing gas and therfore pressure;

(iii) through producing acid which etches the reservoir rocks increasing pore size and therefore flow;

(iv) through producing surfactants and polymers, e.g. xanthan.

A major object of research in this field is to identify bacterial species which can grow at the temperatures and pressures found in oil wells and which have some or all of the properties described, and genetic engineering will be used to improve and combine appropriate characteristics.

Some progress has been made. Dr. Chakrabarty has used bacteria to increase production from an experimental stripper well from one to six barrels per day. There are 500,000 stripper wells in the United States (each producing less than 10 barrels per day). Every increase of one barrel per day per well is equivalent to about five per cent of total United States domestic oil production. If increases are forthcoming from major wells the effect will be important in all oil producing countries.

(c) Transport of oil in pipelines. In discussions at GPC it was mentioned that biowax which blocks pipelines presents serious problems when crude oil is being pumped over long distances. Bacteria and/or fungi offer two possible lines of attack:

(i) The biowax could be degraded by bacteria introduced into the oil during pumping and

(ii) the source of the biowax could be inhibited or eliminated by antibiotics produced by bacteria or fungi introduced during pumping.

(d) Cleaning oil tankers and other installations. Bacteria and/or fungi may be used to degrade crude oil, waxes, sludge, etc.

(e) Reduction in pollution, cleansing waste, oil spills, etc. As in (d).

It was disappointing not to learn of any research and development in any of these areas in GPC.

The Chemical Industry: Bulk Solvents, Fine Chemicals, Pharmaceuticals

33. Genetic engineering and biotechnology are expected to leas to substantial changes in the chemical industry by:

(a) increasing the efficiency of fermentations to produce bulk organic solvents, organic acids, etc.;

(b) increasing the range of products made by fermentation;

(c) replacing chemical conversions by bioconversions in the fine chemical and pharmaceutical industries.

34. There is a pilot plant and related facilities at the NRC and there is some research in the area of bioconversions. The NRC through its staff collaborated in getting the acetone-butanol fermentation under way at Hawamdie.

35. No information was obtained on current research and development in this area either in industry or research institutions.

Enzyme Production

36. One of the largest effects of the new biotechnology is expected to be in industrial scale enzyme production. Only 20-30 enzymes are produced on a large scale e.g. α-amylase, proteases, β-glucanase, amyloglucoside, chymosin (rennin), etc. These "traditional" enzymes will be produced more efficiently and in principle any other enzyme required on an industrial scale will become available as necessary. Thus much international research is being devoted to identifying valuable new enzymes (especially from thermophiles) and amplifying their production by genetic engineering.

37. Some Egyptian scientists at the NRC and elsewhere are clearly informed about this aspect of biotechnology and some useful bacterial strains have been identified in the past, but little evidence was presented of intensive research in this area now. Screening of organisms for valuable enzymes is well within the current research capacity of the NRC. Genetic engineering to amplify enzyme production is not.

Medicine: Vaccine Production

38. There are strong theoretical reasons for postulating that genetic engineering will have an important impact on vaccine production, and in practice some vaccines have already been prepared by the novel methods and are under test.

39. Egypt has an active research programme in vaccine production and is in a strong position to develop this programme as appropriate through genetic engineering if a genetic engineering research group is established.

40. The present programme is centred on the Egyptian Organization for Biological Products and Vaccines (EOBPV) (human vaccines) and the Animal Health Institute (AHI) (livestock). Unfortunately there was not an opportunity to visit the AHI. The EOBPV has some research programmes which have attracted international attention.

Medicine: Genetic Disease

41. Serious genetic diseases - several thousand different Mendelian diseases have been characterized - may be treated in one or more different ways including two which will become more common as genetic engineering is applied to these problems. One method is protein or enzyme replacement therapy. If a genetic disease is caused by the lack of a protein or enzyme in principle these could be supplied. Usually there is just not enough of these materials available and so this therapy is rarely adopted. By genetic engineering they will gradually be made available. A second method, gene replacement therapy is more radical and has not yet been applied to any genetic disease. It is controversial and is unlikely to be introduced for many years. Protracted experimental studies and clinical trials on terminal cases will be required. It does however hold promise for patients with certain forms of thalassaemia, a genetic disease which is relatively common in Mediterranean countries including Egypt.

42. These methods will be important in the development of medicine in Egypt because the incidence of genetic disease in Egypt is relatively high due to demographic factors which also are responsible for the

variety of genetic disease in Egypt. The incidence and variety of genetic diseases have been studied in great detail by Dr. Nemat Hashem at the Faculty of Medicine, Ain Shams University.

43. One project particularly appropriate to the Egyptian situation is the appraisal and development of pre-natal diagnostic tests for thalassaemia. Some forms of the disease are always fatal, affected persons dying at about twenty even after the best treatment which is expensive to administer. Genetic engineering technology provides a new method of pre-natal diagnosis which should be introduced into Egypt and tested for its efficacy. A similar test is available for sickle cell anaemia, also found in Egypt, a disease which is one of the major public health problems in Nigeria and other sub-Saharan African countries. These tests need to be developed for use in district hospitals and clinics - Egypt could take a lead in this.

General Comments on Research and Development in Genetic Engineering and Biotechnology

44. There is a large research establishment in Egypt (700 PhDs and 3300 other staff in the NRC alone) many of whom are microbiologists, biochemists, geneticists, agricultural and medical scientists whose interests are related to biotechnology and who could undertake a substantial and valuable research programme in biotechnology.

45. The laboratories are often badly equipped and badly maintained (dust is a very big problem). Much of the equipment is old. The new equipment recently acquired at the NRC has not yet been fully commissioned. It will not be used to anything like full advantage unless there are other major changes in the R and D system.

46. The budgets of the research groups for consumables (chemicals, enzymes, glassware, plasticware) are low (LE 2000 - 3000 per annum for a group of five at the NRC). With little or no hard currency these conditions make meaningful research in many areas of biochemistry or microbiology or similar subjects impossible.

47. Salaries paid even to senior staff reported to be in the range of LE 100 - 200 per month, are insufficient.

48. There are virtually no incentives for successful research.

49. The research training given to M.Sc. and Ph.D. students is badly organized and badly funded. It takes on average ten years to complete a Ph.D. (The evidence for this can be seen in the staff lists of the Universities.) Such a system must destroy bright young scientific researchers, a great waste of talent.

50. Little evidence was presented of achievements in research. The establishment of Egyptian scientific journals (including the Egyptian Journal of Genetics and Cytology) is encouraging, but few Egyptian scientists have a substantial record of publishing in international journals. A list of publications by the staff of the NRC was not available.

51. The overall impression was that in the field of biotechnology, a large number of scientists are not producing substantial research proportional to their numbers. The infrastructure of research and development is not adequately financed nor organised.

52. There is great potential for research and development in biotechnology. There is no shortage of manpower with basic knowledge in the field. This manpower is presently unused, and is in effect available for retraining and re-direction.

IV. GOVERNMENT REGULATIONS AND POLICIES AFFECTING THE DEVELOPMENT AND TRANSFER OF TECHNOLOGY IN THE FIELD OF BIOTECHNOLOGY AND GENETIC ENGINEERING INCLUDING PATENT AND LICENSING LEGISLATION, TECHNOLOGY IMPORTS ETC.

53. The general impression obtained on these matters was that the government has not yet been able to place a high priority on the wide-spread development of technology-based industry in Egypt. Its priorities have been food, water, communications, health and education with industrial development concentrated on electricity, irrigation, oil, steel, sugar/molasses/organic solvents and acids. Channels for a continuous acquisition and adaptation of new technology for productive industry are not easy to identify. It was difficult to define economic structures which favour this process, Egyptian business enterprises being heavily concentrated on tourism, trading, property and financing rather than production.

54. Except as noted earlier the biotechnology sector appears to be rather weak. For example, Egypt uses large quantities of pesticides and herbicides (it was reported that 60 million dollars are spent per year on importing insecticides for cotton) and pharmaceuticals but only manufactures a small range of these products. It is not clear that there is sufficient widespread experience within Egyptian enterprises of high technology manufacturing processes of the kind employed in pharmaceuticals, micro-electronics etc., nor has Egypt yet attracted large scale investment by international corporations to locate manufacturing operations in Egypt. This is a useful method of introducing high-technology work practices and management which has been adopted successfully for example by Ireland through its Industrial Development Authority (IDA).

55. The Egyptian government and various associated authorities are now seeking to remedy these deficiencies but it will be some time before plans materialize.

V. RECOMMENDATIONS FOR THE DEVELOPMENT OF APPLIED BIOTECHNOLOGY IN EGYPT

The Application of Biotechnology in the Social and Economic Development of Egypt

Introduction

56. As outlined in section I, biotechnology and genetic engineering are being applied worldwide in the creation of new industrial, agricultural and medical enterprises which will have revolutionary effects on society over the next fifty years. Some developing countries are in a position to contribute positively to this revolution and to control and profit from its impact on their own societies, provided they recognise the opportunities and organize their scientific technological and industrial resources to take advantage of them. Egypt falls into this category. It has a long tradition of scientific research for example in agriculture and vaccines; an extensive though inadequately resourced university system; a large though underutilized research establishment with substantial international contacts; a fermentation industry; surplus raw materials (molasses, natural gas, urban and rural waste, straw); a strong geopolitical base. Given these resources a biotechnology industry can be developed in Egypt provided it is planned and organized with care and adequately financed.

The Time-Scale of Biotechnology and Genetic Engineering

57. Projects in biotechnology and genetic engineering depend on intensive research and development. It is rare for such projects to proceed from the drawing board to production in less than five years, although the time-scale is likely to be reduced as more experience is gained in the technology. For a country like Egypt with no experience in genetic engineering it is unrealistic to expect projects to come to the production stage in less than five years from the time that a team of trained scientists is assembled. This time-scale is not significantly different from that which is common in plant and animal breeding programmes or in major civil engineering projects. For such projects to succeed there must be an assurance of sustained support over this kind of time-scale.

Potential Benefits to Egypt from Biotechnology and Genetic Engineering

58. It has been argued in section III that there are many applications of genetic engineering and biotechnology which have the potential to benefit Egyptian society. These can be illustrated as follows:

(a) The oil resources of Egypt may be extended by EOR using genetically engineered microorganisms. There may be other effects on the oil industry as outlined including the manufacture of food (single cell protein) from natural gas.

(b) The fermentation industry may be developed to produce more organic solvents and acids more efficiently.

(c) The pharmaceutical and fine chemicals industry may be extended.

(d) Plant breeding may be accelerated and revolutionized by a combination of regeneration from tissue culture and genetic engineering.

(e) Genetic diseases, including thalassaemia and sickle cell anaemia, may be diagnosed more effectively, and some other genetic diseases may be better treated.

(f) There is a new strategy for developing vaccines against human and livestock diseases which may be applied to bacterial viral and parasitic diseases. It is being applied in research programmes abroad against malaria and trypanosomiasis and should be considered in Egypt for bilharzia.

A Central Question:

59. A question facing Egypt is this: Are all of these projects and many other similar ones to be carried out under licence or through importation from abroad, or should some be developed within Egypt and how?

One Answer to this Question Could be Based on an Applied Biotechnology Programme

60. In order to facilitate discussion on this question, an Applied Biotechnology Programme is outlined below and shows costs for a seven year period including an initial training programme of two years. It is based on four principles:

(a) The programme should be integrated and involve government, industry, research institutes and universities;

(b) The programme should have clearly defined social and economic objectives which can reasonably be attained within seven years, a two year training programme plus a five year research programme;

(c) The progress of the programme should be assessed annually;

(d) UNIDO should be requested to provide support services.

An Applied Biotechnology Programme

Objectives.

61. The objectives of this programme are:

(a) To solve a number of social and economic problems and to develop profitable industrial and agricultural enterprises through biotechnology and genetic engineering;

(b) To establish a corps of biotechnologists and genetic engineers who in conducting the Applied Biotechnology Programme are able to assess the developments in biotechnology and genetic engineering abroad.

Training; Research and Development; Product or Process Assessment; Production; Distribution and Marketing

62. The Applied Biotechnology Programme to be effective should lead to new products or processes which have measurable social or economic value in Egyptian society. The Programme should concern itself with the training of young scientists and technologists in those areas which are relevant to Egypt so that R and D teams can be properly staffed. These teams would have clearly defined objectives, new products or processes, which have to be assessed for their usefulness in industry, agriculture, medicine etc. They have to be developed so that they can be applied in factories, on farms, in clinics etc. and then distributed or marketed as appropriate. An idea in biotechnology is not fully realized until it has an observable effect on society.

The Board of Applied Biotechnology

63. The Applied Biotechnology Programme should be initiated and subsequently co-ordinatied by a Board of Applied Biotechnology. It might consist of about twelve members representing those areas in which applications of biotechnology are envisaged and those disciplines on which the programme will be based. UNIDO might be requested to advise on the appointment of experts as members of the Board. It would need a full time Executive/ Director and a small support staff. It would administer the Applied Biotechnology Programme including the disbursement and accounting of finances, and review assessment and control of the technological and applied aspects of the projects undertaken.

The Applied Biotechnology Programme

64. A scheme is outlined in this section which is designed to produce results within a seven year time-span. It takes into account the most serious deficiencies of the biotechnology research sector and is certainly not a complete proposal. It is put forward for consideration as an example of what an Applied Biotechnology Programme might be; the final programme can only be drawn up with much more substantial input from Egyptian scientists, technologists and industrialists and with advice on feasibility from consultants who are experts in particular aspects of biotechnology. It would be the responsibility of the Board of Applied Biotechnology to present the final programme.

65. This scheme comprises four elements:

(a) Training Programme.

(b) Applied Biotechnology Research Grant Scheme.

(c) Applied Genetic Engineering Research Centre.

(d) Industrial Biotechnology Research Programme.

Training Programme

66. There are apparently very few or even no experienced genetic engineers in Egypt. (It is emphasized that the term genetic engineer is used in its contemporary sense as a person who generates and manipulates recombinant DNA in vitro.) This is the most extreme example but it is likely that there are other gaps in Egyptian manpower, to be identified by the Biotechnology Board. In particular the numbers of industrial microbiologists, industrial biochemists, and process engineers will need to be assessed to ensure adequate staffing of the oil and fermentation industries which should be two important beneficiaries of a successful biotechnology programme.

67. The Training Programme will be necessary to meet demands in the short-term. It should last for two years and should enable thirty to forty Egyptian scientists and technologists to go abroad for training. Of these, twenty should be in the field of genetic engineering. There is no other short-term solution to the present problem of manpower deficiency in genetic engineering. Short courses in Egypt would not provide sufficient experience while long courses, that is lasting for a year or two, could not be staffed.

68. Applicants for this Training Programme should be assessed for their aptitudes as bench scientists as well as for their background in theory and their relevance and commitment to the Biotechnology Programme, UNIDO could be asked to facilitate the placement of these scientists in laboratories with established reputations.

Applied Biotechnology Research Grant Scheme

69. As stated there is a large research establishment which is not proportionately productive. The Biotechnology Board will need to investigate the reasons for this in greater detail but one obvious reason for the low productivity arises because researchers do not have sufficient funds especially foreign exchange to pay for chemicals, biochemicals, glassware, plasticware, small items of equipment, i.e. less than 1500 dollars per item, accessories and spare parts for large items of equipment e.g. rotors or tubes for centrifuges. A second reason for low productivity arises from the fact that the scientists are not paid adequate salaries and so are encouraged to acquire additional posts or responsibilities outside research for which they receive additional remunerations.

70. These two matters can be dealt with by establishing a competitive prestigious research grant scheme in applied biotechnology. Scientists would be requested to submit research proposals to the Biotechnology Board. Successful applicants would receive funds for research expenditure and a salary element. These monies would be channelled to the researchers in such a way that they are held entirely responsible for their management being accountable to the Biotechnology Board for both the finance and the science. Reports and accounts would be received annually. Grants would normally be renewable for three years in all but could be extended if justified by the results. The total number of grants should be about twenty in year one, with an additional ten starting in year two, and another ten starting in year three.

71. It is essential that the grant applications should be assessed by experts. It is routine in many countries with a small scientific establishment in a particular field, for such applications to be sent abroad for assessment and UNIDO might be helpful in this regard.

72. The Research Grants should be directed towards particular areas which might include for example: plant tissue culture; fermentations (to extend the range of organic chemicals in which Egypt is self-sufficient);

biological pesticides and insecticides; the microbiology and biochemistry of oil; disease resistance and salt resistance in plants; food storage: semi-synthetic production of antibiotics; the enzymology of fine biochemicals especially from plants e.g. diosgenin a raw material for contraceptive hormones; vinblastine used in cancer chemotherapy; novel industrial enzymes; biochemical basis of disease resistance in plants; the enzymology of biogas production; recycling of urban waste.

Applied Genetic Engineering Research Centre

73. Genetic engineering is a key element in most sophisticated biotechnology projects. It is itself a complex technology and is only conducted competitively when a critical mass of between ten and twenty experienced genetic engineers is assembled. It is essential that such a group be established in Egypt if advanced biotechnology is to be carried out there. The size of the group should be about twenty trained scientists which is large enough to undertake about five projects. This number is sufficient to ensure as far as possible that at least one or two will be successful in about five years, and yet it is small enough to allow the Centre to be got under way with the sort of resources which can reasonably be expected to be available, both human and financial.

74. The Centre would have a Director who would be responsible to the Biotechnology Board for the overall management of the Centre both financial and scientific.

75. The Centre would benefit greatly from having a Council of Scientific and Industrial Advisers which would review annually the performance of the Centre. This Council should be composed of experts who have specialized knowledge of the projects adopted by the Centre.

76. The Centre should be associated with the International Centre for Genetic Engineering and Biotechnology to be established under the auspices of UNIDO.

77. The Centre should undertake the training of about twenty graduate students to be selected after open competition.

78. The Centre should have a technical staff (technicians) of about twenty.

79. Staff members should be paid salaries which are on the one hand sufficient to ensure that they can devote all their time to their research, and on the other hand sufficient to induce them to remain in Egypt.

80. Senior appointments should be for two years in the first instance, renewable annually after review until five years, when staff members would become eligible for tenure. A system of incentives and rewards should be established.

81. The Centre should be located as closely as possible to the Egyptian Organization for Biological Products and Vaccines to take advantage of the major containment facilities (two P3 laboratories and one P4 laboratory) now being planned there.

82. The research programme of the Centre should be decided by the Biotechnology Board on the advice of the Director and Council of the Scientific Advisers of the Centre and in consultation with those sectors of Egyptian government, industry, agriculture and medicine likely to be related to or affected by the Applied Biotechnology Programme.

83. The research programme of the Centre should comprise of about five projects which have clearly defined objectives, which can be applied to solve or relieve social or economic problems, and which are reasonably believed to be attainable in five years.

84. The research programme of the Centre must be financed with adequate access to hard currency - most of the non-salary costs of the Centre will be hard currency.

85. The research programme of the Centre and the research projects funded by the Research Grants Scheme (see section V, paras 69-72) and in industry (see section V, para 87) would be considered in toto by the Biotechnology Board and integrated as appropriate. Projects initiated

in one place will need to be passed on to another as a matter of course but the Board would be responsible for ensuring that this occurs. It is crucial that scientific breakthroughs are realised in practical terms through full involvement of the industrial sector at all stages of the Biotechnology Programme.

86. When the research programme of the Centre is being drawn up it may be useful to consider projects in the following areas:

(a) Vaccines and Diagnostic Kits
- Gastroenteritis (Salmonella, Shigella, E. Coli)
- Bilharzia
- Leprosy

(b) Enhanced Oil Recovery

(c) Industrial Enzymes
Cellulases, Amylases, Pectinases, Chitinases, Proteases especially of thermophilic bacteria and fungi.

(d) Genetic Diseases
Diagnostic systems for thalassaemia and sickle cell anaemia.

(e) Biological insecticides and pesticides
from microbial and other sources, e.g. venoms.

(f) Plant biochemicals

Industrial Biotechnology Research Programme

87. The impression was gained from discussions and from visiting Egyptian industrial centres that Egyptian industry does not have a strong research and development capacity in biotechnology. Efforts to date appear to have been appropriately concentrated on commissioning processes and products from abroad rather than developing them ab initio in Egypt. But the

Biotechnology Programme is conceived as a source of new processes and products, for example related to the oil industry, the fermentation industry and the pharmaceutical and fine biochemical industry. These industries and perhaps others must be ready to interact with the Biotechnology Programme participating actively in all stages of its development. In order to do this the industries are strongly advised to increase their in-house commitment to research and development. The Biotechnology Board will have an important role in catalysing industrial research and development and may consider whether financing should be shared. The Industrial Development Authority in Ireland has a Research and Development Grant Scheme to encourage industrial investment in research, and this may be a useful model.

A Preliminary Estimate of the Cost of an Applied Biotechnology Programme

88. The cost of a programme has been estimated as set out below. The Estimates must be regarded only as preliminary. They do not take account of:

(a) the capital costs of siting and building the Applied Genetic Engineering Research Centre;

(b) the costs of the Biotechnology Board;

(c) the costs of any projects beyond the laboratory/pilot scale stage;

(d) the costs of the Industrial Biotechnology Research Programme or

(e) the cost of inflation.

The estimates are based on the assumtion that the Training Programme will last for two years. The Research Grant Scheme will start in year one but the Applied Genetic Engineering Centre will not become operational until year three. The programme gives costs to the end of year seven.

SUMMARY

Year	Training Programme	Research Grants	Genetic Engineering Centre	Total
1	450,000	300,000	-	750,000
2	450,000	450,000	-	900,000
3	-	600,000	720,000	1,320,000
4	-	450,000	420,000	870,000
5	-	450,000	320,000	770,000
6	-	?	320,000	320,000
7	-	?	320,000	320,000
	900,000	2,250,000	2,100,000	5,250,000
Hard Currency:	100%	66%	50%	66%

TRAINING PROGRAMME

Year 1 - Twenty grants renewable for three years total at 15,000 dollars per grant, being 300,000 dollars.

Year 2 - Twenty grants continued plus ten new grants, being 300,000 plus 150,000 = 450,000 dollars.

Year 3 - Thirty grants continued plus ten new grants being a total of 600,000 dollars.

Year 4 - No new grants. Thirty grants continuing = 450,000 dollars.

Year 5 - No new grants. Thrity grants continuing = 450,000 dollars.

GENETIC ENGINEERING CENTRE

		dollars	
Year 3	Equipment	400,000	
	Consumables	100,000	
	Library	5,000	
	Travel	5,000	
	Administration	10,000	
	Salaries	200,000	
	Total		720,000
Year 4	Equipment	100,000	
	Consumables/library/travel/ administration/salaries (as above)	320,000	
	Total		420,000
Year 5, 6, 7	Consumables/library/travel/ administration/salaries	320,000 x 3	
	Total		960,000
			2,100,000

Note

It is assumed that the Genetic Engineering Centre will not have P3 or P4 laboratories but will have access to these in the Vaccine Institute.

ANNEX I

Terms of Reference

In co-operation with the designated Egyptian counterpart and keeping in mind the technology advances in biotechnology and genetic engineering, the consultant will specifically be required to:

(a) review the state of technology of biotechnology and genetic engineering and its application in both private and public sectors in Egypt;

(b) review the overall programmes of R and D activities undertaken by various organizations and institutions in the field of biotechnology and genetic engineering and its applicability to industries in this area;

(c) review government regulations and policies affecting the development and transfer of technology in the field of biotechnology and genetic engineering including patent and licensing legislations, technology imports etc.

(d) recommend actions and measure to be undertaken by the government for strengthening national technology in this sector taking into consideration technological advances in the field of biotechnology and genetic engineering and its potential within the Egyptian context.

ANNEX II

Details of Mission

CAIRO

4 May 1982

Academy of Scientific Research and Technology

1. Genetic Engineering Committee, Chairman Dr. A. El-Bindary
2. President of Academy of Scientific Research and Technology, Dr. I. Badran

5 May 1982

Faculty of Medicine, Ain Shams University

1. Department of Paediatrics
   Dr. Nemat Hashem, Chairman of Dept. of Paediatrics, Head of Clinical Genetics
2. Department of Biochemistry
   Dr. Farid El Asmar, Chairman, Dept. of Biochemistry

6 May 1982

Agricultural Research Centre, GIZA

1. Dr. H. El-Hamawy, Chairman
2. Dr. Mohsin Al Didi, Director Cotton Research Institute at ARC

8 May 1982

National Research Centre, DOKKI

1. Dr. M. Kamel, Chairman
2. Dr. Nabiel Saleh, lant Chemist and Biochemist and Senior Administrator
3. Dr. M. Abdel-Samie, Microbial Chemistry and Fermentation
4. Dr. Assem M. Ali, Microbial Genetics

5. Dr. A.M. Allam, Microbial Chemistry
6. Dr. Samir M. Badr-Eldin, Microbial Chemistry
7. Dr. T.A. Elzainy, Microbial Chemistry

Academy of Scientific Research and Technology

1. Dr. El-Bindary, Chairman of ASRT,
   Committee on Genetic Engineering
2. Dr. Abd El Rahman, Institute of National Planning,
   Former Executive Director of UNIDO

9 May 1982

Faculty of Agriculture, Ain-Shams University

1. Dr. Saad Aly Zaky Mahmond, Dean of Faculty
2. Dr. Yussef Abdel Malik, Soil Microbiology
3. Dr. Sayed Hassan Hassanien, Genetics
4. Several members of the Department of Genetics at a Seminar
   and separately.

10 May 1982

Egyptian Organization for Biological Products and Vaccines

1. Dr. Imam Zagloul, Director
2. Dr. Rifky, Virologist

HAWAMDIA

11 May 1982

Organic Chemical Industries Ltd.

Sugar and Distillery Company, UAR

1. Chemist Abdel Moeti El Gazzar, General Manager
2. Dr. M. Abdel-Samie, National Research Centre,
   Consultant to Organic Chemical Industries
3. Members of the technical staff

CAIRO

12 May 1982

Academy of Scientific Research and Technology

1. Genetic Engineering Committee, Chairman Dr. A. El-Bindary
2. President of ASRT, Dr. Badran

15 May 1982

Academy of Scientific Research and Technology

1. President of ASRT, Dr. Badran
2. Dr. Ismail, ex-President of ASRT

16 May 1982

General Petroleum Corporation

1. Dr. M. Fouad Abdel Azim, Laboratories of Production and Geochemistry, Research Manager GPC
2. Dr. A.H. El Said, Research Expert GPC
3. Dr. Sayed M. Gh. tass, Manager Department of Chemical Analysis
4. Dr. M.A.A. El Zeftawi, Manager, Geochemical Laboratory
5. Dr. Omar Nassar, Petroleum Energy Division