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CAPABILITY BUILDING IN BIOTECHNOLOGY AND GENETIC ENGINEERING IN DEVELOPING COUNTRIES*

Four papers prepared for a UNIDO-sponsored symposium held during the 150th annual meeting of the American Association for the Advancement of Science

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PREFACE

During the 150th annual meeting of the American Association for the Advancement of Science (AAAS), held from 24-29 May 1984 in New York city, the United Nations Industrial Development Organization (UNIDO) sponsored the symposium entitled "Capability Building in Biotechnology and Genetic Engineering by Developing Countries". The four persons who presented full-length papers on this occasion were: Dr. S. Riazuddin, a scientist who works in Pakistan; Dr. R. Wu, a scientist from a developing country who has spent his working life in a developed country university and serves as an adviser on biotechnology to the government of the People's Republic of China; Dr. D. McConnell (co-arranger of this symposium), who was born and trained in a developed country, Ireland, and continues to work there while at the same time giving much of his time to helping scientists from developing countries gain knowledge and know-how in genetic engineering techniques; and Dr. R.A. Zilinskas (symposium arranger), an industrial development officer with UNIDO whose main task is to assist in the establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB). As can be seen, the four participants were, and continue to be, directly involved in helping developing countries build advanced capabilities in biotechnology.

It has become almost a truism that recent advances in biotechnology, such as genetic engineering, hold great promise for helping the developing countries solve their pressing needs in relation to health, food, and energy. The question remains how best to make certain these advances, all realized through R&D in developed countries, will actually benefit the Third World. This can be partially done by focusing applied R&D being performed in the developed countries to find answers for specific problems in the developing countries and, over the longer term, by strengthening the capability of Third World researchers to perform advanced biotechnology R&D and encouraging their industrialists to capitalize on the results. Important vehicles for

mobilizing the resources of the scientific community to make certain that the promises of biotechnology are realized include intergovernmental organizations. UNIDO has been active in this endeavour since early 1981, taking four general approaches: (i) promoting and establishing the ICGEB wherein R&D of pertinence to the developing countries will be performed by world-class scientists and where Third World researchers will be trained in advanced techniques; (ii) providing expert advisory services to the governments that are formulating national policies and programmes vis-à-vis biotechnology; (iii) acting as a "technology scout" by catalyzing joint cooperative projects between R&D units in developed and developing countries, likewise by promoting joint commercial ventures; and (iv) seeking the cooperation and involvement of scientists and technologists of all countries in the tasks of boosting national capabilities.

At the AAAS symposium, UNIDO was represented by one of its officials and three working scientists who served as scientific experts. As has already been mentioned, all are involved in building a biotechnology capability in developing countries. This group aimed at achieving the following: (i) clarifying the conditions under which bioscientists work in developing countries; (ii) reviewing the past efforts by UNIDO in biotechnology vis-à-vis the Third World for the purpose of drawing useful lessons for suggesting and/or enhancing future activities, both by UNIDO and other organizations; (iii) stimulating an exchange of ideas between symposium participants and the audience in order to generate further thoughts on the developing countries' prospects and problems; (iv) introducing the ICGEB to a wide sector of the scientific community and discussing its role as a vehicle for capability building in new biotechnology; and (v) compiling a roster of scientists and technologists active in new biotechnology who may wish to lend their assistance for advancing capabilities in the Third World.

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BASIC INGREDIENTS REQUIRED FOR CAPABILITY BUILDING IN GENETIC ENGINEERING AND BIOTECHNOLOGY IN DEVELOPING COUNTRIES: SOME OBJECTIVES FOR THE INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY

by

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I. INTRODUCTION

The new interest in biotechnology in the 1970s can be traced to a number of discoveries in different areas of research in molecular and cell biology. For example, in molecular genetics the discovery of the type II restriction enzymes greatly facilitated the manipulation of DNA molecules in vitro, now referred to as recombinant DNA or genetic engineering technology. In immunology the discovery that immunoglobulin (antibody) producing cells could be hybridized with tumour cells and that resultant "hybridoma" cells would continue to produce immunoglobulins and could be readily cultured made possible the production of monoclonal antibodies and gave new impetus to the use of immunological methods in many areas of biology. Other key discoveries preceded and followed, but these in particular played critical roles in stimulating interest in the new biotechnology.

In 1976 the first genetic engineering company, Genentech, was founded in San Francisco, financed by venture capital, and in 1983 human insulin purified from genetically engineered bacteria was marketed in the United States. In that same year according to the US Office of Technology Assessment (OTA) more than US $1 billion were invested in the commercialization of new biological techniques by the private sector in the US and to US research related to biotechnology (1). Japan, West Germany, UK, Switzerland and France, in that order, have also invested heavily in biotechnology. The OTA report considers that the US has a substantial lead. If this lead is maintained and carried through from the level of basic research to commercial realization on the scale envisaged both by scientists and industrialists, the US and the other free market economies will have masterminded a new industrial revolution, affecting many activities in medicine, agriculture, manufacturing industry and energy.

Most developed countries have been involved to various degrees in the basic sciences which gave rise to the new biotechnology, and, following the lead set by Genentech in 1976, private industries or government agencies, and sometimes consortia involving both the public and private sectors, have set up companies making use of pre-existing

scientific knowledge and technological skills. However, some developed countries, where the basic sciences are not so strong, are faced with the possibility that they may not contribute significantly to the generation of the new biotechnology industry. Further, in 1981 a report for the United Nations Industrial Development Organization (UNIDO) drew attention to the position of the developing countries (2). It concentrated on the technology of genetic engineering and noted that the "recent scientific literature indicates that people in developing countries know little if anything about genetic engineering and the importance of recent advancements in research". This judgement implied that the developing countries will not benefit rapidly from the new biotechnology and that they will be beholden to international science and industry unless the problem is recognized and dealt with. The developing countries have been caught unawares and unprepared and must now set about building capability in biotechnology.

The UNIDO report (2) suggests that the problems faced by the developing countries are on such a scale that international efforts would be required; accordingly, it contains a proposal that "international research and training centres should be established under the auspices of the United Nations". It envisages that this facility would have three purposes: to help in the training of a core of professional scientists who would have the responsibility for furthering education and research in their own countries; to assist in the solution of particular research problems of developing countries by the application of genetic engineering; and to conduct basic research in genetic engineering whose results would be shared with all interested countries. These basic ideas have led to a series of discussions organized by UNIDO over the last three years. The discussions involved scientists, industrialists, government officials and political figures in many different countries and eventually led to the establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB). This entity will have a crucial role to play in the transfer of the science and technology of genetic engineering and biotechnology (GEB) to the developing countries. It seems appropriate at this halfway stage, with the ICGEB founded <u>de jure</u> but not <u>de facto</u>, to record something of the process by which it has come into being.

This process revealed many of the difficulties faced by the developing countries in dealing with contemporary science and technology. It amply confirmed the judgement that genetic engineering is not understood in developing countries and it suggested a series of steps which need to be taken to remedy this situation. In this paper the ideas behind the establishment of the ICGEB and the process of its formation are described. Some proposals will be presented as to how, as a relatively small institution, it may undertake its task of facilitating the growth of GEB in developing countries.

II. EXCHANGE OF VIEWS ON GENETIC ENGINEERING AND BIOTECHNOLOGY IN RELATION TO DEVELOPING COUNTRIES: THE PROPOSAL TO ESTABLISH THE INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY

The paper prepared by Dr. S. Narang was amongst those presented for discussion at a meeting convened at Vienna in February 1981 under the auspices of UNIDO, the International Federation of Institutes for Advanced Study, the Club de Geneve and the Foundation for the Reshaping of International Order. The meeting was attended by nine practising molecular biologists and microbiologists (3), as well as representatives from international groups and industry. The scientists all had close connections with developing countries. They set out:

(i) "to examine the implications of the advances in genetic engineering fo the developing countries";

(ii) "to outline the nature of the technological capabilities to be built up by developing countries in order to take advantage of such advances";

(iii) "to examine the possibility of establishing a broad based international promotional and development facility for scientists and technologists from developed and developing countries to work together" (4).

They were in accord that international action was required and requested UNIDO to take on the responsibility for stimulating and coordinating a programme designed to foster GEB in developing countries. It was agreed that "there is a need for an international centre for genetic engineering and biotechnology". Their judgement was, on the one hand, that GEB was going to be extremely important for developing countries, and on the other hand that there was a "relative lack of awareness in this field in many developing countries". Most of the scientists at this meeting had first hand experience of the state of GEB in both developed and developing countries and understood well the weakness of the underlying basic sciences in the latter. In effect, this report was both scientifically authoritative and culturally sympathetic. Given the scientific reputations of the scientists involved it was likely to be respected. The group suggested that UNIDO prepare a report on the proposed centre to see if the idea of the centre which had come from experimental scientists would attract political and financial support - in effect, they called for a widening of the discussion.

In the following six months consultant scientists and UNIDO representatives visited 16 countries (both developed and developing) and some international organizations and conducted a very wide range of discussions with scientists, officials and political figures. They reported in October 1981 that there was widespread interest in GEB and support for the proposal that the ICGEB be established (5). They noted "the pervasive feeling that unless timely action is taken countries will stand to lose in the structural changes ahead". They identified at first hand the "great shortage of trained scientific and technological manpower in this field", the need for international exchanges and cooperation and for international advisory services at all levels extending from information on experimental protocols to discussions on the development of institutional and national policy. They observed the opportunities and the needs for regional collaboration. It was apparent that the ICGEB would have many more uses than were suggested in the original proposal. More than that, the report concluded that "only the setting up of such a centre will ensure the critical mass of international action and effort consistent with the wide ranging potentialities and implications of genetic engineering and biotechnology" (6).

In reaching this conclusion it is evident that the authors of the report were anxious to emphasise some critical features of GEB. These had been referred to directly or indirectly in the two earlier reports, but at this stage they came more sharply into focus as the authors argued that the ICGEB was not just a useful mechanism to catalyse the transfer of GEB but that it was the "most practical and effective means of assisting, in an integrated fashion, the strengthening of national technological capabilities in this important field". They explained that genetic engineering and biotechnology represented a field which was remarkably wide and dynamic. One of the underlying sciences, broadly referred to as molecular biology, in which this group of scientists had been trained, has arguably grown more rapidly and extended more widely than any field of science in the last thirty years. Yet molecular biology is only a part of biotechnology which derives from a range of sciences extending from chemical engineering to genetics. The report noted that research and training in biotechnology cannot be sustained at the highest level unless a wide range of disciplines are represented. These scientists had first hand knowledge of the way research and training in molecular biology had thrived in the great research institutions of Europe and North America and they envisaged the creation of the ICGEB as sharing the essential characteristics of "transdisciplinarity", but dedicated to the needs of the developing countries. They found that the international scientific community was "overwhelming" in its support for the Centre, but that it was concerned that the ICGEB would not succeed unless it established a standard of excellence from the start: "A sub-critical effort might rapidly erode ICGEB's attraction as a centre of excellence". Scientists would like to participate in the activities of the ICGEB but "the extent to which they actually do would depend on the location and facilities of the Centre". The authors were acutely aware that the international scientific community of molecular biologists, and others who understood the complexities of GEB, would only support a scheme for the transfer of this science and technology, if they were convinced of attention to standards which would be required to ensure its success.

. The report addressed one other possible mechanism of facilitating technology transfer: networking. "The mere networking of existing

institutions will not have the desired effect in itself" (7). Some countries, indeed most developing countries, have no institutions capable of contributing significantly to a network in GEB (as the field had been defined in the UNIDO reports) and those institutions that might conceivably be included were, by implication, considered not to be capable of providing the necessary leadership or impetus in undertaking what amounts to a crash programme to invigorate developing countries with the science and technology of GEB.

In the case of a network of existing institutions the report noted that none of them would have the transdisciplinary character of the range envisaged for the ICGEB. Although it was not stated, it can be deduced from the report that many highly qualified scientists, who expressed doubts about the ICGEB meeting their standards of excellence, would not have given much thought to the idea of participating in a network of existing institutions. The transfer of GEB to developing countries will be accelerated much more effectively with the support of internationally respected scientists; the ICGEB seemed to offer a mechanism for enlisting this support in a way which networking could not match in this particular field.

Although the report did not see networking as an alternative to the ICGEB, the discussions certainly led to a broadening of the concept of the Centre and especially to a much more detailed consideration about how it would be associated with existing institutions and how it should support the establishment and development of national and regional institutions specializing in GEB. It was proposed that the ICGEB should "promote networking of national and regional institutions engaged in genetic engineering and biotechnology so as to mobilize their efforts in the service of the developing countries". This and other references in the report were part of a theme which was to arise again at the subsequent Belgrade meeting and underlay many of the problems that arose at other times, especially in regard to the location of the ICGEB. Developing countries have particularly strong national feelings; they display remarkable diversity in culture, geography and politics and so forth, and usually they have trifling discretionary funds for investment in science. Networking, which implies the expenditure of money in one's

own country, or as an alternative, within a region of common culture, is more desirable politically than the establishment of a single international centre, the financing of which was sure to be a most difficult matter and might lead to the accrual of disproportionate benefits to the country in which the Centre is located. Networking had other potential advantages, for example in ensuring a greater degree of local control in the choice of research programmes and providing a conduit for the transfer of knowledge and skills into each participating country. These matters were certainly regarded as extremely important in the report which emphasized that the ICGEB must establish close connections with national institutions for reasons of science, otherwise it would not be able to implant GEB in the different countries. Networking, although not a substitute for the ICGEB, should be an important objective once the ICGEB was established.

The report outlines some roles for ICGEB in research and development, training, the promotion of cooperation including networking at national, regional and international levels, the provision of advisory and information services, the organization of meetings, and the organization of supplies of critical materials. The ICGEB research programme is discussed, listing the fields within genetic engineering and biotechnology likely to be most relevant to developing countries. A training programme is suggested to be closely linked to the research programme. Trainees would be accepted on much the same basis as post-doctoral fellows to participate for a number of years in the research programme thereby gaining a thorough experience. Additional trainees would be funded to go to other institutions. Trainees are to be chosen on the basis of their potential to create groups around them in their home countries, and with a "commitment made by the sending country" to provide adequate local facilities. The report has a range of imaginative suggestions, which in themselves provide further justification for the ICGEB, and put forward some ideas on the constitution of the ICGEB, and its scale in terms of space, personnel and financing. There would be a Board of Governors drawn from participating countries and a Board of Scientific Directors composed of eminent scientists. The scientific staff would consist of a director, 30 scientists and 30 technicians, and be able to train on site about 100

scientists over a five year period. Capital expenditure (excluding land and buildings which would vary greatly with location) would be US $9.5 million and operating costs US $29 million for a five year period (at 1981 prices).

The report had a last, short section discussing the location of the ICGEB, a matter which has perhaps done most to hold up the foundation of the ICGEB. It was noted that the facilities of the ICGEB would have a crucial effect on the ability to attract staff who in turn will determine the quality of the Centre. Four factors were listed for consideration when the location was being chosen - basic infrastructure, industrial environment, social infrastructure and national commitment.

The recommendations of the Report on the Establishment of an International Centre for Genetic Engineering and Biotechnology are shown in Table I.

III. THE BELGRADE MEETING ON THE ESTABLISHMENT OF THE ICGEB

The UNIDO report Establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB) of November 1981 (5) recommends that UNIDO "follow up its initiative" and "pursue the question of the Centre vigorously", enlisting the support of scientists, consulting with other international agencies and organizations, and negotiating with interested governments. It recommends that UNIDO "convene a meeting of participating governments". In the following twelve months teams of UNIDO officials and consultants prepared more detailed plans for the statutes, staffing, research programmes, financing and other matters for consideration by a meeting of interested governments. Members of the UNIDO Secretariat discussed the ICGEB in many countries seeking political and financial support. There were indications from Mexico, Sweden, Ireland, France, Canada and Belgium of interest in supporting the establishment of the ICGEB, but it was clear that commitments to provide the financial support for the ICGEB would be postponed until the nature of the Centre was more fully described and until it received substantive international political support. This political support emerged at the Belgrade meeting in December 1982.

The High Level Meeting on the Establishment of the International Centre for Genetic Engineering and Biotechnology was convened jointly by the Government of Yugoslavia and the UNIDO Secretariat. Representatives were invited from 35 countries where interest had been expressed in the ICGEB. Representatives came from 28 countries, while seven other countries, some not on the original list, sent observers, as did nine international organizations and one industry.

An introductory address was given by Dr. Abdus Salam, Nobel prize winner and Director of the International Centre for Theoretical Physics (ICTP), the first UN science centre established in 1960 under the auspices of the International Atomic Energy Agency (IAEA). He rejoiced at the prospect of a second UN science centre and continued the theme identified in the UNIDO reports. He referred to two theses; one, that "science transfer must go together with technology transfer if technology transfer is to be meaningful" and two, that "the best vehicles for both science and technology transfers were high level science and technology centres created and run by the United Nations Organization". He argued that such centres give scientists from developing countries "opportunities to contribute scientifically on equal terms" and foster idealism among scientists in the cause of the developing world. He saw too the need to protect biotechnology from the secrecy beginning to impinge upon it as industrial interest developed. His address echoed the ideas of the UNIDO consultant scientists. The ICTP in Trieste, established in Physics for the same reasons proposed for the ICGEB in Biology, has been a success. Each year 2000 physicists, half from the developing countries, visit the ICTP. It is now financed mainly by the Government of Italy with other support from Sweden, Japan, Denmark, USA, FRG, the Netherlands, Kuwait and the OPEC Fund, operating under the auspices of the IAEA and UNESCO.

The meeting was, in overall terms highly successful. The great majority of the delegates spoke in favour of the idea of the ICGEB and the Conclusions and Recommendations (Table II) reflected this clearly (8). There was virtual unanimity that the ICGEB be a "centre of high excellence" and strong sentiment that it should be located in a developing country (Table II, paragraphs (iii) and (iv)). It was

recognized however (Table II, paragraph (iv)) that the location had to be chosen with great care bearing in mind the need to attract outstanding scientists whose work would establish the quality and reputation of the ICGEB. It was also decided (Table II, Paragraph (v)) that preparations be started to develop a network of affiliated "regional and/or national centres".

IV. THE REPORT OF THE SELECTED COMMITTEE

It was decided to pursue the main outstanding matters of location and finance by asking interested countries to submit offers to UNIDO by 31 December 1982. A questionnaire was to be prepared by UNIDO and distributed to the offering countries with replies to be received by 20 February 1983. A broadly representative Selected Committee of scientists was to be established with members from Yugoslavia (host of the Belgrade meeting), Hungary (for the centralized economies), Sweden (for Europe), Nigeria (for Africa), Indonesia (for Asia), Argentina (for the Americas), China and UNIDO. I served as the UNIDO representative and as the Chairman of the Selected Committee. The Committee was to examine the replies to the questionnaires and then to visit each candidate country. It was to report on "its findings including the merits and demerits of the several locations offered from its point of view of realizing the objectives of the Centre"; the report was to be presented to a Ministerial-Level Plenipotentiary Meeting. The terms of reference of the Selected Committee were wide, covering physical facilities, scientific infrastructure, support services, finance and legal provisions, especially those related to the international character proposed for the ICGEB. It considered offers from Belgium, Cuba, India, Italy, Pakistan and Thailand and visited these countries plus Sweden.

The Selected Committee had a unique opportunity to assess the prospects for the ICGEB from many different viewpoints in both developed and developing countries. Extensive discussions were held with political leaders, government officials, planners, administrators, scientists and students and the Committee received many written submissions and supporting material. Visits were made to universities, research centres,

libraries, computer centres, industries and agricultural stations. For two and a half months as the Committee travelled its members listened, observed, questioned, analyzed and discussed, accumulating a body of knowledge and forming opinions about GEB and developing countries.

(a) The political and governmental view

In each country the Selected Committee was received by Cabinet Ministers and in three (Sweden, Cuba and Pakistan), by the Head of State. This level of political contact is a measure of the importance attached to the question of GEB in developing countries at this time. Science and technology have had very large effects on the developing countries, perhaps most noticeably in medicine, and political authorities in these countries perceive the capacity of science and technology to solve major social and economic problems. Moreover, it is certainly the case that if some of these problems are to be addressed through GEB, the State has a much greater role to play than in the developed countries, given that the high technology private industrial sector is either weak or non-existent in most developing countries. The leaders of developing countries whom we met clearly expect GEB to be important in the future and are willing to support it. One question which emerged is whether they will be properly advised on the structures required for teaching and research in GEB, the kinds of research and development programmes, the costs, the time scales and the criteria for success.

It was apparent in several countries that the expectations among some politicians were unreasonably high, that they had not been properly advised and were likely to end up supporting the wrong projects and the wrong people. I shall return to the set of problems underlying these observations later in the paper, as I see a major role for the ICGEB in providing objective advice on GEB to the authorities in developing countries. Allowing for these cautionary remarks, the message was clear that the prospects for GEB had been assimilated at high levels in governments and that the small numbers of indigenous scientists trained in GEB had good contacts with senior politicians and officials. The UNIDO proposal to establish the ICGEB had obviously stimulated and

accelerated the formation of these contacts. New planning boards were being established, policies formulated, new laboratories built, new courses designed, and scientists sent abroad to be trained, all with the immediate approval and sometimes close supervision of senior politicians and government officials. GEB now has a very high political profile in developing countries.

(b) GEB projects in developing countries

The high political profile of GEB is certainly justified by the prospects for the application of GEB in developing countries, even if these prospects may be on a longer term basis than is usually accepted. In each developing country visited by the Selected Committee there were examples of how the new biotechnology might be applied with results in the near future. In Cuba the sugar cane industry is of vital importance. The primary products of molasses and sugar, rich carbohydrates, could be more efficiently utilized. They are potentially valuable feedstocks for the industrial-scale enzymological processes which should emerge from the GEB revolution. The international cane sugar industry has been threatened by the industrialization of one enzymatic reaction (the conversion of glucose to fructose by immobilized glucose isomerase), but this same industry could be revitalized by the application of similar processes. Moreover industrial-scale enzymological conversions should also be applied to bagasse, the by-product of sugar cane. It too is potentially a rich source of carbohydrate, mostly cellulose, which is convertible to sugars and ethanol. The impact of genetic engineering is already materializing with several reports on the cloning of genes for alpha-amylases, cellulases and beta-glucanase. These are some of the enzymes which will be valuable in the catalysis of economically important conversions of polysaccharides. The newly-identified ligninase of Phanerochaete chrysosporium will be an important subject of research in this area.

In Pakistan there is a greater climatic range than in Cuba so the range of economically important crops is correspondingly greater. There

are substantial opportunities to add food value to the crops through better utilization of by-products through industrial-scale enzymology. Prevalent tropical infectious diseases will be more accurately diagnosed through the use of monoclonal antibodies and nucleic acid probes, and more importantly, novel vaccines developed by recombinant DNA will be introduced.

In Thailand striking data were presented to the Selected Committee on the incidence of thalassaemia and HbE, genetic disorders of the blood. These affect a very large percentage of South East Asians but can now in principle be diagnosed in unaffected carriers and in the foetus by using nucleic acid probes. These new techniques can lead to the near eradication of these diseases, provided that they are made available in practical form, and that therapeutic abortion is socially acceptable. These and related genetic diseases are also widespread in East and West Africa and in Mediterranean countries. Another major line of interest in Thailand is malaria, unfortunately reappearing in many tropical countries. Genetic engineering is being used to study the surface of the malaria parasite in its different forms and there are prospects that a novel vaccine may be developed from this work (9).

In India there was substantial interest in the development of many novel vaccines. Leprosy remains an immunological puzzle and has been difficult to study partly because the causative bacterium Mycobacterium leprae is cultured only with extreme difficulty. It will be possible to clone M. leprae genes coding for surface antigens into E. coli and so generate new reagents for the diagnosis and study of leprosy. These lines of research should also lead to novel vaccines, though here one should be cautious given the unusual features of the immune response to leprosy (10). New vaccines against tuberculosis, cholera, typhoid, polio, measles and hepatitis are also expected to be developed by recombinant DNA, as well as a set of vaccines against a variety of animal diseases (11).

These are merely a few reflections of any discussions on the applications of GEB anticipated in the short term in the four developing countries visited. Long term prospects, especially in the genetic

engineering of plants, were often considered, but as in developed countries, many scientific observers were cautious in their assessments. In Cuba there was much interest in interferons and a very well-equipped and well-staffed research centre has been established - the Centre for Biological Research (CIB). Interferon is being produced from buffy coat by the Finnish method, and some clinical trials have been conducted. There is also an active research group working on the production of interferon by genetically-engineered E. coli. The Selected Committee were unanimous in their high assessment of the facilities, the personnel and the quality of the work, and this is the judgement which it is important to record. In my own opinion, shared I believe, by other members of the Committee, the CIB was the best endowed laboratory we visited in the four developing countries. It closely resembled similar laboratories in the US and Europe, although it was small, with less than 50 personnel, and was working in virtual isolation. On the one hand it is an example of what can be and is being done in developing countries and on the other it demonstrates the need for an international centre such as the ICGEB to facilitate the transfer of new ideas and techniques which are emerging at a tremendous rate and which isolated laboratories have great difficulty in keeping abreast of.

(c) The research capacity for GEB in developing countries

In general, the GEB research base, particularly in molecular genetics, at institutes and universities in each developing country visited by the Selected Committee, was observed to be weak. In effect, none of these countries presented substantial evidence of GEB research being conducted at a competitive international level. For the most part the research facilities were primitive, the equipment was out-of-date or non-existent, the libraries were usually incomplete and often poorly maintained, the consumables budget, which must be large for genetic engineering, was usually much less than required and the number of senior staff with recent hands-on experience of modern laboratory techniques was low. Of course, the visits were short. In some countries such as Cuba, most of the major research institutes were visited, whereas in others especially India, only a small proportion were visited. However, in

every country the research centres visited were the top ranking ones in the country. With the exception of the CIB in Havana, not one of these laboratories was sufficiently equipped, funded, staffed or organized for molecular genetics. The usual arrangement was for one or perhaps two faculty or staff members of an institution carrying out or supervising molecular genetic research. One or two graduate students or technicians acted as assistants. In some laboratories where it was purported that molecular cloning was being carried out, the Selected Committee found only one or two relatively junior people working without an experienced supervisor. Reagents were in short supply, especially isotopically-labelled compounds, enzymes and fine chemicals; they were difficult to obtain not just because of finance, but also because of problems of communication, transport and customs clearance. (Many of these problems are discussed by Dr. S. Riazuddin elsewhere in this volume.)

The grim overall picture was relieved by the occasional scientist who thoroughly understood molecular genetics. Usually these scientists had studied and researched abroad, and faced virtually insurmountable problems in recreating the facilities for research programmes in their home countries. These are the people who must be given the responsibility for developing GEB and its underlying sciences in the developing countries. They have shown themselves intensively committed to their countries - the ones referred to could have easily found good positions abroad.

(d) <u>The teaching capacity for GEB in developing countries</u>

Although the apparent quality of the universities in their capacity for <u>teaching</u> GEB varied greatly in the four main cities of developing countries visited by the Selected Committee - Havana, Lahore, New Delhi and Bangkok - the impression was clear that the staff were always working under considerable difficulties. None of the universities visited has strong molecular genetics groups, courses tend to be traditional and it was apparent that the laboratory facilities are not adequate for providing good experimental training at the undergraduate or postgraduate levels. There are too few specialist staff and they are sometimes spread

between several departments or institutions. Library facilities are sometimes good as in the new campus at Mahidol University, Bangkok and the Biological Library of the Academy of Sciences in Havana. In other places libraries were inadequate. Some had been forced to stop taking major journals as funds were no longer available - poignant evidence of the problems faced. Nowhere was there that close and free relationship between books and students which should be so much a part of learning and research in contemporary molecular genetics.

In every centre there were some members of faculty who were well-read in molecular genetics, some had active research groups and some collaborated with laboratories abroad. But none of the university groups were close to realizing their full potential, being always seriously impeded by poor facilities for teaching and research. The experimental scientists, especially those who depend on high quality chemical and biochemical reagents and complex instruments, are at a serious disadvantage in the universities of the developing countries. They are like carpenters without saws, skilled and knowledgeable but often utterly ineffective, stymied by lack of facilities. This condition represents a waste of talent and appears to have had the more serious effect of biasing the main teaching and research programmes in biology towards the observational rather than experimental side of the subject. Such experimental programmes as do exist are of a rather more traditional kind. The overall impression is of biology as it was in the 1930s, with occasional, almost idiosyncratic or capricious accretions, as for example an up-to-date electron microscope in an otherwise very poorly equipped laboratory, or a set of about 20 gamma counters laid out on benches behind double locked doors.

(e) <u>The response by scientists to the Selected Committee</u>

Scientists in each developing country were extremely interested in the idea of the ICGEB. Some had had direct experience of GEB, sometimes abroad, and were trying to develop research and teaching programmes. Many of these scientists were coming up against the problems of lack of resources and lack of understanding. The UNIDO initiative on GEB

provided a point on which to focus discussion. There was already much active discussion of GEB and the UNIDO documents seemed to have been helpful in adding weight to the arguments for increased investment in GEB. After the Belgrade meeting the scientists and administrators in all four developing countries quickly coordinated their efforts and produced offers within 2-3 months to host the ICGEB and answers to the UNIDO questionnaire. This required considerable commitment on the part of the Governments of these countries as well as the institutions involved in the planning, management, and construction of the project etc. The Selected Committee was enormously impressed by the keen broadly-based support which had materialized for the project extending from the scientists to the political leaders. It was plain that the scientists were seizing the opportunity of the ICGEB project to press their case for more support for teaching and research in GEB and that the governments were sympathetic.

(f) The report of the Selected Committee (12)

The Selected Committee summarized its views on its enquiries about the role of GEB in developing countries and the need for an institution such as the ICGEB as follows:

> "The Selected Committee has greatly appreciated the unique opportunity offered to it to meet the working scientists in their own laboratories in so many countries. The Selected Committee has often been impressed by the quality of the science being conducted, sometimes under difficult circumstances and essentially in isolation from the international scientific community. The value of this science is increasingly recognized by the relevant authorities and wide support is being given to the fundamental areas of molecular biology, microbial genetics, biochemistry and fermentation processes, which have in some cases formerly been neglected. Recombinant DNA technology (genetic engineering) which has grown out of these fundamental sciences is now being used in some laboratories in developing countries though the efficiency of the projects is not usually high. It has been difficult to assemble the necessary numbers of experienced scientists to form a "critical mass" and it has often been difficult to arrange for sufficient support in terms of materials, technical support, information flow, buildings, etc. However, the potential of genetic engineering and biotechnology is widely known at high political levels and there is a keen appreciation

of the need to increase the efficiency of the research and development groups in this field. All developing countries visited have started programmes in genetic engineering and biotechnology. These activities in the developing countries show in the first place the need for the ICGEB and in the second place that the ICGEB will be able to construct and act as a resource centre for a network of affiliated regional and national centres.

The Selected Committee, considering the main tasks of UNIDO, has seen at first hand the need to transfer the powerful science of genetic engineering and biotechnology to developing countries. In each developing country it has been made aware of research projects which are unique to that country which would benefit from association with the ICGEB. At the same time in the advanced countries it has noted the gathering speed of the genetic engineering and biotechnology research and development programmes. The need to establish the ICGEB is even greater now than it was two years ago when the idea was conceived. It is therefore important that the potential member countries of the ICGEB assess the urgency of this matter and note that the choice of location of the ICGEB will crucially affect the speed with which the Centre can begin to help the developing countries in a useful way" (13).

The Selected Committee presented its unanimous report to UNIDO on 13th May 1983 dedicating it to Dr. Cesar Vasquez, a member of the Committee until his tragic death from a heart attack on 19 April 1983. The report was one of the documents considered by the Ministerial-Level Plenipoteniary Meeting held at Madrid in September 1983.

V. THE MINISTERIAL-LEVEL PLENIPOTENTIARY MEETING ON THE ESTABLISHMENT OF THE ICGEB, MADRID SEPTEMBER 1983 AND VIENNA APRIL 1984

Forty-four countries participated in the Madrid meeting and seven others sent observers. Fourteen organizations, including the UN University, the European Molecular Biology Laboratory, WHO, FAO, EEC and the Rockefeller Foundation, also sent representatives.

The meeting was in two parts, the first to resolve outstanding questions pertaining to the statutes, finance and location, and the second to adopt and sign the statutes establishing the ICGEB. The draft statutes were modified somewhat and then agreed upon (14). It was not possible to reach agreement on the location and financing. Indeed, the discussions on these last two matters were difficult and the Madrid report (14) indicates that opinion was so divided that it might be difficult to establish the ICGEB at one centre. In the event, 25 countries signed the Statutes (Table IV) without deciding on the location or the financing. A Preparatory Committee, with one representative from each of the countries which had signed, came into being with the signing of the statutes and it was charged with the responsibility of resolving outstanding matters including those pertaining to location and finance. The Plenipotentiary Meeting was adjourned and was to reconvene to hear the recommendations of the Preparatory Committee.

The Committee met twice (in November 1983 and January 1984) and finally proposed that the ICGEB be initially established with two equal components, one in Trieste, Italy and the other in New Delhi, India. The Plenipotentiary Meeting was reconvened in Vienna in April 1984 and accepted this proposal, with ten countries signing the amended Statutes (15).

The decision to establish the ICGEB in two places, one in a developed country and the other in a developing country, reconciled the two decisions of the Belgrade meeting that the centre should be of high excellence and preferably located in a developing country. Several scientific consultants to UNIDO, as well as the Selected Committee, had been concerned that if the ICGEB was located in a developing country it would find it difficult to attract highly qualified and experienced scientists with international reputations sufficient to establish the standards of "high excellence". On the other hand the developing countries are to be the beneficiaries of the ICGEB and their governments' representatives were virtually unanimous, at Belgrade and Madrid, that the ICGEB would not function effectively unless it were part of the developing world, where staff could see at first hand some of the problems to be solved and be more likely to focus their research towards relevant objectives in a practical way. The Vienna decision that the

ICGEB have laboratories in Trieste and New Delhi, and that laboratories in other places be linked to the ICGEB has resolved the matter in a realistic and constructive way. Trieste was highly recommended by the Selected Committee and the Italian Government has offered US $38 million towards the costs of the ICGEB. The Indian Government has offered US $19 million and will facilitate the foundation of the New Delhi component in every way possible.

VI. THE ICGEB AND THE BASIC INGREDIENTS OF BIOTECHNOLOGY

The foundation of the ICGEB has been accomplished because it was accepted there was little or no genetic engineering and related biotechnology in the developing world. The objectives and functions of the ICGEB as defined in the Statutes are shown in Tables V and VI, which can be more easily understood if viewed in conjunction with the reports upon which they are based. It would be superfluous to review all of the ideas contained in these reports but it may be valuable to look behind and beyond them.

The ICGEB will be a small institution with some 50-100 scientists working at any one time; it will undertake a small number of research projects, train a small number of people in the course of these projects, and its immediate impact on science could initially turn out to be small. It will never be able to match in scale either the foreign students' programmes of the United States or other Western countries or the research programmes undertaken in these countries on some matters (e.g. malaria vaccine development) which are directly related to the needs of the developing countries. The question is how the ICGEB as a small institution can exercise a role to distinguish it from the great national universities and research institutes of the developed world, many of which have close ties with developing countries. What will the ICGEB have to offer the developing countries?

The reply to this question is this. The aid programmes of the

developed countries (training of research students, collaborative research projects, etc.) have not succeeded in the field of GEB, nor in the underlying science of molecular biology. This author is not in a position to comment on other fields, but GEB and molecular biology which have thrived in the US, Western Europe, Japan and Australia for twenty years or more, are very poorly established in developing countries in spite of the fact that many students from these countries have been trained abroad. There are many reasons for this failure - students not returning to their home countries; poor laboratory conditions; inadequate research and teaching budgets in the home countries, etc. - but it is clear from the discussions at Belgrade and Madrid that the developing countries believe that international aid programmes are more likely to be successful than national ones, and in particular they will be more successful if they are under the supervision of the developing countries themselves. The ICGEB has been founded with these arguments in mind and its experience will be a test of them. The ICGEB is not just another research institution. It has been founded under the auspices of a UN organization (although it is an independent intergovernmental organization) and so should be able to act and speak with an authority and objectivity enabling it to have an influence which far exceeds what would be expected for an institution of its size. It will have the chance to influence people in universities, research organizations and governments about GEB and molecular biology in a way no other body can at the present time. It is planned, desired and expected to achieve a position of authority for the developing countries comparable with, for example, that which the National Institutes of Health has for the US.

It is of course not enough to talk of this position of authority. The authority of the ICGEB will not be established as a birthright just because it is an international institution. The authority will be established as a result of the work of the ICGEB in its early years. How should it go about achieving authority?

The scale of the task facing the ICGEB is enormous, with the prospect of choosing between a great range of research projects on many species of plants, animals, bacteria and viruses endemic in different climates in over a hundred different countries of the developing world.

Plainly, the ICGEB must be organized so that its influence extends far beyond its immediate day-to-day concerns. It must set out to be a prophet of its science, enlisting the faithful and training its disciples so that its effect permeates the universities and research institutes of the developing world. In the following paragraphs I want to draw attention to some ways in which the ICGEB might respond to this challenge - how can a small international institution significantly influence the development of a major field of science and technology in such a large number of developing countries?

Of course this question was posed by the authors of the reports to UNIDO and some answers were suggested. There was clear emphasis on the necessity of establishing the highest possible standards of science in the appointment of staff. This was accepted as the primary initial objective for the ICGEB - appoint outstanding staff. I will not labour this point further - sine qua non - except to say that the international scientific community will watch how these appointments are made, and it is the collective opinion of this community which will signal whether the ICGEB is setting off on the right track.

The ICGEB will have as one of its most important elements a group of visiting researchers from developing countries who will spend a number of years at its laboratories and then return to their home countries. They will be accepted by the ICGEB in the expectation that they will return to their home countries and play important roles in the development of GEB there. They will be vectors providing one of the most valuable ways of extending the effect of the ICGEB, carrying with them knowledge of the latest discoveries and techniques, imbued with the intellectual standards of the ICGEB and, in many cases, having won for themselves reputations in their fields of research. It is therefore of paramount importance that when these scientists are chosen they meet the highest objective standards of intellect, scientific knowledge, experimental experience, commitment and personal qualities, and that the process of selection does not take undue account of qualifications not germane to science. It would be wise to avoid rules reserving places for scientists from particular developing countries, but if such rules have to be introduced then they must include stipulations on two further matters. A

scientists, to be accepted, must meet a set of objective criteria in respect of his ability as a scientist, and his country must show that when he had completed his study he will be able to pursue his science under reasonable conditions.

The reputation of the ICGEB as a research institute will be based initially on the reputations of the newly appointed staff. They in turn have to fulfill the trust placed in them and produce outstanding research results, comparable to those coming from the leading institutes of the world. This research, as it is published, will reach the international scientific community, carrying the influence of the ICGEB to all countries. Much depends on the way the research of the ICGEB is organized - for example, on the balance between directed or contract research and independent research. How many major projects will be undertaken and in what areas? How much of the research will be aimed at short-term applications and how much at longer term results? What will the balance be between pure and applied research? It may at this stage be helpful to tease some of these questions out further.

UNIDO consultants did specify six major areas for research projects (16). Work programmes for five of these and for the additional area of Bio-Informatics were drawn up (17). The titles of these documents describe the areas.

These work programmes cover an enormous range of projects from enhanced oil recovery by genetically engineered microorganisms to the development of novel vaccines. There is no question of the ICGEB being able to carry out significant programmes across this range and this was not the intention of the consultants. The projects as described were mainly to show the range of applications of genetic engineering, so that developing countries would be alerted to the potential value of GEB. The work programme of the ICGEB will very likely include some of the projects outlined in the original documents but the number of different ones must be rather small and carefully selected with respect to their chances of success, either in terms of scientific or applied value.

The balance between directed or contract research and independent research will be an important factor in attracting staff of high quality. It will also be important in helping to maintain a balance between pure and applied science. I argue below that the ICGEB must pursue strong programmes in pure molecular biology, and this may best be ensured through a policy of supporting independent work of the staff members, say up to 60 per cent of their time.

The questions of the number of major projects to be undertaken and the areas of research for these projects are difficult to answer. The scale of the ICGEB (50 permanent scientific staff plus 26 postdoctoral fellows and 40 technicians) and its facilities suggest that perhaps it might undertake about 5-10 major projects at the beginning, dropping some as others show promise of success. Some projects should be chosen in the expectation that within four years they will have a good chance of being perceived as successful in the developing countries, for example, programmes to develop novel vaccines against polio or typhoid, or to construct expression vectors for use in E. coli, Streptomyces, S. cerevisiae and Bacilli. Others, for example, the development of molecular cloning systems for monocotyledons (perhaps based on mobile genetic elements) and vaccines against malaria are of such importance that the ICGEB could probably have groups working on them even if success is not likely to be achieved in five years. The ICGEB personnel will at least be able to give advice on these topics of major concern to the developed countries as well.

One result of the process by which the ICGEB was founded was a serious revelation about science in the developing countries. One whole field of science, molecular biology, hardly exists in the developing countries. The scientists who participated in this project travelled to many developed and developing countries; in my case to Egypt, Yugoslavia, Hungary, Kuwait, India, Pakistan, Thailand and Cuba. In extensive discussions amounting to several man-years of work, there was no dissent from this conclusion which was recorded in each of the reports. The question is what the ICGEB should do about this. I suggest that it would be extremely important for the ICGEB to recognize that it has a role in fostering basic molecular biology as well as GEB in developing countries. Although the ICGEB has been established with a wide brief

(Table V), it is at this stage too early to say how this will be interpreted. It will be extremely important that in its advisory capacity the ICGEB uses its influence to drive home the point that the basic ingredient of biotechnology is basic science in the relevant fields (R. Wu discusses this point elsewhere in this volume). It is worth repeating again the advice of Abdus Salam that "science transfer must go with technology transfer if technology transfer is to be meaningful and lasting".

There are two questions to be posed in pursuing this point. The first is how can molecular biology be implanted in the developing countries in order to sustain the transfer of biotechnology? This question is the main matter I shall deal with for the remainder of the paper, but thinking of how the developing countries might avoid another situation equivalent to the one in genetic engineering I want to pose a second question. It is this: what other areas of mainstream science, which have yet to show obvious applications, are not represented in the developing world? I am sure the answer to this is known, but has it been addressed in the proper international fora and are steps being taken to redress the deficiencies so that when novel technologies emerge from these other sciences, the developing countries will be able to benefit from them more quickly? The example of genetic engineering must be used to support the case that the developing countries cannot afford to neglect pure science.

The basic ingredients of genetic engineering and biotechnology are knowledge and skills of many fundamental sciences and technologies. The title in a wide ranging symposium and the name of the ICGEB emphasize the role of genetic engineering, a field which is often subsumed within the general heading of biotechnology. This reflects the way in which the new biotechnology has been influenced by genetic engineering which more than any other field has been a source of inspiration, motivation and inventiveness for biotechnology. It is also an area of biotechnology in which the developing countries were found to be extremely weak by the scientific consultants who drew up the early reports. Moreover, because genetic engineering is composed of many different experimental procedures ranging from organic chemistry through biochemistry to microbial

genetics, because these procedures are being constantly changed and added to, and because they are bench skills demanding a high degree of experience, intuition and theoretical knowledge, it was apparent that the transfer of genetic engineering to the developing countries vividly exemplifies the problems of technology transfer, exacerbated by the neglect of the underlying basic science. Unlike say applied microbiology or applied botany which are parts of biotechnology for which the basic sciences exist in many developing countries, the basic science underlying genetic engineering is essentially absent. Not only is the technology of genetic engineering exceedingly complex, but there is virtually no base for it in the developing world - and the ICGEB must participate in building this base of molecular biology at least as much as it concentrates on the application of the technology.

There is of course a major task of influencing the policy makers within developing countries that the pure science of molecular biology must be fostered. The ICGEB will not be successful unless this argument is put forward and won. Let us assume that it is won, then how should the ICGEB advise the developing countries on the mechanism for implanting molecular biology, remembering that the ICGEB has been planned as a relatively small institution.

The ICGEB must be viewed as a catalyst, or perhaps as the provider of the seed corn. Its effects will be spread by its "graduates" who return to their home countries and impart knowledge and skill through their teachings and their research groups. These graduates of the ICGEB will be under great pressure to produce "meaningful" results, as will the ICGEB itself. The case for pure science is crucial to the international perception of whether the ICGEB and its scientists are succeeding; that being so it will be prudent as well as proper for the ICGEB to establish a programme for molecular biology in the developing countries, which reaches many more scientists within the developing countries than can be accommodated on long-term research fellowships at the ICGEB.

The situation of molecular biology in the universities of the developing countries is extremely poor (this situation is described by Dr. S. Riazuddin), yet at the same time faculty members in these

institutions could become powerful allies of the ICGEB. Molecular biology is virtually absent from the biology curriculum in developing countries. A curriculum approved by the ICGEB could be drawn up, textbooks, journals and laboratory manuals recommended, external examiners appointed, and courses ratified. Many faculty members in developing countries have had good experience abroad but have not been able to institute courses, perhaps because of entrenched traditional interest, lack of resources, lack of colleagues in related areas, lack of suitable preliminary courses and so forth. The ICGEB might be asked to participate in reviews of national capacities for teaching molecular biology and perhaps to advise on how resources should be allocated. It would seem appropriate for the ICGEB to collaborate with UNESCO in these endeavours. The object must be to ensure that many more students graduate with degrees in molecular biology which meet international standards.

In advising about molecular biology in the universities it is important to advocate that resources are concentrated in a small number of universities so that the critical mass of suitably qualified staff can be achieved. "An essential pre-requisite for the successful application of modern biological technologies to the needs of development is the creation in developing countries themselves of integrated scientific and technological communities large enough to be effective" (18). This is crucial for the universities which have the responsibility of undergraduate education in molecular biology. About 20 faculty members are required to form a core group in molecular biology, although even at that number it is necessary to be cautious about spreading the interests too widely across molecular biology. It should be agreed that a core group of this size should concentrate its research (though not necessarily its teaching) on a relatively narrowly defined topic, thereby making it easier to achieve an international reputation.

In implanting molecular biology at the universities, it must be accepted that faculty members are required and permitted to conduct research. Without research the teaching will not prosper. More than the formal permission, which is usual in the conditions of appointment of university staff, the permission must mean that the university will

provide full facilities for carrying out research (though at times permission at most universities in developing countries is meaningless since they do not usually have suitable laboratories, equipment or money for support staff, consumables, etc.). Furthermore, university research in molecular biology must be carried out with graduate students who submit theses for higher degrees. In many developing countries, universities have extensive postgraduate research programmes but these need to be extended to include molecular biology, and monitored to ensure that they meet international standards. The ICGEB could serve a most useful function in establishing a system of external examining of B.Sc., M.Sc. and Ph.D. degrees in molecular biology awarded in developing countries.

The appointment of staff in universities always poses problems. No country has the perfect answer but in many cases it has been found useful, if not essential, to enlist the help of university colleagues from other universities, located perhaps in other countries. Those developing countries with small peer groups in molecular biology might value the institution of an international system organized by the ICGEB to provide external assessors for critical appointments. No doubt external assessors are used by developing countries, but I suspect it would be useful to have a formal mechanism supervised by an international body dedicated to the developing countries and controlled by them. The ICGEB could also have a role in devising an international system to review national research proposals in molecular biology, once again fulfilling an essential function which cannot be properly exercised when peer groups are small.

The peer group problem in developing countries has many consequences so it is useful to further elaborate on this point. Peer groups everywhere tend to coalesce, with cooperation growing at the expense of competition and criticism. There is the real danger of peer groups becoming cartels which carve up funds, competing only with other cartels operating in quite different fields. Proposals in very different fields cannot be compared easily on scientific merit, so political manoeuvring determines how the cartels operate. This becomes a time consuming activity for the main group of scientists in the country. Political

institutions are much impressed by the number of conferences held, especially if these are international, as they are impressed also by the foundation of national societies, or journals. Political figures and officials seem to appreciate journals, conferences about policy, especially multi-disciplinary discussions. Committees, commissions and subcommissions, reports and reports about reports add up to be a frenetic merry-go-round on non-science. This pattern is represented to some degree in every country but in developing countries it seems to be much more pronounced. The scarcity of resources and the poor organization of distribution divert scientists from science to politics. It is important for the future of molecular biology in developing countries that this problem is recognized and minimized. International agencies have a role and responsibility in advising on this, perhaps in the formulation of reports similar to those produced by the OECD on science in member countries.

Scientists in developing countries are frequently isolated from the mainstream of science. The isolation will be reduced if the scientists are formed into groups of critical mass, but the conduct of modern science in every country depends on frequent visits to other laboratories and countries. As a country is smaller and more distant from the main centres of the US, Western Europe and Japan, it is even more important that visits abroad should be frequent. These occur, but not sufficiently often. Sabbatical leave should be one year in four, and should be mandatory in new centres of excellence in molecular biology. It is urgently required that UNESCO and other organizations establish and expand fellowship programmes in molecular biology to facilitate this.

Scientists in developing countries frequently found journals where most of the results of local research are published. This is a very large enterprise in some developing countries and at face value may suggest that science is in a healthy state. These publishing enterprises deserve great respect, but of the kind shown to Sisyphus, "son of Aeolus, who was punished by the underworld by having to roll uphill a huge rock which as soon as it reached the top always rolled down again". At the risk of offending national sensitivities outside the developing world, it is evident that there are few major journals of molecular biology

published outside the US or Western Europe. In Western Europe the main countries which contribute to the list are the Netherlands, Germany and the United Kingdom. Of course the list of countries from which the editorial boards are drawn is much wider, and includes many developing countries, but the overall picture is that the journals with international reputations in molecular biology are produced and edited by the developed countries of the West. Scientists from developing countries are at a great disadvantage in dealing with this system. On the one hand, the facilities for their science are not usually sufficient to carry out experiments which are routine in developed countries, meaning that papers as submitted are judged to be incomplete. On the other hand, they often do not have the benefit of personal contacts to help establish credibility. Although it is clear that science from developing countries is not so easily published in international journals, the response of publishing their science in national journals has been counterproductive. There it is in effect lost, not being read, or given credence, and not being cited. The ICGEB should found two new journals; one on the applications of GEB and the other on molecular biology, with special emphasis on publishing results from developing countries and results which are related to them in these fields. These journals will have a similar role for the developing countries as the EMBO Journal has for Europe. The international credibility of the EMBO Journal was assured by the reputations of the editors and the link with the European Molecular Biology Organization and the European Molecular Biology Laboratory. The ICGEB should be able to do the same for journals founded under its auspices.

There are now more than 100 universities and research institutes in North America, Western Europe, Japan, Australia and elsewhere, with prominent research reputations in molecular biology, and some have close connections with developing countries. The goodwill of international science towards developing countries is reflected in the readiness to accept visiting researchers and students, but much more could be done. Funding of exchanges is frequently difficult. There is a lack of continuity and too often the relationships are based on personal connections which are easily lost. There is a need for a wider use of institutional connections; for example, where a department or faculty in

a developed country is twinned with a corresponding one in a developing country. Close connections of this kind have certainly benefited universities in Thailand, facilitating exchanges of staff and students, establishing confidence in standards and leading to joint research programmes. The ICGEB will have a network of affiliated institutions, but it could have a much larger effect if it initiates and coordinates a much wider set of linkages between "third parties".

Finally, I want to draw attention to the interplay between science and politics which has pervaded the process by which the ICGEB has been founded and which will be a powerful factor in its future role as the axis of molecular biology in the developing world. The Statutes were amended in Madrid to the effect that the Director must be a citizen of one of the member states. This is a regrettable imposition equivalent to having a rule that the head of a university or a research institute within a country must be a citizen of that country. If such rules exist, and I am sure they do, they should not be emulated. Coming from a country which was colonized for 750 years and which has its own special cultural strengths and weaknesses, I find it easy to discern sentimentality in the developing world. It serves not the interests of the people but merely the vanity of the diplomats and politicians to exclude from consideration for the directorship the great majority of eminent molecular biologists.

I make this point, not because I believe that it is going to matter in the end, in that I am confident a good appointment will be made, but a great principle, the internationality of science, which the ICGEB seeks to take advantage of and to strengthen, has been challenged and I am concerned that this sort of action must be strongly resisted as the ICGEB begins to operate. It is easy to foresee the pressures which will arise for example in the appointment of other staff, representatives of regions, countries and so forth, and the Board, composed of representatives from member nations, must endeavour to resist and protect the ICGEB and the Director from these pressures. The Statutes provide for a Council of Scientific Advisors of up to ten scientists and technologists. It will not be representative, except that members are to be elected by the Board "on a balanced geographical basis" (19) and it

has a function to advise the Director on the appointment of senior staff and other matters. It will act to some extent as a buffer against unwanted and unproductive political interference.

Having made these cautionary remarks, I am optimistic that the ICGEB will succeed in avoiding most excesses of political meddling. The reason for my optimism is that in the process of its foundation it has already experienced substantial political pressures and a great majority of these have been accommodated in one way or another without damaging the main scheme. The intrinsic idea of the ICGEB, the strength of the underlying science and the international scientific community, the skills of the UNIDO's Division for Industrial Studies and ultimately the wishes of the developing countries have carried it through. The evidence is that the ICGEB is a recipe for success. The antipathy between science and politics emerged with science at the Renaissance and it will not go away, but in this project many scientists, officials and politicians have worked together, usually in agreement but often with obvious tensions and difficulties. Usually principles have been adhered to, the scientists staying out of the politics and the politicians respecting the scientists' views. It is quite remarkable that the ICGEB has been founded, if anything on a grander scale than was hoped for, while retaining the essential ideas of its proposers.

The omens are right for success. Now there is nothing for nations to gain by staying aloof from the ICGEB and a great deal to lose. At this symposium of the American Association for the Advancement of Science it is opportune to ask what the US has to gain by eschewing success in international science. Owen Sheehy Skeffington, an educator, sadly little known outside Ireland and France, resigned once from an educational institution and regretted it all his life because it opened the way for others who were not so well qualified as he.

Table I. RECOMMENDATIONS ON THE ESTABLISHMENT OF THE ICGEB (20)

(i) An International Centre for Genetic Engineering and Biotechnology (ICGEB) should be established on the lines suggested in the report.

(ii) UNIDO should follow up its initiative, pursue the question of establishment of the Centre vigorously and continue to fully and actively associate itself in this activity.

(iii) It should continue to associate the leading experts in the field in the setting up of the Centre.

(iv) It should initiate further consultations with interested United Nations agencies such as FAO, UNESCO, UNU and WHO and other international organizations such AMBO, EMBO, ICRO and IFIAS.

(v) It should mobilize resources to create a small unit with a full-time project coordinator who would pursue the several activities leading to the establishment of the Centre.

(vi) It should carry out negotiations with interested governments and convene a meeting of participating governments where they could announce their participation and financial contributions and formally establish the Centre.

Table II. THE BELGRADE MEETING: CONCLUSIONS AND RECOMMENDATIONS (PART A) ON THE ESTABLISHMENT OF THE ICGEB (21)

(i) There is an urgent need for broader and more effective international cooperation in the field of genetic engineering and biotechnology.

(ii) International cooperation should be promoted in the first place for the benefit of the developing countries and for strengthening their scientific and technological capabilities and industrial development.

(iii) An International Centre for Genetic Engineering and Biotechnology of high excellence should be established soonest possible with activities covering, inter alia, training, research, application and information, etc., taking into account the proposals in the UNIDO documents on these subjects.

(iv) It is most desirable to set up such a Centre in a developing country provided that such a country can meet the conditions envisaged in the UNIDO reports and can provide an attractive environment for the scientists.

(v) Within the framework of the International Centre it is necessary to support activities of affiliated regional and/or national centres to be sited in different regions on a broad, geographical distribution. Financial support for these affiliated centres should be pursued through national and international financing schemes based on the advice of the ICGEB. Preparatory activities should be started as soon as possible to achieve this goal.

(vi) There should be an emphasis on lower operational costs and a minimization of operational problems of the International Centre.

Table III. THE BELGRADE MEETING: TERMS OF REFERENCE OF THE SELECTED COMMITTEE (22)

(a) The mandate of the Selected Committee is within the framework of the consensus reached in the meeting.

(b) The Selected Committee is required to seek additional information and examine in detail information from the host governments, UNIDO and other sources about the suitability and advisability of accepting the offers submitted.

(c) For this purpose, it will examine the details of the offers received in regard to:

(i) physical facilities, including the site and location;

(ii) scientific infrastructure and supporting services;

(iii) availability of scientific and technological and administrative personnel including language services;

(iv) finances and ability to attract membership and other sources of finances; and

(v) legal and other privileges to retain an international character.

(d) The Selected Committee will visit the countries to ascertain all the details in (c) above and to acquire first-hand information about the submitted offers.

(e) In order to assist the Ministerial-Level Plenipotentiary Meeting to reach a decision, the Selected Committee will offer a critical and objective analysis on the merits and demerits of each case. Therefore, the Selected Committee will be advisory in character to the Ministerial-Level Plenipotentiary Meeting.

Table IV. SIGNATORS OF THE STATUTES OF THE ICGEB AT MADRID (23)

At the ceremony for signing the Statutes plenipotentiaries from the following countries signed:

Afghanistan
Algeria
Argentina
Bolivia
Bulgaria
Chile
China
Congo
Cuba
Ecuador
Egypt
Greece
India
Indonesia
Italy
Kuwait
Mauritania
Mexico
Nigeria
Spain
Sudan
Thailand
Trinidad and Tobago
Yugoslavia
Zaire

Table V. OBJECTIVES OF THE ICGEB
STATUTES AS ACCEPTED AT MADRID (24)

(a) To promote international cooperation in developing and applying peaceful uses of genetic engineering and biotechnology, in particular for developing countries;

(b) To assist developing countries in strengthening their scientific and technological capabilities in the field of genetic engineering and biotechnology;

(c) To stimulate and assist activities at regional and national levels in the field of genetic engineering and biotechnology;

(d) To develop and promote application of genetic engineering and biotechnology for solving problems of development, particularly in developing countries;

(e) To serve as a forum of exchange of information, experience and know-how among scientists and technologists of Member States;

(f) To utilize the scientific and technological capabilities of developing and developed countries in the field of genetic engineering and biotechnology; and

(g) To act as a focal point for a network of affiliated (regional, sub-regional and national) research and development centres.

Table VI. FUNCTIONS OF THE ICGEB
AS ACCEPTED AT MADRID (25)

(a) Carry out research and development including pilot-plant activities in the field of genetic engineering and biotechnology;

(b) Train at the Centre and arrange the training elsewhere of scientific and technological personnel, particularly from developing countries;

(c) Provide, upon request, advisory services to Members to develop their national technological capacity;

(d) Promote interaction between the scientific and technological communities of the Member States through programmes to enable visits of scientists and technologists to the Centre, and through programmes of associateship and other activities;

(e) Convene expert meetings to strengthen the activities of the Centre;

(f) Promote networks of national and international institutions as appropriate to facilitate activities such as joint research programmes, training, testing and sharing of results, pilot-plant activities, information and material exchange;

(g) Identify and promote without delay the initial network of highly qualified research centres to serve as Affiliated Centres, promote existing national, regional, sub-regional and international networks of laboratories, including those associated with the organizations mentioned in Article 15, active in or related to the field of genetic engineering and biotechnology to serve as Affiliated Networks, as well as promote the establishment of new highly qualified research centres;

Table VI (continued)

(h) Carry out a programme of bio-informatics to support in particular research and development and application for the benefit of developing countries;

(i) Collect and disseminate information on fields of activities of concern to the Centre and the affiliated centres;

(j) Maintain close contacts with industry.

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CAPABILITY BUILDING IN BIOTECHNOLOGY AND GENETIC ENGINEERING BY DEVELOPING COUNTRIES

by

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I. INTRODUCTION

Biotechnology has emerged as a new revolutionary technology which offers tremendous opportunities and inexpensive solutions to some of the most urgent and difficult problems facing mankind. It has the potential to broaden the base of industrial structure and impart new directions to the economic growth of developing countries. The vast panorama of possibilities for the use of biotechnology is just unfolding and I believe that the fruits of the new technology will be with us for at least the next fifty years. The most important impact of biotechnology will undoubtedly be on agriculture, energy and health areas, within which the major problems of developing countries can be found. The new technology has thus the potential for helping alleviate hunger and improve the quality of life in the developing countries.

Biotechnology revolves mainly around microbes which may be considered as compact and efficient biochemical factories. These factories can divide and multiply into billions, with an average doubling time of 30 minutes, thereby resulting in an enormous increase in productivity. The factory functions are controlled through genetic messages contained in a computertape-like molecule called DNA. A particular DNA molecule can direct the same functions whether present in bacteria, plant, or animal cells. Recent advances in chemistry and biology have made it possible to generate tailor-made DNA which can be inserted into a chosen microbial host where it amplifies quantities of those compounds which are otherwise difficult or uneconomical to obtain either through chemical synthesis or through extraction. Progress in molecular biology, cell biology, plant physiology and immunology will undoubtedly lead to further uses of newly generated DNA.

The new biotechnology integrates several recent advances in basic molecular biological research and encompasses many facets of management and manipulation of biological systems for which neither expertise nor infrastructure is available in developing countries. In order for these countries to reap harvests from new biotechnology, several measures are needed to develop and advance their capabilities.

II. CREATION OF WILLINGNESS

First and foremost, it must be realized that capability building is expensive and it inevitably involves a long-term political commitment. Efforts must therefore begin with creating awareness, willingness and desire among the administrators and policy-makers in the developing countries to make such a commitment. Some recent developments such as the bacterial production of insulin, growth hormone and vaccines that have been widely reported upon in Newsweek, Time, New Scientist, etc. have helped a great deal in creating the desired awareness. Rapid proliferation of public and private bioscience-based companies in Europe and USA has provided an incentive to the progressive industrialists in developing countries. In particular, UNIDO's attempt to organize the establishment of an International Centre for Genetic Engineering and biotechnology (ICGEB) has played a significant part in educating the policy-makers in developing countries (the ICGEB is discussed in detail by D. McConnell elsewhere in this volume). For example, while preparing for the establishment of the ICGEB, UNIDO-organized visits by experts met many top-ranking officials including two heads of state (President Fidel Castro of Cuba and President Zia-ul Haque of Pakistan). As a result of these meetings and discussions, long-range political commitments have been made and national biotechnology plans have been formulated in some developing countries in order to advance their capability in biotechnology.

Although UNIDO's attempts have been successful and significant results were obtained, this has so far been on a very limited scale. The results obtained justify expansion of this activity into a full-fledged international activity. More could be done by such means as video lectures to promote the concept of the new technology. Popular articles highlighting future possible applications and the expected dividends will obviously provide incentive to private industry (usually not a party to research and development activities in developing countries).

III. IMPROVEMENT IN UNIVERSITY TEACHING

Major ingredients necessary to educate and train biotechnologists have already been discussed elsewhere in this volume by R. Wu. Taking into consideration the ingredients as explained by Wu and the experiences which I have had in setting up and performing research in developing countries it will be seen that undertaking high quality research in developing countries involves overcoming almost unsurmountable constraints. As was mentioned by Wu, genetic engineering and biotechnology utilizes recent developments in biochemistry, microbiology, molecular biology and genetics. These are rarely taught as separate subjects in developing countries and there are very few universities where separate departments in these subjects exist. Teaching in genetics is mostly confined to classical genetics and very little, if anything, pertaining to molecular genetics is offered. Botany and zoology courses are confined to comparative biology, classification of plant and animal kingdoms and the other topics which are usually taught at the secondary school level in most developed countries. Modern concepts on transposable elements, tumour viruses, DNA replication and recombination, single stranded DNA viruses, RNA viruses, etc., are beyond the scope of university teaching in most developing countries. Modern techniques such as immobilized enzymes, tissue and cell culture in plants, RNA-DNA hybridization, synthesis of DNA probes and DNA sequencing are neither taught nor practically demonstrated in most universities.

There are several reasons for the poor standard of university teaching in developing countries. Firstly, there is an acute shortage of well-qualified teachers who are familiar with recent developments taking place in the field of genetic engineering and biotechnology. Secondly, the teachers in most universities are heavily burdened. The average teaching load of a science professor is 40-60 hours per week and if one considers the time spent in routine administrative and bureaucratic procedures, there is no time left for him to keep abreast of the scientific developments requiring intensive library reading and literature consultation. The result is therefore that the subject material taught to students is the same as that which most professors

learned when they were students themselves. Thirdly, there is no specialization in teaching. A professor of biochemistry who may have specialized in fatty acid metabolism often is expected to teach reactions and biochemical kinetics. Usually, an entire subject course (be it biochemistry, genetics or microbiology) is taught by one or two professors who would have obviously specialized in a narrow area in that subject.

Another important factor contributing to poor university teaching in the developing countries is the weakness in laboratory practicals. The sciences underlying biotechnology are practical, meaning that much of the knowledge a student is expected to gain is dependent on the experience and expertise of sophisticated techniques which should be learned and mastered through practicals during university education. Furthermore, genetic engineering and biotechnology are new areas of R+D having a multidisciplinary character. Most universities in developing countries are, however, still confined to traditional monodisciplinary teaching and research.

To alleviate the above-mentioned shortcomings and to improve upon the standard of teaching in universities which are the main producers of trained manpower in developing countries, efforts should be made to: (a) regularly upgrade teaching courses by accommodating recent developments; (b) considerably strengthen the teaching facilities; (c) provide laboratory facilities to accommodate experiments in molecular biology and molecular genetics on which the new technology is based; (d) adopt curricula in biosciences based on the concept of multidisciplinarity and transdisciplinarity; and (e) promote the intensive use of computers in teaching and research.

IV. LIBRARY AND INFORMATICS

University libraries in developing countries are not well stocked and this has prevented even the best students and teachers from updating

their knowledge. Almost all of the books on modern biology and scientific journals containing information on most recent developments in genetic engineering and biotechnology are published by European and US companies and they are prohibitively expensive. A new molecular biology or genetics book may cost between US$ 100-200, which in many developing countries is close to the monthly salary of a university assistant professor. This makes availability of new books to university students and teachers extremely difficult, if not impossible.

Literature information is not up-to-date in most libraries in developing countries. Most publishers of scientific journals require advance payment in hard currency which many universities cannot afford to pay. Further, shipping is invariably via surface mail in order to save huge air transportation costs. The result is that most journals are not shelved, and thus available for use, until as much as 12-18 months after their publication, by which time the information is old, if not obsolete. Developments in biotechnology is causing an explosive increase in literature information. This has enormously increased the number of relevant journals, often beyond the reach of a moderately funded library to acquire. The result is that no library in a developing country can afford to subscribe to and house all the journals related to genetic engineering and biotechnology. The best that a research worker can do is to scan "Current Contents" (which fortunately most libraries do get by air) and request free reprints. They are therefore forced to depend on the mercies of authors, some of whom may be too busy to mail their reprints.

In view of the enormous amount of new research information that is coming out every day, it is becoming impossible for an active scientist to scan through all the journals. To facilitate information retrieval, most libraries in the developed world are storing literature information in computers which has proved extremely useful and resulted in a tremendous saving of precious time to laboratory workers, allowing them more time performing experiments. At present, most universities in developing countries do not have access to computer facilities. Nevertheless, it would prove useful to teaching and research in developing countries to establish "lending libraries" at the "national"

or "regional" levels. These libraries must be equipped with duplicating, photography, microfiche and related equipment and otherwise be able to help disseminate information to where it is needed. Cheap and paperback printings of biotechnology and genetic engineering books, similar to those prepared by the Asia Foundation, should be published for sale to students in developing countries.

V. CREATION OF WELL-TRAINED MANPOWER

One of the most important measures required to build capability in developing countries is to create a core of well-trained scientists that can be used to: (a) generate more manpower through improved university teaching and (b) apply know-how in genetic engineering and biotechnology to solve their own specific problems. To accomplish this task, a two-pronged programme will be needed. Firstly, specialized short training courses will have to be organized for university teachers, exposing them to recent developments in biochemistry, molecular biology, molecular genetics, immunology, virology, fermentation technology, chemical engineering, etc. Such courses must include laboratory practicals during which techniques routinely used in new biotechnology are demonstrated. Secondly, long and thorough courses leading to Ph.D. degrees in molecular biology and genetics should be initiated. Syllabi for these courses must be designed by experts who should also participate in teaching them. It is proposed that young researchers possessing a M.Sc. in Physics, Chemistry, Botany, Zoology, Microbiology, Chemical Engineering, etc. may be selected for such programmes. During the first year, the trainees may be taught courses and be allowed to conduct laboratory experiments in molecular biology, molecular genetics and chemical engineering. During their second year the trainees may be assigned research projects in line with their country's national priority areas (see below). Project research work must be initiated in the laboratories in their respective countr[illegible] At the completion of the second year arrangements may be made fo[illegible] trainees to spend six months to a year in foreign laboratories engaged [illegible]ilar or related areas of

scientific investigations. This will help to give them an exposure of the excellent academic environments which exist in the universities in developed countries. However, it is extremely important for the trainees to initiate and complete most of the project work in their native laboratories.

It should be borne in mind that living conditions, as well as laboratory working conditions, in developed countries are completely different from those prevailing in developing countries. For example the quality of water, the environmental level of contamination, the ambient temperature, the regularity in voltage and power supplies are all very different. In the developed world, the emphasis is on automation, whereas in developing countries the tendency is to utilize the vast resources of semi-skilled manpower. This, quite naturally, necessitates different designs of equipment and different planning of experiments.

The proposed three-stage training, besides being economical, will lead to the early creation of better trained and well-adapted scientific manpower, adapted to working under the unique conditions prevailing in developing countries. Furthermore, this will help to create infrastructure and facilities to promote R+D work in developing countries.

VI. STRENGTHENING OF BASIC RESEARCH

The tradition of performing basic research is usually non-existent in developing countries. This may be attributed to lack of financial support from national and international funding agencies. Where resources are limited, it is logical to intensify work that has clear applications. However, it must be borne in mind that various discoveries which led to the advent of genetic engineering were clearly an out-growth of basic laboratory research. For example the discovery of restriction endonucleases resulted from studying defence mechanisms against the invasion of bacteria by foreign DNA. Reverse transcriptase (an enzyme central to most methodologies in genetic engineering) was discovered from

studying the life cycle of a tumor virus, an experiment that had no relation whatsoever to biotechnology.

As more information is becoming available through hybridoma research, cell culture and tissue culture work, immunology, DNA hybridization and a variety of similar researches, the new biotechnology is becoming broader in scope. It is of paramount importance, therefore, to support investigator-initiated basic research in the university laboratories in developing countries, so that new initiatives and techniques are developed locally and those devised elsewhere can be relatively easily modified and adapted.

VII. COMMUNICATION AND INTERACTION WITH THE ADVANCED WORLD

Research workers in developing countries are awfully isolated and work in small groups which quite often do not have the personnel to form a "critical mass". The density of scientists and technologists is extremely low and there is no criticism of their work and no cross-fertilization of their ideas. New ideas reach them slowly and eventually, their intellectual powers begin to die, slowly but certainly. To forestall this fate, many scientists leave their countries to join active research groups in the already developed countries where their gifted talents can be harnessed, but definitely not where they are most needed.

The process of capability building in developing countries can be greatly hastened by improving communication and interaction between biotechnologists of the developing and the developed world. To improve communication and interaction, I propose the following actions: (a) to establish collaborative research programmes between laboratories of the developing and advanced countries working to achieve similar goals; (b) to arrange for exchanges of scientists and visit programmes; and (c) to hold truly international seminars, symposia and workshops in developing countries with the participation of scientists from the elite groups in

various regions of the world. Such activities will help to overcome the isolation of scientists working in the developing countries, provide opportunities for cross-fertilization of their ideas and serve as vehicles for the recognition of their discoveries. Besides, this will reveal to the foreign scientists the inherent difficulties and problems of researchers in developing countries to practice day-to-day laboratory science and thus help win their moral and material support.

VIII. REQUIREMENT OF A RELIABLE SUPPLY OF RARE BIOCHEMICALS

The new biotechnology does not necessarily require sophisticated and expensive machines which are difficult to run in industrially poor countries. This makes the technology especially attractive for the developing countries. Nevertheless, the heart of the technology is the regular and reliable supply of rare biochemicals which include nucleic acids, enzymes (restriction endonucleases, reverse transcriptase and replication enzymes), DNA metabolites and specialized chromatography media. Acquisition of these materials by the scientists in developing countries, presents the following difficulties:

(a) Hard currency: Since all of these materials have to be imported, payment is required in hard currency. If extra funds are available to the scientists in developing countries, they are in local currency. Conversion into hard currency, if possible, is very time and effort consuming.

(b) Transportation: Most enzymes and related materials are unstable at ordinary temperatures and are generally shipped in dry ice. The standard size cartons cannot take more than a few kilogrammes of dry ice that normally lasts for 24-48 hours. However, the journey time to many cities in Asia and Latin America is usually more than 48 hours. Increasing the quantity of dry ice makes air

transportation charges prohibitively expensive. Further, there are usually no facilities for cold storage at the receiving airports in developing countries. Therefore, goods collection by the customer has to be extremely efficient, which is not always the case.

(c) Procedural formalities: The procurement procedures to be satisfied by a developing country scientists are usually lengthy and cumbersome. Customs clearance is time consuming and communications between the customer and the supplier tends to be poor. To advance the biotechnology capability of developing countries, a regular supply of continually needed materials must be ensured. No one group can make all of the enzymes it requires, so it must depend on commercial sources simply because the time and energy required to make them is beyond the capability of any one institution.

To overcome the obstacles I have described, it is proposed that interested governments in developing countries should: (a) make budgetary provision for such materials; (b) introduce quick procedures for the import of biotechnology materials; and (c) make customs clearance easy and quick.

IX. LABORATORY INFRASTRUCTURE

Provision for the constant source of electricity necessary to run equipment, maintain an air-conditioned work environment for cold storage of vital substances, secure sterile conditions must exist in all laboratories engaged in genetic engineering and biotechnology research. Such laboratory infrastructure is generally non-existent in developing countries. There are frequent power failures and voltage fluctuations that not only damage equipment and materials, but may also ruin experiments, resulting in a tremendous waste of experimental efforts.

It is proposed that all laboratories devoted to research in genetic engineering and biotechnology be air-conditioned and that they have a provision for the steady flow of sterile air. A standby power generator, linked to vital points such as constant temperature rooms, ultracentrifuges and incubators, should keep these vital equipment running in the event of power failure.

X. REPAIR AND MAINTENANCE OF EQUIPMENT

While performing research and development in genetic engineering and biotechnology, equipment such as ultracentrifuges, spectrophotometers, high pressure liquid chromatographs, electron microscopes, fraction collectors and radioactivity counters are used Their operation and maintenance in developing countries presents two problems. Firstly, there is a lack of proper staff to operate and look after equipment. Secondly, there is usually a shortage of qualified technicians to repair faulty equipment as well as a lack of replacement parts. Any equipment, no matter how rugged and soundly built it may be, can develop faults through continuous use. Experience has shown that once a piece of equipment breaks down, even due to a minor fault, it has to wait for many months to be put back into operation.

Any effort to advance biotechnology capabilities must include measures to ensure the proper repair and maintenance of equipment through training of two categories of personnel; firstly those trained on the machine to use it properly and secondly electronics engineers who can diagnose faults, repair the machine and if necessary design and fabricate minor components.

XI. AWARENESS OF BIO-HAZARDS AND SAFETY

There are two sides to this problem. Firstly, administrators and policy-makers in the developing countries often identify genetic engineering as being associated with special safety hazards. This impression is based on the fears expressed during the recombinant DNA debate in the early days of discovery of this methodology. In spite of the most careful scrutiny no problem has yet been encountered, so it is safe to assume that none should be expected. Secondly, the use of the new technologies will involve a large number of unskilled persons who will obviously not be familiar with routine safety measures. It must be borne in mind that our experience with the new technologies being safe, although reassuring, is limited. It is certainly important to remain vigilant. The technical supporting staff must therefore be given safety courses. Comprehensive manuals describing safety procedures and measures to be taken if emergencies occur must be prepared and made freely available.

XII. RAPID ACQUISITION AND ADAPTATION OF THE NEW TECHNOLOGIES

Developing countries most often have no mechanism for technology transfer, nor do they possess efficient extension services for the dissemination of research results. It is of high priority to create industrial estates together with efficient extension services which can facilitate the mechanism of transfer of technology (the horizontal and vertical transfer of biotechnology is discussed in depth by R. Zilinskas in this volume).

XIII. NATIONAL POLICY AND SETTING OF NATIONAL PRIORITIES

The strength and thrust of capability development will ultimately depend on sound formulation and implementation of national policy, including a most judicious fixing of national priorities. It must be realized that capability building is both difficult and expensive. However, bioscience R+D does have a way of becoming simpler, cheaper and more economical as it matures. Quite inevitably, it involves a long-term commitment both by the scientific community and national decision-makers.

The resources available for R+D and needs of developing countries vary widely and therefore different priorities and national policies will have to be established by different governments in order to enhance their capability in biotechnology. However, two major problems common to all developing countries are that they have poor management and they have not identified their true national priorities. In particular, problem identification and setting of priorities, when done, are more influenced by politics than by genuine needs. Unfortunately, the most acceptable solution politically, is often not the best from either the economic or scientific points of view.

It would be useful for developing countries to adopt the following two measures. Firstly, to constitute high powered national committees comprising local scientists-planners, policy-makers, finance people and foreign biotechnologists of high repute. Such committees would have the tasks obtaining an in-depth knowledge of existing problems, gauging the availability of trained manpower and infrastructure and determining the economic and scientific feasibilities of proposed projects. On this basis, the committees could draw up the following: (a) a list containing proposed basic research projects which would supplement ongoing applied programmes or serve to adapt foreign technologies to specific and unique needs; (b) a list of short-term applied projects to address immediate national problems in order to solve them within a given period, taking into account the limited resources of manpower and finances available for these projects; and (c) a list of long-term projects which have national importance but are considered difficult to solve as a result of limited

resources but that have the potential for gaining momentum as more trained manpower becomes available in time for these projects. Secondly, a joint committee of R+D organizations and universities should be set up and endowed with a certain amount of funds to allow it to stimulate new projects and co-ordinate R+D efforts towards solving national problems.

New projects of basic research which have direct relevance to biotechnology and are accorded high priority on the list prepared by the high-level committees, must be initiated in the university laboratories. Other short- and long-term projects enumerated on the list of the high-level committee can be undertaken in designated single laboratories or in several laboratories (if it is deemed advisable to pool available resources). The joint committee must strengthen existing laboratories and act as a steering group to coordinate their activities. Since the available resources of men and material are extremely limited in some developing countries, they should consider multinational cooperation. However, the latter is a difficult step incurring political problems.

For the advanced developing countries, I believe that each should consider establishing a national centre for genetic engineering and biotechnology solely devoted to the exploitation of the new technologies for the economic development of the teeming millions in third world countries. The subject of biotechnology centres is given fuller discussion elsewhere in this volume by D. McConnell.

XIV. ROLE OF INTERNATIONAL AGENCIES IN CAPABILITY DEVELOPMENT OF DEVELOPING COUNTRIES

For most developing countries, it is probably too expensive to make the necessary commitment to accomplish the training, infrastructure and support of the type and magnitude described above. In view of the expense, difficulty and time required, the question arises whether it is necessary for developing countries to advance their capabilities to master the new biotechnologies. The logical answer is clearly "yes".

The major reason is that it is not practicable to maintain a continued dependence on the developed world. Further, in recent years much of the applications of biotechnology has been spearheaded by private companies whose work programmes are driven more by the profit motive than by anything else. There are few, if any, signs that companies in developed countries are willing to undertake projects related to the needs of the third world. So it is encouraging to see that international agencies such as UNIDO, US AID and UNESCO are taking measures focussed more on need than on profit.

As discussed elsewhere in this volume by Dr. D. McConnell, UNIDO is in the process of establishing an International Centre for Genetic Engineering and Biotechnology which will: (a) train selected scientists from developing countries; (b) arrange regional and international seminars, symposia, workshops and specialized training courses; (c) conduct R+D work on some of the pressing problems faced by the third world countries; and (d) act as a focal point for a network of affiliated centres. The US AID has also designated priority areas in biotechnology and is supporting research projects in the developing countries. Since the two agencies are working for the same goal, an ideal situation should be possible where collaboration be undertaken aimed at complimenting each others efforts for the promotion of new biotechnology in developing countries.

Being familiar with the work of these two organizations, I propose that they adopt the following measures:

(a) Organize visits of scientists from the advanced world to the developing countries. These scientists should meet top-ranking officials, hold discussions with administrators and scientists and give seminars in various laboratories. Such activities will promote rapport among scientists from various regions of the world, thereby contributing to the global sharing of knowledge. Furthermore, young scientists in developing countries can have first-hand accounts of the achievements of human intellect.

(b) Organize regional workshops and specialized laboratory courses to enhance the capabilities of local scientific and technical manpower.

(c) Arrange visits of foreign scientists of the elite group to physically work in the laboratories in developing countries. By working on the priority projects of the host country, help would be provided to improve university teaching, build infrastructure and train local manpower. This is obviously the most economical means of training manpower.

(d) Set up a number of production and service units located in geographically different regions. A network of such units could prove extremely useful in capability building. These units may stock biochemicals and rare enzymes; deposit books and journals; stock spare parts for various equipment; store bacterial strains; offer facilities for a gene bank; manufacture and distribute video-tapes on various techniques used in genetic engineering and DNA sequences, etc. The proposed units may acquire these important materials through the courtesy of ICGEB or by bulk purchase and provide them at cheap prices payable in local currency. The establishment and successful running of these units will ensure for the working scientists a reliable supply of materials considered to be the heart of the new technology.

These measures, in my opinion, will greatly help the developing countries in strengthening their biotechnology capabilities.

BUILDING BIOTECHNOLOGY RESEARCH AND DEVELOPMENT CAPABILITY IN DEVELOPING COUNTRIES

by

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I. INTRODUCTION

There are many definitions of "biotechnology". For this paper, I adopt the definition given by the International Union of Pure and Applied Chemistry: "the application of biochemistry, biology, microbiology and chemical engineering to industrial processes and products (including here the products in health care, energy and agriculture) and to the environment" (1) I agree with the statement that "agriculture and traditional crop and animal breeding are not regarded as biotechnology" (2). However, biotechnology does include the use of modern genetic manipulation techniques for the development of novel plant and animal varieties.

The development of biotechnology is of vital importance to all nations, both developing and developed. Biotechnology will make important and long-lasting contributions in the following areas: agriculture, biological products, chemicals, energy, enzymes, food, health care, mineral recovery, enhanced oil recovery, pollution management and waste treatment.

The first step in building biotechnology research and development (R+D) capability in a developing country is to clearly identify, and then to establish, biotechnology as a national priority. Priority assessment by a country requires the joint efforts of its policy-makers, economists, expert scientists and engineers. One problem a developing country often faces is the lack of such experts to provide sound and realistic advice. It is then necessary to ask a group of experts from abroad to help identify specific areas in which to concentrate. Expatriate scientists and engineers who are now leaders in specific disciplines of biotechnology can be especially helpful, because they understand the problems in their homeland and they are usually willing to put in the required effort. After priorities have been specified, funds must be appropriated for building new facilities and for training biological scientists and chemical engineers (these two groups will henceforth be referred to jointly as biotechnologists). Long-term commitments must be made by the government to support biotechnology programmes in order to reap long-term benefits.

There is both a training and a production component in building up biotechnology R+D capability. A first-rate university can serve as a model for the training component, and a successful biotechnology company can serve as a model for the production component of a national programme. My choice of factors which I believe are vital for capability building comes mainly from my experience as a biological scientist who has been working in a first-rate university for 20 years, and as a consultant for two biotechnology companies. Since the starting point in building R+D capability is to develop a system for training a group of highly competent biotechnologists, and then to provide them with a supporting environment for them to practice R+D, these aspects will be stressed throughout this paper.

II. TRAINING OF INDIVIDUAL BIOTECHNOLOGISTS

The training of biotechnologists in developing countries has the same requirements that it has in industrial nations. The biotechnologist must have a solid grounding in the basic sciences at the undergraduate level and advanced training at the graduate level. Additional laboratory or practical experience through postdoctoral research or traineeship is equally desirable.

A. Training at the undergraduate level

Adequate undergraduate training includes studying a broad range of subjects including both elementary and advanced courses in biology, chemistry and mathematics. For example, basic biological sciences may include lecture and laboratory courses in general biology, biochemistry, microbiology and genetics. Some students may also take botany, animal physiology or cell biology. Basic chemistry may include general chemistry, quantitative analysis, organic chemistry and physical chemistry. Mathematics should include calculus and differential equations. Furthermore, some knowledge in computer sciences is a must

for all students and chemical engineering courses for the engineering students are also essential. In addition, students must learn to express their ideas clearly in speaking and writing. In all courses mastery of fundamental principles must be stressed and students must be trained to use their knowledge in problem solving. However, certain experience can only be gained through laboratory work.

B. Training at the graduate school level

Training at the graduate level includes advanced courses in a cluster of related subjects. The most crucial component in the training of graduate students comes from the carrying out of an independent research project, which involves the planning and execution of experiments in a logical and elegant way. Learning from fellow workers is as important as learning from senior faculty members. It is essential for the students to develop the ability to think through problems and design experiments to solve them. Frequent interaction with other students and critical readings of the relevant scientific literature are important activities in gaining advanced knowledge and for developing sound judgement.

C. Training at the postdoctoral level

After completing their Ph.D. degrees (or equivalent) it is most helpful for scientists to take on further post-doctoral research training in a different laboratory to gain new skills and perspectives, and for engineers to obtain practical training in a modern biological, chemical or genetic engineering company.

D. Training or retraining of already established investigators and technologists

There is a possibility of providing already established investigators and technicians with additional training or retraining. In general, it is productive when the further training is in a closely

related discipline or involves similar techniques. The retraining of investigators or technicians to acquire new knowledge or learn new techniques in a different discipline is usually more difficult, especially if they are over 45 years of age. For these reasons, it would be more desirable and productive to retrain young postdoctoral fellows or technicians.

Each developing country must decide where to have its students trained. Some can provide their students with adequate undergraduate training or even graduate level training within their own countries. Other countries are better off training a certain proportion of their undergraduate or graduate students in a developed country. In most cases, advanced post-doctoral training for biotechnologists should be carried out in carefully selected laboratories, research institutes or companies in developed countries. After a sufficient number of well-trained biotechnologists have returned to their own countries, they can gradually take over the responsibility of training undergraduate and graduate students. However, since biotechnology is a fast moving field with frequent introduction of new methods or technologies, the majority of post-doctoral training should probably continue to be carried out in developed countries.

III. DEVELOPING TEAMS OF SCIENTISTS AND ENGINEERS

Frequent interaction with other biotechnologists is indispensable to a productive scientific career. Any research institute or genetic engineering company must possess a "critical mass" of scientists and engineers. The principle behind the idea of "critical mass" is that five biotechnologists working in the same place are more effective and productive than the same five biotechnologists working in five different places. This is related to the benefit derived from frequent interaction and help among biotechnologists, which is much easier and more effective when they are working in the same place. Within a particular field, it is invaluable for colleagues to raise questions and help solve problems. This principle also applies to scientists or engineers in other

disciplines. In order to use different concepts or techniques to solve a certain problem, it is essential that a team consists of biotechnologists from a range of disciplines. For example, a successful team of workers in biotechnology must have at their disposal several independent scientists in each of the following basic disciplines: biochemistry, microbiology, immunology, cell biology and biochemical engineering. Depending on the type of projects, a team may also need one or several experts in specialized fields such as genetics, virology, pharmacology, plant science, animal science or food science.

The size of a team of biotechnologists in an institute depends on several considerations:

(a) The number of problems on which the team is expected to concentrate. Even if the team intends to solve only one problem, it may need well-trained biotechnologists from two or three disciplines. In general, the critical mass can be achieved with approximately five well-trained independent workers (Ph.D. level or its equivalent, plus others possessing several years of postdoctoral training and work experience) in a given discipline. To achieve high productivity, each independent worker needs an average of four to six support personnel, including senior assistants, laboratory technicians and administrators (see section III-C).

(b) Whether the team is expected to carry out separate basic research in addition to goal-oriented R+D. In order to benefit the country the most, at least in the long run, the biotechnologists should devote a portion of their time to carrying out basic research without specific application. Basic research is needed to build up broad-based background information and later on some of it may turn out to be extremely useful in solving practical problems. Certain breakthroughs with theoretical or practical significance can come only from basic research. For example, the discovery of restriction enzymes in 1970 came from basic research on the molecular biology of bacteria. Shortly after their discovery,

the application of restriction enzymes (by now more than 100 have been found) in genetic engineering and biotechnology has become an indispensable tool in the splicing of DNA. In fact, goal-oriented developments often depend on first carrying out basic research. For example, before interferon could be produced in large amounts in bacteria for commercialization, basic research was needed in cloning the interferon gene, and then in finding the most suitable promoter and microorganism for its efficient synthesis. Therefore, I strongly urge that policy-makers and directors of biotechnology institutes allow their biotechnologists to devote approximately 50 per cent of their time to basic research.

(c) Whether the team of biotechnologists is also expected to train more biotechnologists. If it is, the team may include six to 10 independent workers in each of the basic disciplines of biochemistry, microbiology, immunology, cell biology, and biochemical engineering. In addition, it may be necessary to also include three to five independent workers in each of several other disciplines, such as genetics, chemistry, plant physiology, animal science, virology and pharmacology. I believe that it is most desirable to combine the training function with research and development. The benefits are two-fold: (1) the students will get the most up-to-date information and training from the experienced and active biotechnologists; and (2) the established biotechnologists may be stimulated by the young and eager students, who may also contribute new ideas and additional help to the laboratory.

The number of teams of biotechnologists to be established in each country depends on the size of the country as well as the financial and human resources it can mobilize. A small country may start with one team while a large country may start with several teams in parallel. The optimum number of trained biotechnologists needed in a country has to be decided by its policy-makers. There is a close correlation between the number of university faculty involved in biotechnology and the number of students that can be trained. As stated by Bull, et. al. (3); in the

United Kingdom and in the United States of America, on the average each Academic Member can train four to five undergraduates, five Master's students and one to one and a half Ph.D. students per year. Thus, in order to increase the number of students to be trained in biotechnology, larger university faculties are needed.

One problem related to sending students abroad for training, especially for students starting from undergraduate years, is that a high percentage of them may not come back. The problem of "brain drain" (losing the most able and intelligent students from the country) has to be considered, and effective means devised to deal with the problem. The best way to minimize the problem is to make the research environment at home as attractive as possible so that the expatriate students will want to come back to serve their countries.

IV. NURTURING RESEARCH ENVIRONMENT

An environment which fosters success and productivity includes the following components:

A. Sufficient high quality laboratory space, library and computer facilities

The biotechnologists need high quality laboratory space to carry out their work efficiently. Generally, in a given research institution it is desirable to have shared instrument rooms, cell culture rooms, temperature controlled rooms, a recombinant DNA room, animal quarters and greenhouse space. Computer facilities and a good library are also indispensable. A good library should include current journals on biotechnology and related topics (around 500 journals may be needed), important books and monographs. A computer terminal that is connected to a major computerized information source in a developed country will allow instant access to important and up-to-date information.

B. Adequate and long term financial support

It is essential that adequate financial support is available for salaries, equipment, consumable supplies and other necessary items. Major instruments can be shared by an entire institute. These may include: an electron microscope, a protein sequencer, a DNA synthesizer, high speed centrifuges and fermenters. It is also essential to include a reserve fund in the annual budget to purchase items whose need cannot be easily predicted a year in advance. It is equally important to work out an efficient ordering and receiving system so that perishable supplies can be obtained without delay.

In scientific research and development, short-term projects may take a year or two to complete; long-term projects may take five to ten years. Certain challenging and important projects are long-term in nature. Thus, for any biotechnology institute (or company) to succeed, long-term financial commitments must be made by the government to allow inclusion of such projects.

C. Competent support staff

In order for highly trained scientists and engineers to be productive, they must be assisted by a competent support staff. The support personnel for each independent biotechnologist may include one or two experienced senior assistants (or postdoctoral fellows, if available), one or two laboratory technicians (bachelor's degree), and a laboratory aide (high school graduate fo outine laboratory work). In addition, a biotechnology institute needs: a far-sighted director, a business administrator (for managing the general operation of the institute), one or more machinists and electronic experts (for the repair and maintenance of equipment), one or two accountants (to be in charge of business and finance) and one or two persons for ordering consumable supplies and equipment. In short, the support staff takes over routine laboratory work, maintenance, and administration in order to free the biotechnologists for creative and productive work.

D. The freedom to choose directions and approaches within a given project

There are different ways, approaches and methods for solving a given problem. The scientists and engineers should be given sufficient freedom to choose approaches which they believe are the most likely to succeed. It would be counter-productive for a director, who is less knowledgeable on a specific project, to give specific orders.

E. Seminar programmes and meetings

Each institute should include an internal weekly seminar programme to keep its members informed of current research projects being undertaken internally and to review recent literature reports. It should also include a second seminar programme that invites first-rate biotechnologists from abroad to report and discuss important new developments, especially unpublished results. Each biotechnologist at the institute should be given the opportunity of attending one or two international meetings annually to keep up with new developments and to make useful contacts with leaders in the field.

It is advisable for members of a biotechnology institute to form close contacts with both the faculties of universities and the biotechnologists from industries, especially pharmaceutical industries. A monthly joint seminar programme should be arranged to exchange information on recent findings and to promote personal contacts between these three groups. This will help speed up the transfer of useful research results from the biotechnology institute and the universities to the industries. It is also necessary to have a small committee consisting of members of the biotechnology institute, major universities and key industries to promote the speedy commercialization of research results.

F. Annual symposium and review of progress

It is advisable for an institute to sponsor an annual symposium and to invite a number of experts to the meeting. These experts can discuss in depth certain topics of interest and can also serve two other important functions: (1) Some of the outside experts may serve on a review board to review the progress of biotechnologists doing related work at the institute; and (2) some of them may help in identifying new areas of research important for the institute to consider. Different topics will be chosen each year for the annual symposium so that after three or four years, all the important topics of interest to the institute will have been covered, and, equally important, the work of its biotechnologists in the field will have been thoroughly reviewed, also once every three to four years.

G. Subsidiary facilities

Adequate housing and recreational facilities, schools, stores, etc., preferably near the Institute, are among the stabilizing factors that would allow the biotechnologists and support personnel to concentrate on their work and stay in place for longer periods of time.

V. ORGANIZATIONAL REQUIREMENTS

A. Advisory boards

Clearly, the development of a strong biotechnology base in developing countries requires serious consideration by decision-makers of organizational mechanisms. A government is responsible for making the operation of its biotechnology institute as simple and as smooth as possible. As I see it, two advisory boards, one government and one scientific, need to be organized to advise and to assist the director of the institute. The government board may consist of two members, from each of the following:

(a) the national science and technology commission, to transmit government decisions to the director and to assist him in solving problems related to customs, transportation, manpower supply, and so forth;

(b) the department of budget or treasury, to assist the director with problems related to finance; and

(c) the city government (of the city in which the institute is located), to assist the director with problems related to buildings and grounds, roads, water and electricity supply, and so forth.

The scientific board may consist of the director and around 10-15 prominent scientists and technologists, including expatriate biotechnologists, to guide the overall scientific programme and oversee the long-term progress of the institute. The director would supervise the scientific operation of the institute and transmit the needs of the biotechnologists to the board members. An open and healthy communication between the board members and the director, and between the director and the biotechnologists must be maintained.

B. National biotechnology center

Each nation interested in building a biotechnology R+D capability should form a national biotechnology centre, which not only serves as a biotechnology institute to carry out R+D but also covers several additional functions. If a country has only one biotechnology institute, it can also serve as the national centre by the addition a coordination committee. If a country has several biotechnology institutes, the largest one will logically also serve as the centre. The functions of the national centre should include:

(1) The coordination of all the national biotechnology R&D activities including those being carried out in all the biotechnology institutes (if more than one exists), in universities, in other research institutes and in industries.

The national biotechnology centre should include a Co-ordination Committee constituted by some members of the scientific board and the director(s) of the biotechnology institute(s). The primary task of this committee is to find out what major projects related to biotechnology are being carried out in the country and elsewhere in the world. A secondary task is for it to help plan a national biotechnology programme and to establish priorities for both long- and short-term projects within the biotechnology centre.

(2) the promotion of cooperation between biotechnologists from universities and industries with those at the biotechnology centre. This can be done through a joint seminar programme (see Section II-E), or via bi-annual or annual joint national meetings. Further incentive for co-operation may be promoted by awarding special research grants for joint projects between members in the university or industry with those from the biotechnology centre.

(3) The fostering of contacts with national biotechnology centers and institutes in other countries, as well as with international agencies. For example, the national biotechnology centre could make co-operative arrangements or initiate exchange programmes with the UNIDO sponsored International Centre for Genetic Engineering and Biotechnology (ICGEB). Unquestionably, it will be easier and more effective for the ICGEB to make contacts or arrangements with a national centre than with individual biotechnologists within a country. Members of the national coordination committee may also make contacts with other international agencies having interests in different aspects of biotechnology, such as the World Health Organization (WHO), the Food and Agricultural Organization (FAO), the Consultative Group of International Agricultural Research (CGIAR), Microbiological Resource Centers (MIRCENs), International Cell Research Organization (ICRO), and so forth, for the exchange of culture collections, gene libraries, cloning vectors, seed banks and germplasm collections.

It is also important to exchange information with other national and international centers or agencies through computer systems, abstracting services, and special publications related to biotechnology.

VI. APPLICABILITY OF GENERAL PRINCIPLES

The aim of this report is to outline the basics of organization necessary for productive scientific research and development. However, one point that should be noted is that while certain efficient models for research and development have worked well among developed countries (such as the U.S.A., Germany and Switzerland), there is no guarantee that these same models will work in a particular developing country. However, there is a good chance that they will, if a few fundamental provisions are made in the way these countries value the contributions of their scientists and engineers. For example, related activities such as the procedure for ordering and receiving of supplies could be streamlined. In some developing countries, supplies ordered from abroad takes months instead of weeks to arrive because of cumbersome ordering procedures and inflexible customs regulations. Many of these problems are discussed by S. Riazuddin in this volume.

It should be pointed out that the general principles and specific examples cited in this report may work well with a number of developing countries but may not work as well with all of them. It is clear that some developing countries are more highly developed than others, and that the needs and problems of each country are likely to be different. It is also clear that certain countries may have certain unique problems which must be solved in different ways.

VII. SUMMARY

In summary, if a nation truly wants to build a strong research and development capability in biotechnology, it must make the necessary commitments and arrangements to train biotechnologists, and create the supportive environment needed by the biotechnologists in order for them to work creatively and efficiently.

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CAPABILITY BUILDING FOR BIOSCIENCE-BASED INDUSTRY BY DEVELOPING COUNTRIES

by

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I. INTRODUCTION

It is now well recognized that a revolution is taking place in biotechnology; a revolution which began in the early 1970s when the first of several powerful genetic engineering techniques was discovered. It is also well recognized that the applications of biotechnology and genetic engineering hold promises to help developing countries solve their pressing problems related to health, shortage of food and shortfalls in energy. These conclusions were already reached in 1981 when a symposium organized by the United Nations Industrial Development Organization (UNIDO) brought together bioscientists from far-flung places in the world to consider biotechnology vis-a-vis the developing countries. The symposium participants felt advances in biotechnology were indeed so relevant for developing countries that their scientists and technicians should, as soon as practicable, begin biotechnology R+D offering possibilities for payoffs to their home nations in the short and medium terms (1). More recently, a workshop held by the US National Research Council came to a similar set of conclusions (2).

Here consideration will be given to several approaches available to developing countries for developing and building advanced capabilities in biotechnology and the assistance which international organizations can render in this process. In particular, the focus will be on the vertical and horizontal transfers of bioscience and biotechnology. The vertical transfer of technology in its simplest form refers to concept development, i.e. the transformation of ideas or findings from basic research into a technology or a product. The horizontal transfer of technology refers here to the dissemination of research findings, concepts and technologies between nations, particularly from developed to developing countries. It will be seen that international organizations can positively affect both types of technology transfer. Of course, in an ideal situation of capability building, one kind of transfer will complement the other. However, as will be seen, the ideal is rarely, if ever, accomplished.

Due to the recent origin of dramatic developments in biotechnology and since the fields have unique characteristics, it has been argued that

past or on-going capability building in other technological fields offers little guidance to capability building in biotechnology. This contention has not been validated and here it is therefore presumed that much can be learned from past activities, especially those undertaken by nations and international organizations to formulate policy for industry to set up mechanisms for international technology transfer and establish and/or advance the capability of nations to perform R+D. Furthermore, quite a bit is known about present-day bioscience-based industry in developed countries. By combining the lessons learned from past activities to that which is known about the characteristics of present-day bioscience industry, suggestions can be formulated for capability building in biotechnology by developing countries. More relevance will be given here to this process by attempting to discern directions of future R+D and the industrialization of the results thereof.

Accordingly, this study has four sections. First, concept development in developed countries and the mechanisms that have evolved for the international transfer of technology are considered. Next, the present-day biotechnology-based industry in developed countries is characterized. Third, relevant findings from the first two sections are used to formulate suggestions for capability building in developing countries. Last, tentative conclusions are reached as to steps which could be taken by developing countries to accomplish capability building in biotechnology R+D and industrialization.

Before proceeding with the substantive part of this study, it is useful to define terms related to technology (3):

- Technology: A collection of physical processes which transform inputs into outputs, together with the social arrangements, that is organizational modes and procedural methods which structure the activities involved in carrying out these transformations.
- Technological mastery: Operational command over technological knowledge manifested in the ability to use this knowledge effectively and achieved by the application of technological effort.

Also implied by the term "technological mastery" is the capacity to further improve on a given technology (to derive further technology from technology). The term "mastery" connotes a thorough knowledge of the fundamental aspects of technology, including its scientific underpinnings.

II. CONCEPT DEVELOPMENT AND MECHANISMS FOR THE INTERNATIONAL TRANSFER OF TECHNOLOGY

A. Concept development

Figure 1 represents an ideal situation of concept development; i.e. the selection of an idea from the store of fundamental knowledge and the series of stages through which it passes before reaching the consumer in the form of a product or process. In the ideal situation we find a large store of fundamental knowledge continually being replenished and augmented by results from basic research. The store is freely and easily accessible to whoever wishes to use it. Worthwhile ideas are selected from the store by industry possessing the capability and resources to turn the ideas into commercial products and processes. Products and processes are developed and marketed because consumers require or want them.

Reference should now be made to Figure 2 (4) which is an expansion of the central part - Industry - of Figure 1.

There are four main components existing either apart or, in some cases, under one roof (for example, a transnational corporation, or TNC, will commonly have a basic research laboratory, several applied research laboratories, manufacturing units, marketing and sales units and retailers). These are:

(a) Store of fundamental knowledge (characterized above).

(b) Research unit. An independent research unit should be capable

of selecting ideas having the potential for industrialization from the store of fundamental knowledge and developing them to the point where sufficient information is available for making a decision whether or not it is marketable (the feasibility determination stage). If the conclusion is no, the idea is dropped. If the answer is yes, the idea is presented to a manufacturing unit with relevant information. If insufficient data prevent a decision, the idea can be further developed until the stage where a technology can be said to have resulted. At this point, the technology can be transferred to the manufacturing unit. When the research unit is part of a firm, all the foregoing apply; additionally, the unit must have the ability to respond to feedback from consumers. Feedback and the appropriate response to it can lead to either present technologies being improved or new ones being created. An important function of the research unit is for it to form effective linkages with universities to draw on their fund of knowledge and expertise.

(c) Manufacturing unit. This unit, the core of an industrial firm, must have the capability of assessing the many ideas and technologies emanating from both its own research unit (if one exists) and from outside sources, whether public or private. After assessment, those very few possibilities for commercialization must be selected and developed to the point where the feasibility of marketing the technology can be determined. Factors which enter into the determination include projected production costs, results from market surveys, evaluation of profit margins, etc. If a determination to proceed is made, the manufacturing unit should have the capability of scale-up and manufacture, while making certain that adequate quality control can be maintained in the production stage.

(d) Marketing and sales unit. The unit should have the ability to conduct a market survey before a technology is introduced in order to estimate market acceptance and market size. After a

technology is manufactured, the unit's responsibility is to make certain the technology reaches intended markets, that it is packaged correctly, and that the market is aware of the technology. Consumer response to the marketed technology should be accurately gauged and used as a basis for improvement or to generate new ideas.

The ideal, as represented in Figures 1 and 2, is never wholly realized. Almost invariably three barriers will affect concept development. First, the linkage between universities and industrial research units may be weak or non-existent. As S. Riazuddin points out elsewhere in this volume, this is an especially acute problem among developing countries. The second is the transfer of research results to the manufacturing unit, an event difficult to achieve under the best of circumstances. This could be a national problem: several nations have histories of being unable to transfer results from their basic research establishments to their industry. The problem is not limited to countries; potentially useful research performed in basic research laboratories owned and operated by private firms is to a great extent not applied by parent companies (5). Third, there will always be severe restraints on the availability of resources; even the largest company can only undertake a small number of projects at one time. For a small or medium-sized firm, sound project selection is of utmost importance since failure of a project wastes meager resources - a small firm may not be able to survive even one major failure. Quite probably a parallel situation exists in this regard with developing countries. Due to a scarcity of resources, each country will have to take extreme care when selecting development projects.

The ideal situation depicted in Figure 1 is approached by only a few nations. Individual developing countries have reached different levels of development; a few may possess all the elements of the ideal situation, at least in rudimentary form, while others have only limited manufacturing and sales units. Although these great differences exist, it is probable that all developing countries (in fact all countries) strive to achieve self-sufficiency to the greatest possible extent. Self-sufficiency is achievable if a country develops self-reliance - the

ability to control its own resources. Control is only possible if adequate knowledge about resources is available, and this knowledge can only be obtained through science (6). Once the requisite knowledge is available, a technology (or technologies) may be developed in order to utilize science's fruits. Their effective mobilization and use requires their wielders to achieve technological mastery. It follows, therefore, that for a country to control and exploit its resources, it must have both the capability of performing scientific research and the means to translate the knowledge into products and processes, i.e. the ideal situation depicted in Figures 1 and 2. The question is then how a country can take the appropriate actions to come close to the ideal situation in biotechnology, a question which will be taken up in the next section.

B. International transfer of technology

Accessing science and technology (S+T) in developed countries inevitably involves the co-operation of foreigners. The role of foreigners can be relatively passive, for example when a developing country sends its nationals abroad for study, when it acquires foreign publications or when it copies foreign products. More generally, the concept of technology transfer includes an active role for foreigners. The following are examples of mechanisms for technology transfer that have evolved in international trade (7); all include foreign involvement to varying degrees:

- A technology-based company in a developed country establishes a subsidiary in a developing country and provides the imported technology, capital investment and management. The host nation provides infrastructure, unskilled labour and protects the investment.

- A company in a developed country forms a joint venture with a unit in the host country. Of course, contract terms will vary but both parties usually share the capital investment burden, management and control over the imported technology. The host provides unskilled labour, protection of investment and, at times, raw material.

- The developing country buys a production plant and the technology needed for production. The terms of the contract may require the seller to provide training to nationals of the host nation and whatever other assistance is necessary to operate the facility. Theoretically, all the buyer must do to begin operation is to turn the key in the plant's front door.

- As a form of foreign aid, a developed country's government may provide a technology to a developing country, usually for infrastructure building.

- An R+D unit in a developing country may have developed a technology but is unable to scale-up and industrialize results. To do so, it could find value in engaging the services of an engineering firm in a developed country.

- In a few cases, technological capabilities of a developing country could be relatively high. If so, it may only need the services of expert-consultants from developed countries to review plans and programmes.

- A government unit or a firm in a developing country may possess some degree of technological capability. If so, it may, after negotiation, purchase the rights to commercialize an invention. The purchase could be in the form of license, rights to a patent, or rights to share in a trade secret. In any case, the buyer is responsible for any further development (if needed), manufacturing, quality control, marketing, etc.

- A unit in the developing country may purchase a finished product in bulk and package it for marketing.

- A unit in the developing country may purchase the finished, packaged products and concentrate solely on marketing it.

From the foregoing it is clear that a range of options face decision-makers of developing countries who wish to either develop a new capability in S+T or improve existing capabilities. The options range from taking substantial steps of developing an independent capability in R+D and being able to scale-up and industrialize results from indigenous or foreign R+D to doing very little, i.e. importing a finished product and selling it on the local market. Whatever option is chosen the importing country needs to take adequate steps in order to avoid becoming dependent on the provider. A necessary precaution to avoid dependence is for a country to strengthen its capability in assessing its needs for

technology and for negotiating contracts on technology transfer. In this way the importing of unnecessary technology is prevented while that which is procured will have pertinence and be obtained under the most favourable terms.

III. CHARACTERISTICS OF THE BIOSCIENCE INDUSTRY

Since a bioscience-based industry has only recently come into existence in developed countries, its history provides few clues as to whether this field is likely to follow patterns of other technology-based industries when they were in their infancy. One must therefore begin a consideration of the field by regarding bioscience industry as it now exists and by trying to discern the direction of its future growth.

To begin with, it should be noted that biotechnology research has some unique characteristics. In other areas of science it is possible to differentiate between basic and applied research: basic research has always been considered as knowledge for the sake of knowledge, that research findings cannot be predicted, that much basic research cannot be applied and that the time between the basic research stage and the product stage is lengthy. Biotechnology research in many instances proves to be exceptional; results from so-called basic research in this field tend to be applied quickly. For example, the genetic control over cellular production of insulin was clarified through research in 1976; the genetic coding sequence for rat pro-insulin was inserted into the bacterium Escherichia coli (E. coli) in 1977; expression by E. coli of the two chains making up human insulin was accomplished in 1978, and by July 1980 sufficient quantities of human insulin were being produced by E. coli for medical researchers to begin clinical trials. In the autumn of 1982 the US Federal Drug Administration granted market approval to the form of human insulin produced by E. coli called Humulin (8).

An even more striking example involves the protein growth hormone-releasing factor (GRF). In June 1982 the protein's chemical structure was determined, three days later the protein itself was synthesized and only two months after these findings were reported to a scientific meeting, a bioscience firm had synthesized the gene coding for GRF and was selling it (9).

It can be seen that a scientist publishing the results of basic DNA research may, in the instance, be providing information applicable to producing new substances or modifying existing industrial practices. Therefore, for the purposes of this paper, it is not worthwhile to attempt to differentiate between basic and applied research but rather to accept that bioindustrial-related research considerably adds to the store of fundamental knowledge, thereby advancing science as well as biotechnology.

The bioscience-based industry which is now emerging can be characterized as follows: It is overwhelmingly based in the developed world, primarily in the US and Japan. In the US it consists mostly of small- and medium-sized firms (10). Many firms are controlled by scientists who tend to hold equity positions in companies; strong industry-university linkages are the norm; industry is largely in the idea development phase, i.e. few products have been marketed; companies tend to concentrate on high-value products, usually related to the health field. Information from several sources indicates that large companies, including TNCs, are actively building their capabilities in biotechnology R+D. Steps taken or being taken in this direction include strengthening internal research facilities, setting up joint ventures with small bioscience firms, and buying equity in these firms. The latter three may include terms for the investing TNC to share the developed biotechnology and related know-how.

Health-related products have so far received major public attention because by fortuity much of the initial research which led tc the development of genetic engineering techniques was performed by molecular biologists using microorganisms important in disease and who were funded by agencies active in medicine. It is also axiomatic that it is easiest to procure research funding in developed countries if the research

pertains to diseases afflicting their populations, such as cancer and heart diseases. The emerging bioscience industry has for similar reasons tended to enter R+D areas where the potential for early pay-off is the greatest. It follows that much of the research taking place in the industrialized world has little relevance to developing countries.

A commonly held opinion among industrialists and investment counsellors is that many small bioscience firms will fail in the short-term, either because of under-capitalization or due to poor management (or both); others will be bought out by larger firms and only a few will survive and prosper. Signs of contraction have already appeared: firms are narrowing their fields of activity, usually by concentrating on projects having a high possibility of short-term pay-off. Concomitantly, the hiring of bioscientists has declined while the demand for bio-engineers has increased - a demand likely to remain unsatisfied because of a lack of suitably trained people.

From the foregoing characterization of bioscience-based industry, it is clear that biotechnology R+D is in an early phase of maturation while its derivative industry is in its infancy. This situation offers both disadvantages and opportunities to developing countries. The major disadvantage is that so much attention is given by both researchers and industrialists to idea development and to infrastructure building, that it is doubtful whether much energy or resources remain to assist developing countries or their scientists.

The opportunities, however, could become quite significant: first, since the bioscience-based industry in developed countries is in its formative stage and is not yet ready to branch out into the third world, and since the governments of developed countries have not yet organized more than the rudiments of foreign assistance in biotechnology, the probability of developing countries becoming technologically dependent on industrialized nations is small in the short- and medium-term. The opportunity is thus presented for setting up and making use of mechanisms for the international transfer of biotechnology most favourable to the recipient countries.

Second, biotechnology, being an emerging S+T area, allows the possibility for third world researchers to enter on the "ground floor". In order to do so, it is beneficial for developing countries to strengthen their abilities to perform R+D in the biosciences.

Third, as a consequence of the foregoing two points, one may conclude that developing countries will largely have to develop and depend on their own resources to advance biotechnology. This implies a requirement for each developing country not only to strengthen its ability to perform bioscience R+D, but also to be able to industrialize research from such R+D.

IV. BIOTECHNOLOGY CAPABILITY BUILDING IN DEVELOPING COUNTRIES

For the purpose of this study, a working assumption is made that national decision-makers in several developing countries have made, or are making, national commitments to advance biotechnology (nations known to have formulated national policies in biotechnology include Brazil, India and Thailand). At the same time, it must be recognized that a wide range in the level of national capabilities exists in biotechnology. At one end of the scale several of the advanced developing countries, such as Brazil, India and Thailand, have universities where basic research in molecular biology is performed; they have applied research facilities where projects are undertaken to solve national problems and they possess manufacturing units capable of producing bio-products such as antibiotics and vaccines. At the other end, there are countries which have fermentation plants capable of producing only fermented foods and beverages. Obviously, the national strategies for developing potentials in biotechnology of the first group would be quite different to those of the second group. Nevertheless, certain basic requirements will have to be met before a country not advanced in biotechnology is able to more fully develop its potential in this field where science and technology are inextricably mixed. In the following pages two broad requirements will be discussed: the importance to each country of having people

available who are capable of performing biotechnology R+D and the necessity for each country to have a firm basis upon which a bioscience industry can become established and grow. It will also be seen that various international organizations are positioned to assist countries in fulfilling these requirements.

A. Capability Building in Biotechnology R+D

Nobel prize winner D. Baltimore has pointed out that although biotechnology is "... a very high technology in terms of being at the forefront of basic science, it is a very appropriate technology for solving the problems of people at all levels of development" (11). Furthermore, he holds that it is most important for developing countries to have a national capability in biotechnology because its applications "go to the heart of the basic necessities of life" (12). In order for a country to develop the necessary capability of understanding and using the new biotechnology techniques - i.e. to perform biotechnology R+D of high quality - three prerequisites are required as to education, infrastructure and support. Since these elements, are discussed at some length by two other authors in this volume (S. Riazuddin and R. Wu) they will only be briefly mentioned here:

Education

In order to perform high quality R+D, well-educated researchers must be available. Availability can only be guaranteed by taking long-range action at the national level ensuring that certain educational opportunities are made available to all those persons with aptitudes for science. Opportunities include making available physical facilities, qualified teachers, textbooks and other implements necessary for students. Experience indicates that it takes approximately 30 years (from early maturation through post-doctoral studies) to rear a biotechnology researcher.

It goes unquestioned that opportunities exist for promising scientists from developing countries to study and train in the industrialized nations. Some opportunities for study abroad come about as a result of bilateral treaties and others are occasioned through support made available by private organizations and through schemes such as the Rhodes Scholar Programme. But in the final tally, most of the developing countries' promising students will have to receive their education and training at home. To do so in an adequate manner, assistance for national action in education can be sought from international organizations.

UN associated organizations, particularly the United Nations Educational, Scientific and Cultural Organization (UNESCO) has been active in helping countries upgrade their educational systems. On a general level, assistance has taken the form of UNESCO providing model instruction plans, helping in training teachers, helping in procuring textbooks and supplies, etc. More relevant to the thrust of this paper is UNESCO's work in applied microbiology.

UNESCO, in collaboration with the International Cell Research Organization, was responsible for setting up the Panel on Microbiology in 1965 to develop and foster an international network of organizations for the purpose, inter alia, of exchanging information about microorganisms, particularly their potential for improving the welfare of human beings (especially in the third world). In 1975 the United Nations Environment Programme also became involved in this project and as a result it was expanded. Thus, the world-wide network of Microbiological Resource Centres (MIRCENs) came into existence (13).

The first step was to set up a World Data Centre on Microorganisms as a MIRCEN at the University of Brisbane, Australia. Since then a regional MIRCEN has been set up in Bangkok to serve South East Asia, and one in Guatemala to serve Central America. Additional MIRCENs are sited in Stockholm (Sweden), Cairo (Egypt), Nairobi (Kenya), and Porto Alegre (Brazil). The latter two specialize in nitrogen fixation, with specific reference to Rhizobium. The work programme of MIRCEN has been reviewed elsewhere (14), and it will only be noted here that MIRCEN affiliates have taken on the important role of training several hundred persons from

developing countries in microbiology applied research. Experience gained from MIRCEN activities indicates that in the short term much can be accomplished by retraining, or upgrading the skills of available technical people (15). For example, fermentation workers in breweries can be retrained for work in antibictic producing plants, while researchers in industrial plants can upgrade their skills by participating in intensive workshops concentrating on rDNA or monoclonal antibodies. (Retraining as part of capability building is discussed at greater length elsewhere in this volume by R. Wu.)

The activities of another non-governmental organization, the Committee on Genetic Experimentation (COGENE), has somewhat paralleled the activities of MIRCEN but with a much heavier concentration on raising the ability level of persons to perform basic research. COGENE was established in October 1976 by its parent organ the International Council of Scientific Unions in order to consider the alleged risks posed to society by rDNA research. When the risk issue faded in the early 1980s, COGENE shifted its focus to three areas of interest:

(1) the organizing of workshops and other training activities;

(2) the arranging of a future conference on interventions in plant and animal genomes;

(3) a consideration of university-industry relationships.

The activities of COGENE have been reviewed elsewhere (16), nevertheless, for the purposes of this paper, it is of interest to consider the first area.

The concept of COGENE workshops is rather innovative. Typically, the two-week workshops will provide intensive training in genetic engineering techniques to students of the natural sciences from nations not advanced in biotechnology. COGENE will supply the instructors (usually highly regarded molecular biologists from France, UK, USA and the Federal Republic of Germany) and retains the right to select trainees. The host nation provides facilities for holding the workshop and pays all expenses. It must allow at least 50 per cent of the trainees to come from foreign countries.

Lack of resources is the main hindrance to COGENE furthering its good work. The organization limps along on a budget of approximately US $15,000 per year plus ad hoc funds raised from private sources to hold its annual meetings. Of course, its major value lies in the knowledge and skill vested in COGENE member-scientists, deployed as a matter of good will and personal sacrifice on behalf of scientists needing added skills. Yet the activity level of COGENE is low and is likely to remain so.

By setting up workshops and training scientists from developing countries, COGENE becomes a conduit for the international transfer of scientific knowledge to scientists of the third world. It is impossible to measure at this time the extent to which this COGENE activity will affect the developing countries' ability to perform basic and applied biotechnology research. For example, the first three workshops were held in Brazil, India and Yugoslavia (others have since been held in South Africa and Costa Rica). The first four nations are now actively involved in biotechnology. In Brazil, a small infrastructure of basic research has been set up and the government is now trying to decide on future directions (17). A similar situation exists in India where a basic research establishment is in place and is performing research (19) and the governme t has set up a Biotechnology Board under the Council of Scientific and Industrial Research (19). India has recently announced a national plan in biotechnology (20). Yugoslavia has been performing molecular biology basic research for some time; recently three industrial enterprises decided to set up a Genetic Engineering and Biotechnology Centre (21). Although it is not possible to conclude that the COGENE workshops resulted in, or hastened these developments, it is reasonable to believe that the training scientists received in the workshops added to those nations' total capability of performing biotechnology R+D.

Of the international organizations involved with new biotechnology, UNIDO appears to be in the most favourable position to influence future biotechnology developments in developing countries. Its major effort has so far been focused on establishing an International Centre for Genetic Engineering and Biotechnology (ICGEB) (22). The progression of events which lead up to the fruition of this effort is related by D. McConnell

elsewhere in this volume as are some of the lessons that were learned while attempting to realize the ICGEB. In this chapter more attentionis paid to other UNIDO activities, such as its attempts to develop joint R+D programmes, promote joint ventures in industry and provide advisory services to governments.

Other than the foregoing organizations, the contributions of international organizations to less developed nations in the form of assisting them to educate and train biotechnologists has not been remarkable and their contributions are not likely to grow soon, primarily because funds are lacking for expanding present programmes or undertaking new ones.

Infrastructure

Requirements pertaining to infrastructure are discussed in this volume by R. Wu; here it is sufficient to note that biotechnology R+D is perforce dependent on support as provided by a strong infrastructure, especially on adequate and dependable services for supplies and utilities. Infrastructure also includes the presence of an academic environment (including libraries) to nurture scientists and technicians. The building of infrastructure and the implementation of plans are almost wholly dependent on national decision-making. Measures which may have to be taken by individual countries to build or strengthen infrastructure could include:

- Establishing procedures whereby the import of vitally required reagents and equipment is facilitated and the continuity of supply can be assured.
- Establishing avenues of communication so knowledge generated in other parts of the world can be made available to national researchers.
- Adjusting national legislation pertaining to intellectual property rights to encourage innovation.
- Taking internal measures to encourage import of necessary biotechnology.

- Making certain scientific libraries exist which possess adequate numbers of books and representative periodic literature.

Although the usefulness of taking these steps cannot be denied, the difficulties facing an individual country attempting to do so are formidable (as is described in this volume by S. Riazuddin). For this reason, regional co-operation to set up centres where facilities are shared would be useful. For example, regional document distribution centres could facilitate the procurement of scientific books, journals or articles; regional purchasing organizations can be set up to purchase supplies in bulk; and networking arrangements could facilitate the sharing of information. The last mentioned measure could include an international component; for example, it should be possible for regional centres to be able to connect with the MIRCENs network. In the future, the planned affiliated regional centres of the ICGEB will offer possibilities of increasing regional co-operation in biotechnology.

Support

A nurturing environment of the development and growth of biotechnology results in the first instance from favourable political and economic conditions. If these conditions are present, specific actions must be taken to support science and technology. For small and developing countries it is important to husband resources; it is only the rare country that can afford to undertake R+D activities over the whole range of biotechonology. An important step for a nation can be for it to formulate a thoughtful national policy in a field deemed important. For most developing countries, a carefully thought-out national policy becomes invaluable as a reference aid; administrators and researchers will have guidance as to what kind of project shall be entered into, what the projects will attempt to accomplish, and the resources a country is willing to devote for goal accomplishment. Of course, national policy formulation must be followed by operational action which makes available the funds necessary for achieving policy objectives and provides the mechanism for their disbursement. The availability of funds must be

guaranteed for as long as possible; few events in life are as inefficient and demoralizing to scientists as research projects abandoned before completion because funds are suddenly not available. It is clear that economic and social stability is an absolute prerequisite for scientific achievement and only governments can provide these to its scientists.

Regional co-operation could be useful in order to define problems which affect several countries and to formulate a common approach for their resolution. For example, no one country in Africa should tackle trypanosomiasis in isolation; its conquest would have to involve all afflicted countries. Similarly the cost of R+D and the performance of actual R+D required before a potential resource common to a region can be commercialized is best shared by several countries according to a regional agreement.

The role of international organizations for support activities will be mostly advisory. Several organizations have had extensive experience managing policy related to science and technology and have also built up considerable expertise in biotechnology. A government might find it worthwhile to turn to UNESCO for formulating policy in matters related to education and basic research, to UNIDO for advice on formulating policy related to bioscience industry and to the World Health Organization (WHO) on health-related matters.

B. Capability Building in Bioscience-based Industry

At this early stage one cannot ascertain whether actions required to build capacity in the bioscience industry are different from those in other advanced technologies. Certain common traits can be detected: Industry based on advanced technologies is research-orientated; manpower requirements are more exacting than for other industries; the cutting edge of innovations is usually found in small- and medium-sized firms; and cost of entry is usually high. Bioscience-based industry may differ in some aspects from these general rules: the initial investment required to start up is often lower than for other advanced technologies and much biotechnology appears to be singularly appropriate for developing countries (23).

The generic problems and obstacles preventing the building of industry in developing countries is beyond the scope of this paper, though some of those that have been identified as significant to the forming of a bioscience industry will be presented and briefly discussed. These more of less generic problems pertain to financing, innovative climate, assessing information and fulfilling manpower requirements.

Financing

UNIDO's First Consultation on Industrial Financing found that serious impediments exist to raising capital for industry in developing countries; small- and medium-sized firms face the most challenging difficulties. The gap between available funds for investment in industry and those needed is large at present and is expected to grow to perhaps US $50 billion by 1990 (24). The question then is whether the obtaining of adequate financing for the establishment of a bioscience industry in developing countries will be hampered by a lack of capital investment. The answer is still unclear; perhaps a situation similar to that of the bioscience industry in developed countries will also arise in developing countries. There has been an impressive in-flow of capital investment funds to this new industry, partially caused by investors foreseeing a profitable future for biotechnology and partially due to the creation of tax incentives by governments favouring risk taking. If capital is available in developing countries that could potentially be invested in a budding bioscience industry, then this would be done by investors with the vision of biotechnology as a growth area holding promise for a fair return on investment. The instilling of such a vision demands an information campaign, run either by industry and/or governments, which makes the potential of biotechnology clear. In any event, the procuring of funds to promote growth in bioindustry must have the highest priority to those attempting to assist developing countries.

Innovative Climate

It is very difficult to identify what constitutes a favourable climate for innovation. Its core is most probably the entrepreneur - an individual who has the vision, acumen, resources and desire to make things happen. A recent study conducted by the Industrial Research Institute in the US supports this contention; it found that "overwhelmingly, an individual, not a group, recognized the scientific and technical opportunity. Statistical tests showed that this recognition ranked first among factors affecting the innovative process" (25). However, the entrepreneur must be able to function and this means that the environment in which he works must provide apt financial and intellectual rewards. Financial incentives include a favourable tax structure which is kind to risk-takers and allows for equitable rewards in case of success. Intellectual rewards may include proper recognition by authorities, accolade accorded to the innovator by popular and elite groups, just intellectual property rights to innovations, etc.

One characteristic of a bioscience-based industry is that its founders and promoters tend to be scientists active in universities or other research facilities. It is probable that the future bioscience entrepreneurs in developing countries will also be scientists and technologists. Recognizing this possibility, UNIDO has suggested that high priority be given to training individuals at the ICGEB who show promise of being able to use their training in setting up, or advancing, bioscience industry in their home countries (22).

Access to information

The innovator must have access to the previously described store of fundamental knowledge, partially in order to access results from research and partially to make certain he is not duplicating previous or ongoing work conducted elsewhere. These reasons also necessitate a continuous updating of information. However, the many services based on computer accessing now available are expensive to subscribe to and communications of sufficient efficiency for these services may not be available in developing countries.

The future ICGEB may be instrumental in alleviating this problem since one of its functions will be to collect and collate information, then distribute requested information to affiliated R+D centres in its member states. It is expected that the Centre will avail itself of the latest communications and computer equipment and will therefore be able to access information derived from past R+D and to collect information about ongoing publicly funded research in developed countries (26). Affiliated centres will have ready access to this communications network.

Manpower requirements

Bioscience industry requires staffing by researchers, bio-engineers, managers and technicians. Observation of the budding bioscience industry in the developed nations indicates that the delineations between these groups tend to blur - an interdisciplinary approach to problem-solving appears to work best. The multidisciplinary nature of biotechnology has been explained by a UNIDO group of experts:

> Actually, the principles of the methods and techniques employed in the fields of concern form a body of knowledge which is so large and so dynamic that no single discipline (eg. chemical engineering, bacteriology, virology, mycology, immunology, etc.) or problem area (food, fuel, vaccines, biological control agents, etc.) can be expected to carry its development (27).

For this reason, one of the functions of the future ICGEB is "...to build technological and scientific manpower in genetic engineering and biotechnology so that the developing countries can form multidisciplinary core groups which can carry out sustained research and development activities" (28).

The interdisciplinary approach in education may create problems for the many countries in which both education and training have been geared to produce experts in one particular discipline. The effort developing countries will have to exert in order to adjust their educational systems to the multidisciplinary demands of biotechnology (and other advanced technologies) will be sizeable. Since S. Riazuddin and R. Wu deal

elsewhere in this volume with this subject, here it will only be suggested that as national decision-makers become sensitized to the demands of biotechnology and other technologies, they will then be able to take steps to change educational systems in an appropriate manner. The experience several international organizations have in this area, particularly UNESCO and UNIDO, may be tapped by those contemplating change.

From the foregoing, it can be seen that severe generic problems are likely to substantially hinder the process of capability building in biotechnology by developing countries. To recapitulate these problems:

- Even if developing countries undertook to revamp their educational systems and greatly increase support for the education and training of scientists (neither likely to happen soon), positive effects would only become apparent in the long-term.

- The efforts by international organizations on behalf of developing countries, although valuable, are minute when compared to what is required and are not likely to have a measurable impact, at least in the short- and medium-term.

- Efforts by international organizations most active in this area, such as UNIDO, are still in their formative stages, and will not, therefore, have a measurable impact for some time on the world community.

- A lack of capital investment funds could hinder the formation of small and medium-sized bioscience-based firms; i.e., the type of firms probably most needed for the industrialization of results from R+D.

- Communications networks of sufficient adequacy to enable researchers and industrialists in the Third World to access information sources and stores will not become readily available for some time.

In view of these restraints to capability building, the question is whether means exist or could be created to overcome them and to advance biotechnology R+D and the applications thereof in developing countries. UNIDO's experience suggests that partial solutions do exist that can be brought into play in the short term. Palliative measures can be taken under the broadly termed headings of international co-operation and of the international transfer of biotechnology and relevant information.

International co-operation

An expert group of scientists brought together in 1981 under UNIDO auspices stated that developing countries needed to participate on an equitable basis in the further development of biotechnology as well as in its commercialization (29). This, the group thought, "... would call for an imaginative approach, extending beyond the traditional modes of technology transfer" (30). One suggested approach could be via international co-operative efforts "... through an international facility and transfer from such a facility" (31).

This idea was expanded through an iterative process and eventually formed the basis for the establishement of the ICGEB. The ICGEB and its position as a lynchpin for international co-operation in biotechnology, particularly by the developing countries, is described in detail by D. McConnell elesewhere in this volume. Mention will only be made here that the scientists who explored the idea of the ICGEB in 1981 concluded that due to "... the general lack of infrastructure and financial resources to support adequate R+D effort in biotechnology , the Centre may well be the only means by which developing countries can get a start in this field and ensure that optimal technology choices are made, local problems addressed and major natural resources fully utilized" (32). At the same time, these scientists did not expect that the fully operational ICGEB would hinder either bilateral co-operation, other institutional efforts in this area, or commercial flows of biotechnology. Actually, it was felt, these other processes may actually be boosted and "opened up" by the wider sharing of biotechnology brought about by the ICGEB and the affiliated network of R+D centres which it will occasion.

In view of the many and varied activities being undertaken in the field of biotechnology by both public and private international organizations, mostly with the aim of sharing the likely fruits from research with the populations of the Third World, an outline of a tremendous global effort is becoming discernible. The outline has several dimensions and many interlocking parts but it is not yet clear how they will all fit together. The dimensions are the different fields

of human endeavour including scientific research, therapeutics, agriculture, mining, energy production and the many industrial activities. The parts are the human components (scientists, engineers, administrators) working most often as teams in various facilities (private and public laboratories, universities and international organizations). The threads connecting it are the sinews of biotechnology, particularly the recent developments of genetic engineering. Into this as yet vaguely outlined structure flow inputs - that is the ideas, accumulated knowledge of mankind, manpower, and financial and material resources. The output has been a great outburst of knowledge, some of it elucidating for the first time nature's most closely held secrets of genetic control over inheritance and differentiation. A trickle of products and processes is also beginning to emerge; a trickle which is certain to turn into a flood within a comparably short time. Will the main stream only bring the promise of bountiful harvests to the rich, the industrialized, and those that have? The tremendous international effort which is beginning has as its aim that at least part of this stream is diverted to serve the needs and desires of the less fortunate populations in developing countries where biotechnology may positively affect the very basis of life as well as add to its quality.

The international transfer of biotechnology

From a recent survey of bioscience-based industry (33) a conclusion can be drawn that a number of firms are desperately attempting to survive. Out of the approximately 150 US bioscience-based firms, it is likely that less than 10 per cent will survive the next ten years in a recognizable form. At the same time, the large TNCs are just entering the field, and of them only a few, such as Monsanto, ICI, Hoechst, and General Electric, have large in-house biotechnology R+D facilities. The present situation holds implications for the international transfer of biotechnology:

(a) Due to the importance of ideas and research to bioscience industry, firms tend to be secretive about their R+D programmes. Therefore, little is known about the details of research taking place in bioscience industry. Under present circumstances, it is doubtful whether more than a

few firms are sufficiently secure to willingly transfer knowledge and know-how of potential commercial value to developing countries.

(b) Only a few processes and products based on, or resulting from, genetic engineering applications are as yet available on the international market. Manufacturers of health-related products in particular, will face time-consuming clinical trials before their products can be marketed on an international scale. In addition, early products are not likely to be economically competitive (for example Humulin).

(c) No early possibility exists for a developing country to procure a turn-key bioscience facility employing new techniques.

(d) The TNCs are not yet involved in biotechnology to the extent that they can be considered as conduits for the international transfer of new biotechnology.

(e) Smaller bioscience firms in developed countries have neither the financial nor manpower resources to establish subsidiaries in developing countries, nor will there be sufficient incentives to do so in the foreseeable future.

In considering the mechanisms for the transfer of technology as presented above (pp. 6-7) it can be readily seen that only a few are germane, at the present time, for the transfer of biotechnology to developing countries. This is particularly true when one takes account of the requirement that technology transfer should add to the recipient achieving self-reliance through technological mastery. Thus, past patterns of developing countries becoming technologically dependent on the conferrer must be avoided. With this important caveat in mind, available mechanisms include those where foreigners play a passive role, i.e. a developing country can send its nationals to R+D facilities in developed countries for training and education, and can act to secure foreign R+D and trade publications. Possibly more important are active mechanisms. Only two are relevant in the short-term: the formation of joint ventures and the purchase of intellectual property rights. An additional two will probably become significant in the medium-term - bilateral aid and contract R+D.

Joint Ventures

Though specific contract terms would, of course, vary from venture to venture, it is likely that each will have two common elements: the developed country bioscience firm provides the technology while the developing country entity supplies a valuable raw material and/or a worthwhile market to a product. For example, the berry from a bush indigenous to East Africa, Maesa lanceolata, has been used by traditional healers for many years to combat cholera. Recent research in Japan suggests that the active ingredient of the plant, named Maesanin, stimulates an as yet unidentified defense mechanism in animals. For this reason, the substance appears to offer the possibility for use as an antibacterial prophylactic substance (34). The African country which desires to exploit this plant could approach a bioscience firm for the purpose of setting up a joint venture. The joint venture could include terms for the firm to develop and share the technology necessary for Maesanin exploitation and for the fair division of future profits. The minimum gain for the developing country under this arrangement is the training of its researchers in some aspects of biotechnology; at the maximum, not only will the nation gain trained personnel but the substance could also prove profitable and earnings will accrue to both firm and country.

Joint venturing arrangements between bioscience firms and developing country entities have two disadvantages but several advantages. The major disadvantages are that the developing country is temporarily dependent for technology on the bioscience firm and that it must share the gains earned from the exploitation of a national resource. These disadvantages are mitigated by several advantages. First, biological resources are renewable so exploitation does not deplete a finite resource. Second, the dependency will lessen with the passage of time since an evergrowing number of scientists and technologists from the developing country will gain expertise in biotechnology R+D. Third, R+D can be performed at locations most favourable to the developing country. Fourth, the imported technology can be adapted as required to fulfill local needs; help for adaptation may be provided by the technology conferrer. As a result of these advantages, successive joint ventures

can be entered into with the comforting knowledge that terms will become more and more advantageous to the developing country. Other benefits may also accrue: the terms of the joint venture may free the developing country from making cash investment in the project; and dealings with recently established small and medium-sized bioscience firms would not be hindered by considerations which apply when dealing with TNCs. In particular, there would be no historic "baggage" of suspicions of motives derived from past questionable activities - relations can be established de novo on the healthy basis of shared mutual interests.

Industrialists representing bioscience firms have expressed enthusiasm for setting up joint ventures with entities in developing countries (35). One example of the form such joint ventures may take is at hand. Recently, a joint venture between the US bioscience firm Biotech Research Laboratories Inc. and China's Shanghai Cancer Institute was entered into. According to a published report (36), the venture will concentrate on developing diagnostic monoclonal antibodies against a variety of cancers including those of the esophagus and nasopharynx, both forms particularly prevalent in China. During the initial three-year contract period, Biotech Research will train researchers in the US, supply reagents and equipment and provide marketing support in selling products. The Institute will provide research personnel and laboratory facilities in Shanghai. Products will be jointly owned but the Institute will have the right to market them in China while Biotech research has market rights for the rest of the world. No funds have been exchanged.

Other, illustrative examples are appearing with mounting frequency. One of which less is known at the time writing, is the joint venture between Merck, Sharp and Dohme International and Singapore Biotech. The first named will transfer to the second the technology to manufacture anti-hepatitis B vaccine which will be used by Singapore to immunize high-risk populations (37). Another is between the Chiron Corporation of California and the South Korean firm Lucky to produce products such as interferon and hepatitis B vaccine through genetic engineering (38). These three examples of joint ventures between firms in the developed and developing countries are only the beginning of what is certain to become a flood in the next five years.

As mentioned above, the lack of resources prevents all international organizations from undertaking large, wide-ranging programmes to bring biotechnology and its benefits to the third world. Nevertheless, they can fulfill important roles by catalyzing projects that can have significant effects at the local level and provide timely, accurate advice to decision-makers who are not so knowledgeable on biotechnology or its scientific underpinnings. All this is in fact being done. International organizations which have had considerable experience in the field of biotechnology and developing countries do play an important role in ensuring that joint ventures proceed according to the steps described in a following section of this paper. Furthermore, UNIDO is in an extremely favourable position to catalyze joint venture arrangements between bioscience-based firms in developed countries and enterprises in the developing countries as a result of it having built up an extensive network of contacts among bioscience researchers and industrialists in the industrialized countries and among researchers, industrialists and decision-makers in developing countries. For these reasons, UNIDO could act as a "technology scout", seeking out on-going R+D in universities and bioscience firms relevant to developing countries. UNIDO could then bring this research to the attention of interested third world industrialists and decision-makers and, if requested, catalyze the formation of joint ventures. Such activity would be likely to satisfy all involved parties - the developed country research unit would receive impetus for its R+D in the form a funds and direction, the developing country enterprise would gain as described above, and the international organization would satisfy its raison d'etre.

Issues pertaining to intellectual property rights

The 1981 UNIDO expert group previously mentioned found that two types of proprietary rights are primarily involved in biotechnology transfer, namely trade secrets and patents. The group estimated "...that the vast majority of transferable technology and know-how is in the form of trade secrets"(39). However, it was also clear that trade secrets were uniformly protected throughout the developed world and the maintenance of trade secrets effectively surpresses the dissemination of technology and know-how. However, issues pertaining to trade secrets

will most probably not be any different in reference to bioscience-based industry than when dealing with any other high technology industry. The situation is one that has to be lived with. Probably the best means of doing so is through licensing agreements (see below).

Theoretically, patent law acts to make information more available than it would otherwise be. Practically speaking, patent law as applied to living organisms and their end products is in a state of flux throughout the developed world. The situation is even more complicated when considering developing countries; some do not have bodies of patent law, while the ones that do most often do not include biotechnology inventions within their structures. What to do about developing countries, patent law and biotechnology is still unclear and is certainly beyond the scope of this article.

In view of the reality of trade secrets and due to the murkiness of patent law as applied to biotechnology and practiced in the developed countries, it may be useful to consider licensing. In the preceding review of bioscience-based industry (pp. 8-10), it is indicated that licensing agreements are very common between bioscience firms and large companies. Generally, the bioscience firms advance an innovation from the idea phase to, or through, the pilot plant stage. At this point the facilities of the large company are required to scale-up the innovation for down-stream processing and to market it.

The same procedure can be employed by entities in developing countries interested in marketing a biotechnology product. For example, a vaccine manufacturer in a developing country may decide that the market for a type of recombinant vaccine is potentially lucrative in its home country or in its region. The manufacturer may find it useful to contact a firm possessing the requisite technology and negotiate a license for the manufacture of the vaccine. As has been pointed out in a UNIDO study:

> Licensing can meet the needs of proprietors of technology and the needs of enterprising citizens and commercial interests in developing countries. The normal rules must be carefully tailored to special conditions in each area if the chances of success are to be realistic. Through skill, patience and a genuine effort to understand the requirements of the other party, licensing can be an effective medium and catalyst for development (40).

There is every reason to believe that licensing will become an extremely important method for biotechnology transfer. Further, as developing countries develop their potentials in biotechnology, licensing agreements will most likely be the primary means whereby results from biotechnology R+D in those countries are transferred to the developed world. When this happens, previous experience vested in developing countries and international organizations regarding the making of licensing agreements will be most valuable for negotiating mutually beneficial contracts.

Bilateral aid

During the next few years governments in developed countries are likely to begin formulating policies and mechanisms for assisting developing countries in building infrastructures by providing training to researchers and technicians, by making funds available for R+D in developing countries, and through various in-kind donation schemes.

Active consideration of bilateral aid programmes are presently being considered by the US and the EEC and possibly other developed countries. These programmes are likely to be negotiated and administered on a case by case basis. It should, however, be borne in mind that bilaterial aid may not address the real needs of recipient countries but aid may instead be provided to fulfill foreign policy objectives of the donor country (41). If so, the usefulness of this mechanism could be severely curtailed.

Contract R+D

A developing country may decide that the solution of a problem may best be accomplished by contracting R+D out to a bioscience firm. For example, a disease may be so damaging that a decision is reached to manufacture a vaccine against it. If a bioscience firm which has the ability to quickly respond to the challenge can be identified, the afflicted country may find it effective to contract this firm to perform the necessary R+D for vaccine development and, as necessary, to manufacture it.

This mechanism, if used judiciously, could be extremely effective especially in those cases when a particular problem plaguing a country is already being researched by a bioscience firm. The difficulty is, of course, bringing the two together. Similar to the possibility discussed above of UNIDO acting as a technology scout, it could serve a similar role in situations where a developing country is facing a problem and is trying to decide what to do about it. In such a case, UNIDO could act to identify an appropriate research unit and help the developing country to negotiate a favourable contract. In fact, several activities of this type are under way: one involves a research unit in the US with a counterpart in Kuwait and is focused on hydrocarbon microbiology; another concentrates on developing cellulase overproducing yeast and is between research units in Ireland and Pakistan; and yet another is being set up between R+D groups in Sweden and the Far East centering on malaria vaccine development.

Of the four mechanisms explored above, two are found to be particularly applicable. Yet, the terms under which biotechnology transfer will take place will have to be negotiated on a case by case basis. The conditions under which the international transfer of technology takes place have been discussed in numerous publications so there is no need to go into this topic here (42). But to reiterate an important point, the recipient country must take great care when entering into transfer agreements, making certain that the agreement being entered into increases its probability of achieving self-reliance and technological mastery. To help developing countries gain these goals, it is suggested that their decision-makers avail themselves of the services of various international organization with experience in this area. As has been noted by UNIDO:

> United Nations bodies like UNIDO and UNCTAC, the regional commissions (Economic and Social Commission for Asia and the Pacific, Economic Commission for Africa, Economic Commission for Latin America, and Economic Commission for Western Asia) and the specialized agencies, such as the World Intellectual Property Organization (WIPO), should play a much greater role in guiding the developed and developing countries in the transfer of technology and in negotiating licensing agreements. They should draw equitable guidelines that Governments could take up and use as the basis for drawing

their own guidelines. When developing countries are not in a position to determine the proper choice of technology and conditions for its transfer, the United Nations bodies should be in a position to extend expeditious help to them when required. To this extent these bodies require strengthening (43).

V. CONCLUSIONS

As a result of exceptional advances in biotechnology, such as genetic engineering, and as applications from research are industrialized, the development rates of developing countries will be profoundly affected. Impacts are likely to be felt in most areas of industrial activity. A UNIDO group of experts has suggested that a wide scope of problems common to the developing countries may be amenable to solutions worked out via biotechnology, such as improved biofertilizers, vaccines against tropical diseases afflicting mankind, animals and plants, to decompose xenobiotics, etc. More specific uses can also be mentioned, including:

(a) Argentina's annual loss of approximately US $2 billion due to foot-and-mouth disease may be greatly alleviated by the application of a safe and efficient vaccine produced through genetic engineering;

(b) Oil producing countries could find it worthwhile to explore the potentials of hydrocarbon microbiology for the production of SCP, to enhance oil recovery or to manage oil spills;

(c) African countries could benefit from the introduction of hardy, drought-resistant strains of agriculturally important plants;

(d) Tropical countries able to exploit renewable biomass may wish to develop genetically improved strains of bacteria or yeast to produce alcohol and biogas.

As developing countries grow aware of the potential benefits of biotechnology, many of them are beginning to take steps which will allow their researchers to perform goal-directed R+D and their industrialists to capitalize on the results of both indigenous and foreign research.

However, as is pointed out throughout this volume, these efforts face severe constraints. The educational systems of the Third World may not be geared for the education and training of the high quality, multi-disciplinary researchers required in biotechnology. Many countries do not have either the resources or the capacity to individually take up bioscience R+D or to develop scale-up and down-stream processes. Capital investment funds for setting up a bioscience-based industry may be lacking and indirect curbs such as, for example, non-existent or inappropriate patent law and poor tax incentives, may discourage industrial initiatives.

Many of these constraints can be overcome or circumvented through international co-operative actions, some of which were pointed out in this chapter. National decision-makers can become informed about biotechnology through the informative programmes run by UNESCO and UNIDO. Furthermore, if assistance is required by countries to formulate national programmes or establish national biotechnology centres, UNIDO can provide the requisite advisory services. UNESCO's assistance may be requested to reconstruct educational systems or formulate retraining programmes. UNIDO may provide help in formulating appropriate industrial policy, drafting intellectual property legislation and in drawing up contracts for international biotechnology transfer.

In the medium-term, the ICGEB will positively affect the capability of developing country researchers and technologists to perform advanced biotechnology R+D, to scale-up laboratory procedures and undertake down-stream processing. This will be partially done by having the Centre's scientists perform important in-house research for developing countries, and partially by the ICGEB and its affiliated centres providing thorough training for a comparatively speaking large number of third world researchers. A primary objective of the ICGEB's training programme is "... to give advanced training to individuals who have the potential to create innovative groups for industrial activity in the home country. This type of training should be such that it would open the road to a wide range of applications, and it definitely presuppose participating in active research processes" (44).

In this volume an attempt is made to demonstrate that capability building is an extremely complex process involving the fitting together of many elements. Most of this process will inevitably have to be done by the individual countries themselves. However, the difficulties in doing so can be greatly eased and progress accelerated through international co-operation whereby the researchers of developing countries may come to generate a great force for the common good when they concentrate their efforts on achieving collective goals. And, as has been noted throughout this volume, international organizations have an important catalizing function to initiate international co-operation and make certain that activities undertaken continue and come to fruition.

The overall purpose of capability building is to allow a developing country to achieve self-sufficiency - a concept which means more than just being able to perform research and establish industry. It means taking steps to achieve mastery over biotechnology, i.e. having knowledge of the scientific basis and dynamics of the bioscience; being able to manipulate results from research to reach practical goals (the developing of a technology); and being able to adapt and improve developed technologies. Only after a level has been reached where these functions have been realized can a country establish a bioscience-based industry capable of significantly aiding the process of development.

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