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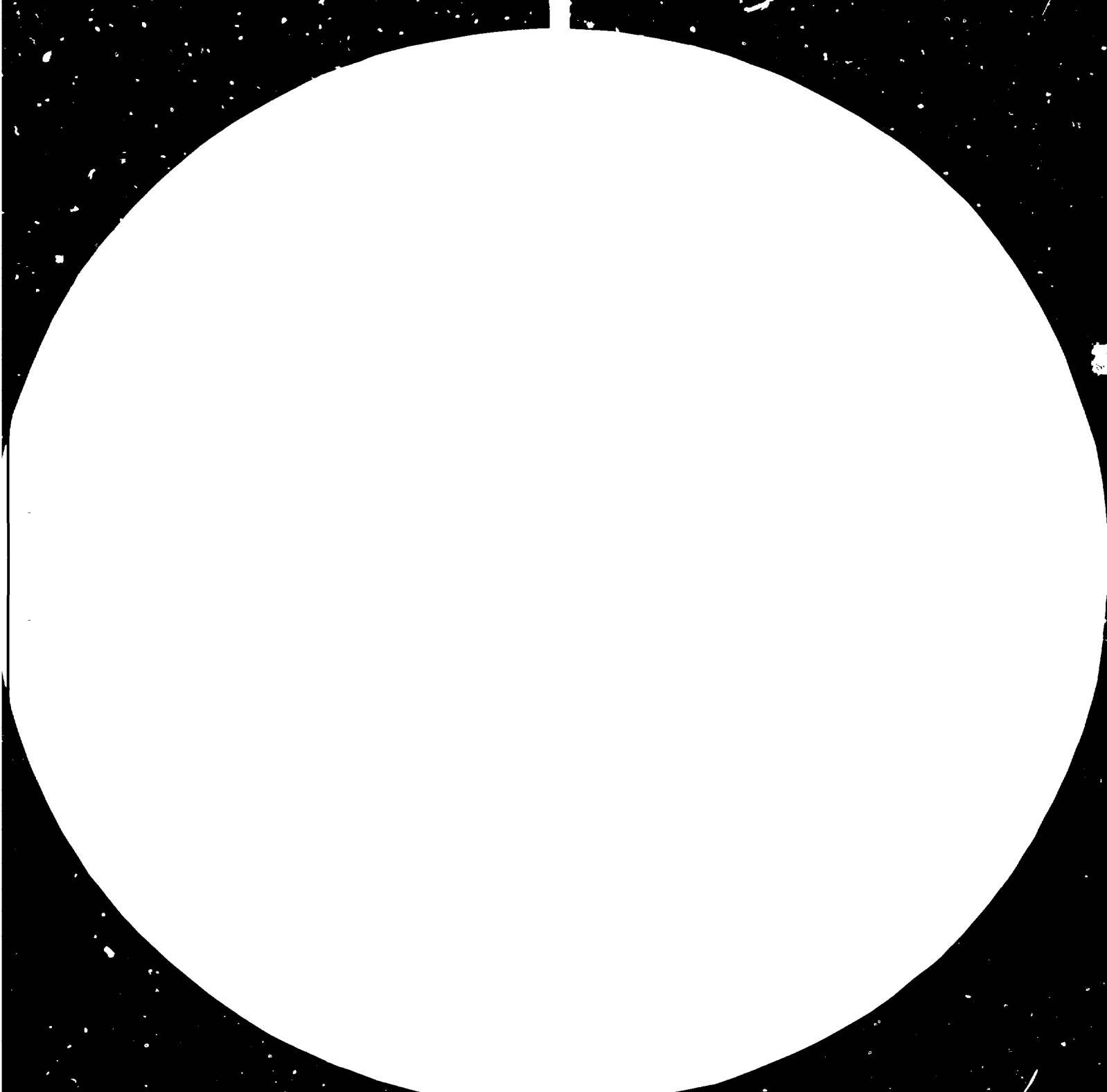
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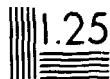
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3.2



4.0



Resolution Test Chart
1.0 1.1 1.25 1.4 1.6 1.8 2.0 2.2 2.5 2.8 3.2 4.0

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ENGLISH

CENTRES FOR THE PRODUCTION OF ENZYMES*

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Genetic manipulations employ a battery of enzymes such as restriction endonucleases, polymerases, polynucleotide ligase, terminal transferase, polynucleotide kinase, exonuclease, etc. These enzymes are readily available in the western world and at present 80 per cent of the world's demand is being satisfied by companies like New England Biolabs, Bethesda Research Labs and Boehringer Mannheim Biochemicals, located in USA. Acquisition of these biochemicals by scientists working in the developing countries, presents the following difficulties:

(a) Transportation

Since all the enzymes are unstable at ordinary temperatures, they must be transported under refrigeration. Generally, the manufacturers ship them packed in dry-ice. Air-transportation makes it prohibitively expensive for labs located in Asia. Further, there is no direct flight to many cities in Asia and Latin America and this increases the transportation time. The standard size cartons cannot take more than a few kg of dry ice which can last for only 24-48 h. Increasing the amount of dry ice makes it both difficult and uneconomical. Besides, there are no cold storage arrangements at the receiving airports and once the package arrives, it must be delivered to the customer without serious delays (which is a miracle if it happens). Experience has shown that it is almost impossible to receive the package before the dry-ice finishes.

(b) Availability of foreign currency

Another difficulty which the scientists in the developing world face, is the availability of foreign currency. Since all the enzymes (and other biochemicals) have to be imported from Europe or USA, the payment is required in dollar currency which is hard to come by. The grants from international agencies are usually given as aid to the receiving country and, therefore, Government restrictions of foreign exchange are applicable. Funds, if available to the scientist, are in local currency.

(c) Procedural Formalities

(1) Ordering

There is a lot of time and effort needed before a firm order can be placed. A permission from the State Bank is required because foreign exchange is involved. The procurement procedures are usually lengthy and cumbersome (such as a minimum of three quotations and advertising in the press) resulting in slowing down the rate of work below the acceptable levels.

(2) Customs Clearance

All incoming parcels, packages must be cleared by the customs authority before entry into the country. This causes delays and since no cold storage facilities are available at most airports, the enzymes get inactivated.

(d) Poor Communication between the Customer and the Supplier

Personal efforts and an initiative on the part of the scientist concerned can help to overcome some of the difficulties such as early clearance from the customs after the parcel has arrived in the country. However, poor communications between the customer and the supplier rules out this possibility. Usually, telephonic or telex contact does not exist between the two parties; in some cases where it may be present, it is prohibitively expensive. Telegrams take much longer than expected and sometimes do not reach their destination at all.

It is evident from the above-mentioned problems existing in developing countries that all efforts of the UNIDO aimed at promoting research in the field of genetic engineering in developing countries can go to waste unless a regular and reliable supply of DNA reagent enzymes is ensured to these scientists. One possibility is that UNIDO may provide dollar grants which may be used for purchasing enzymes. This may help to solve the problem to some extent although the time factor is still there. Besides this is an exceedingly expensive solution and in the future when the number of groups increase, this solution may become economically unacceptable. The other possibility is to set up enzyme production centres in developing countries. Successful running of these centres will ensure cheap and reliable supply of the required enzymes to the scientists and at the same time generate

a collection of DNA enzymes and bacterial strains (within easy reach) which is bound to stimulate other labs in the area to engage in this kind of research work. These units will also satisfy the enzyme requirements of the proposed International Centre for Research in Genetic Engineering.

It is proposed to set up a network of 3-5 enzyme production centres in different parts of the world. These labs will be located in selected laboratories/institutes and each lab will look after the needs of all the scientists in a group of countries. The grouping will be done very carefully on the basis of relative ease with which the scientists in the group countries can communicate. The enzyme units will be equipped with telex computer system and the serving labs will have direct connections.

It is estimated that it would require an initial investment of approx. US\$ 200,000 to start an enzyme production unit in a host institute which can offer for this purpose, a moderately equipped biology laboratory (see Annex). In addition, training of one scientist each in enzymology and culture collection work will have to be arranged and a network of telecommunication systems connecting this unit with other labs in group countries provided. After the unit is functional, it will involve an annual recurring expenditure of approximately US\$ 24,000, including a foreign exchange component of US\$ 16,000 and excluding salaries of the personnel involved.

Inventory for radioisotopes, rare biochemicals and useful strains of bacteria

In order to ensure a speedily available supply of radioisotopes and rare biochemicals which are generally unavailable in local markets in the developing world and therefore their acquisition presents many difficulties, an inventorying stores in enzyme production centres should be set up. All of these materials will be procured and purchased in bulk (which will make them cheaper), and stocked. Scientists in group countries requiring these materials can purchase from those stores and payments will be received in local currency.

Usefulness of the network

Setting up of national centres in developing countries and well arranged co-ordination will greatly help to overcome the shortage of

trained manpower in these countries and at the same time give the scientists a sense of participation in an international activity. The collaborating measures lead to better chances of success. Setting up of reagent enzyme centres and inventory stores will ensure quick supply of routinely used materials to scientists working under condition where acquisition of such essential materials presents innumerable problems. Availability of these materials within easy reach will stimulate research on the various applied aspects of molecular biology in other laboratories and universities in the developing countries. Better communication between the participating laboratories will encourage scientific discussions and cross-fertilization of ideas and thus greatly help in overcoming the drawbacks of working in isolation in the developing countries.

Annex

Manpower and space requirements with estimated costs

The host institute where the unit will be located, will provide the laboratory space and may be pursued to provide (a) basic equipment generally available in a biology laboratory, (b) skeletal manpower. UNIDO or other agencies may supplement by adding more equipment required in the enzymology work and trained manpower. The following lines present an account of requirements for such units:

(1) Manpower

An enzymologist having sufficient training and experience in enzyme isolation, identification and biochemical characterization.

A Microbiologist having experience and training in bacterial culture collection and maintenance.

Three technicians, two of which will help the enzyme work and one will help the culture collection work.

Two laboratory attendants and a secretary to help in the overall working of the unit.

(2) Equipment

Category A

<u>Item</u>	<u>Quantity</u>	<u>Cost</u>
<u>Ultracentrifuge</u>	1	\$ 40,000
It will be used mainly in the preparation of substrate DNA.		
<u>Medium speed centrifuges</u>	2	\$ 40,000
These will be used in enzyme isolation and purification work.		
<u>Fraction Collectors (with peristaltic pump etc.)</u>	5	\$ 20,000
These will be used to collect hundreds of protein fractions as these are eluted from columns during purification of enzymes.		
<u>Slab Gel Electrophoresis Apparatus</u>	3	\$ 7,500
These will be used in assaying restriction endonucleases.		
<u>Polaroid Photographic Camera</u>	1	\$ 5,000
This will be used to take pictures of the gels.		

<u>Item</u>	<u>Quantity</u>	<u>Cost</u>
<u>Glass Chromatography Columns</u>	20 (various sizes)	\$ 1,000
These will be used in the chromatographic purification of enzymes.		
<u>Cold room</u>	1	\$ 10,000
All enzyme isolations and other such manipulations requiring low temperature will be done in this room.		
Deep freeze - 85°C	1	\$ 5,000
<u>Ultrasonic Disintegrator</u>	1	\$ 3,000
This will be used to break up cells for extraction of enzymes.		
<u>Liquid Scintillation Counter</u>	1	\$ 45,000
This will be used for measuring low levels of radioactivity in biological samples.		
<u>Laboratory bench fermenter</u>	1	\$ 12,000
This will be used to grow up 10 l batches of bacteria which will be used as source material for the isolation of enzymes.		
UV-Visible Spectrophotometer	1	\$ 15,000
This will be used to measure the optical absorbance/transmission of various samples.		
Total Cost of Equipment in Category A		Approximately \$ 200,000

Category B

Refrigerators	5	
Incubators	5	
Water bath shaker	3	
Glassware - Routine requirements (flasks, petri plates, test tubes pipettes etc.)		
Vortex shaker	4	
Magnetic stirrers (various sizes)	12	
Balance analytical	1	
ordinary	1	
Colony Counter	1	
Water Distillation units	1	
Water Deionizer	2	
Total Cost of Equipment in Category B		\$ 40,000

Consumables

Category A

This includes materials such as column chromatography resins, radioisotopes, nitrocellulose filters, and other such material which are generally not available in local markets in developing countries

\$ 10,000

Category B

This includes such materials as buffer ingredients, bacterial growth media and similar chemicals ordinarily available in local markets in developing countries.

\$ 4,000

Transportation of Enzymes

\$ 3,000

Travel

Category A (outside the country)

\$ 3,000

Category B (within the country)

\$ 500

To attend meetings and seminars.

Repair and Maintenance

Category A - all components imported

\$ 500

Category B - everything arranged from within the country

\$ 500

Indirect Costs

Category A

\$ Nil

Category B

\$ 3,000

Total: Non-recurring: Category A US\$ 200,000

Category B US\$ 40,000

Recurring: Category A \$ 16,500

Category B \$ 3,000 (+ salaries)

Category A represents that portion of the expenditure provided by UNIDO or other agencies and Category B represents that portion which may be borne by the host institute/country.



