Overseas Development Institute

Briefing Paper

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AGRICULTURAL BIOTECHNOLOGY AND THE THIRD WORLD

The impact on less developed countries (ldcs) of advances in agricultural biotechnology was recently examined at an ODI conference. This Briefing Paper draws on some of the work of the conference to explain the nature and likely potential of agricultural biotechnology; to examine the main concerns it has aroused over regulation, genetic diversity and commercial exploitation; and to consider the range of possible applications and consequences for developing countries. The Paper shows the growing importance of private sector research and development in industrial countries and indicates the need for expanded publicly-funded research in ldcs and support for the International Agricultural Research Centres (IARCs). The Paper explains that the main reason for a declining share of ldc agricultural exports in world trade remains northern subsidy policies, not biotechnology, but shows that there is likely to be an increasingly adverse impact on ldc trade in specific crops as substitutes become available. On the other hand, there are some direct benefits of western biotechnology for ldcs, which include improved veterinary products and some tissue culture techniques.

What is different about agricultural biotechnology?

Biotechnology applies scientific and engineering principles to enable materials to be processed by biological agents, resulting in faster and more accurate breeding programmes for animals, plants and micro-organisms. It differs from established methods used in the field (e.g. plant breeding) and in the factory (e.g. fermentation) in the following ways:

Genetic engineering

Genetic engineering allows scientists access to the building blocks of living organisms so that cells or molecules can be manipulated, and the gene pool available for 'crossing' is widened beyond the limits of sexual compatibility. A secondary set of techniques, based on tissue culture, permits the rapid regeneration of cells into full-sized plants and animals, and allows the effects of intervention to be monitored closely. Apart from their function in 'servicing' genetic engineering, these techniques are also a useful addition to conventional breeding programmes.

Linkages across sectors

Biotechnology is characterised by strong linkages across agricultural and industrial sectors through:

— *techniques:* genetic engineering, **cell fusion** and **culture**, **embryo rescue** and hybridisation.
— *processes:* **enzyme** catalysis in starch, detergent and dairy industries
— *materials:* intermediate products (glucose, fructose, dextrins, lactose) which can be manufactured from a variety of sources so that efficient production is less dependent on individual raw material availability and price.

Cross linkages favour higher returns per unit of research and development (R & D) investment among large firms, and it is this which has led to some mergers and takeovers among the small venture capital companies initially established. Other factors which have influenced the trend towards larger firms include the long lag between research outlay and revenue from the product or process, and the uncertainty of outcome. For example, it costs at least $1 million to **clone** a single gene; it takes at least 20 man-years to isolate a commercially useful new enzyme; and only one useful new antibiotic is found for every 20,000 strains of organism screened.

Box 1: Glossary

Amino acids: The chemical units of which all proteins are composed.

Anther: The fertile segment which surmounts the stamen (the male organ of a plant) and carries the pollen sacs.

Cell culture: A group or colony of cells propagated from a single cell in a specifically formulated nutrient medium.

Cell fusion: The fusing together of two or more cells to become a single cell.

Chromosome: A thread-like body found in cell nuclei, comprising genes arranged in linear order. While genes are the units of heredity, chromosomes are the units of transmission from one generation to the next. During cell division chromosomes may break, rejoin or cross over giving rise to new genetic combinations.

Clone: A collection of genetically identical cells or organisms derived asexually from a common ancestor.

DNA (De-oxyribonucleic acid): This carries the genetic hereditary message and controls all cellular functions in most forms of life.

Embryo rescue (also termed embryo capture): When cross-pollination occurs between genetically different plants, the resulting embryo may be aborted because of parental mutual incompatibility. Such embryos may be extracted and grown on an appropriate medium.

Enzymes: Specific proteins which act as biological catalysts to stimulate essential biochemical reactions in all living organisms.

Genome: The entire hereditary message of an organism.

Germplasm: Often synonymous with 'genetic material' it is the name given to seed or other material from which plants are propagated.

In vitro: Literally 'in glass'. Experimental reproduction of biological processes in isolation from a living organism.

Monoclonal antibody: An extremely pure antibody derived from a single clone of an antibody-producing cell. Invading pathogens, viral or bacterial, carry a large number of different antigens each capable of stimulating the host's immune system to generate a corresponding antibody.

Polygenic: Deriving from more than one gene.

Protoplast: A plant cell from which the cell wall has been removed by mechanical or enzymatic means.

Recombinant DNA (r-DNA): A strand of DNA synthesized in the laboratory by splicing together selected parts of DNA strands from different organic species or by adding a selected part to an existing DNA strand.

Somaclonal variation: Somatic (vegetative non-sexual) plant cells can be caused to propagate *in vitro* in an appropriate nutrient medium. The resultant progeny are called somaclones and theoretically, should be genetically identical with the parent. In fact *in vitro* cell culture of somatic cells frequently generates cells significantly different, genetically, from the parent. Such progeny are called somaclonal variants and provide a useful source of genetic variation.

Tissue culture: *In vitro* methods of propagating cells from animal or plant tissue.

Source: *Biotechnology: opportunities and constraints*, IDRC-M110e, Ottawa, 1985.

Private investment

There is greater private, and less public, investment in biotechnology R & D in industrialised countries than is the case for conventional agricultural research. Agrochemical companies with in-house biotechnology R & D capacity now spend three times the average for R & D in the industry as a whole, reflecting their confidence in the long-term commercial potential of genetic engineering and the prospect of patenting the outcome of research. Agrochemical companies can exploit the complementarities between their own products and those generated by biotechnology. For example, companies can 'package' a plant by genetically engineering resistance in it to a particular herbicide. They can thus retain a marketing advantage even after patents on the herbicide have expired. It is becoming cheaper to tailor a plant to an agrochemical (rather than vice versa) given the high costs of conforming to environmental restrictions imposed on pesticides.

The prospects for biotechnology

Biotechnology is still largely a matter for developed countries. Many techniques relevant to ldcs are at an early stage of development, and the application of those currently available is constrained by limited local research facilities, a dependence on public funds, and patent difficulties. Except for a few products, private companies at present see the returns to investment in biotechnology for the Third World as insufficient and too slow. In the north, however, the prospects are significant in a number of areas, and some have direct relevance to developing countries.

Markets

Estimates of the value of the world market for all biotechnology products by 1990 vary widely depending on how biotechnology is defined, and market forecasts are hazardous, given the long R & D lead times, the unpredictability of results, and the uncertain regulatory environment. The production of diagnostic kits, however, is not subject to strict control and is estimated to have a US annual market of $1.3 bn by 1990, and that of **monoclonal antibodies** with both veterinary and human applications of $1.1 bn. The value of the US pharmaceutical market is likely to be $5.5 bn p.a. by 1990, overshadowing an agricultural market of only $0.3 bn. This gap is not expected to close for at least 10 years, and reliable crop- or animal-specific market estimates are not available. It is likely, however, that biochemical products will be substituted for petrochemical products as agricultural prices decline relatively. **R-DNA** will facilitate this process, leading to an estimated market of $40 bn p.a. by the year 2000 for petro-chemical substitutes, compared with present global sales of crude oil of $450 bn p.a.

Plant and animal breeding

Certain genetically engineered plants have now reached the stage of field trials (e.g. frost resistant strawberries and potatoes in the USA), but progress has been slow with many plant types (including cereals), particularly those with traits which are **polygenically** determined (e.g. yield; tolerance to drought). Not enough is known about how genes interact and what gene structures produce particular plant characteristics, and material still requires testing by growing plants to maturity and by interaction with conventional breeders.

By contrast, progress has been rapid in supporting technologies such as **tissue culture**, a technique becoming possible for most plant types and already in commercial use for fruit and sugar cane, and under trials with tree species such as oil palm, where conventional reproduction is very slow. Similarly, **in vitro** cultures theoretically allow millions of individual cells to be screened for suitability within a short time (to screen 2 million sunflower plants conventionally would require over 30 hectares of land). *In vitro* techniques complement conventional plant breeding and **germplasm** management, reducing the size of some collections by one-third by eliminating duplication.

A number of 'engineered' seeds are likely to be available commercially by 1992 in industrialised countries, including herbicide-resistant tobacco, and pest-resistant tobacco, potato and tomato. Field trials are expected to be under way by then with some 50 cloned genes of economic importance, including those for modifying soya plants to produce oil with the characteristics of sunflower oil.

Substantial progress seems likely in improving the quality of a number of products which do not require complex combinations of genes. Prospects include modifications to fatty acids in oilseed rape, and genetically enhanced storage characteristics in legumes, as well as the improvement of shelf life, fruit texture and flavour in tomatoes.

However, some polygenically-determined traits, such as nitrogen fixation, are extremely complex. Even if incorporated in 20-30 years, plants will only be able to create modest amounts of their own fertiliser in this way. Progress has also been slow in identifying mechanisms for resistance to bacterial and fungal diseases because no naturally-occurring resistance genes have yet been isolated and cloned.

New techniques will lead to gradual increases in the efficiency of conventional plant breeding in the next decade and will be passed on to the farmer. These include the various methods of germplasm management and disease-free propagation already being used at the International Agriculture Research Centres (IARCs) which were set up partly to prepare and distribute genetic material to ldc breeding programmes (Box 2).

In animal breeding, biotechnology provides a major commercial potential in enhancing the quality of offspring and reducing the time required for reproduction. More than 100,000 animal embryos with predetermined characteristics are now being transferred annually to surrogate mothers in the USA, and 30,000 in Europe.

Veterinary products

A variety of new veterinary products will be marketed widely in the next five years, including diagnostic kits, particularly those relying on monoclonal antibodies, and growth hormones for poultry, swine and cattle provided that government regulations can be met. Developing countries can currently purchase kits for rinderpest virus diagnosis, and research is underway to help in distinguishing this from peste des petits ruminants in the early stages of infection, and to assist in tracing the sources of outbreaks.

Vaccines based on r-DNA products are also being developed for extensive veterinary use, including preventing neonatal bacterial diarrhoea, foot and mouth disease and certain herpes viruses.

Fermentation

Industrial fermentation produces both finished products and food components or additives. Conventional selection and breeding of the organisms used in fermentation has already led to high production efficiencies, so that the scope for further gains through the introduction of 'engineered' organisms is limited, especially in high volume, low unit value products. More expensive products (such as the less common **amino acids**) offer scope for yield increase, but their complex polygenic pathways have hitherto prevented rapid progress.

Plant cell culture

Certain plant cell cultures which are used to improve varieties can be designed to generate commercial products directly. However, not enough is known about where and how these products are synthesised within plant organs, and the process is more costly than bacterial or yeast fermentation. Only synthesis of expensive compounds such as drugs or fragrances (with a value of over $100/kg) is likely to be economic. The only product currently manufactured commercially by cell culture is shikonin, a dye and pharmaceutical used in Japan, where consumption has been about 150 kg/year at $4,000 per kg.

Regulating biotechnology

Regulation affects two aspects of research in particular: patents and health and safety.

Patents

The strong commercial stake in biotechnology R & D requires patent protection of successful products and processes. But this may reduce competition and — an important possible consequence for ldcs — may prevent new knowledge from entering the public domain. Fears about competition may be overstated since there are many firms involved in

biotechnology R & D, there is continued public funding for it, and patents are difficult to enforce.

There are several impediments to full regulation by patent in many countries. The extensive descriptions required often give sufficient detail to allow competitors to 'design around' the patent. Samples deposited in patents offices may be forfeited if the application is unsuccessful, allowing competitors access to them. An added difficulty is that international patents remain largely unenforceable in countries not signatory to certain conventions.

Health and safety

The spectre of the uncontrollable spread of dangerous mutations is feared by organisations and lobby groups seeking to widen the debate on possible future environmental degradation and ecological imbalances arising from the use of biotechnological processes. A Dag Hammarskjold Seminar addressed this question at Bogève, France, in 1987 and concluded in the Bogève Declaration that an international biotechnology policy agreement was required which met "the needs of the majority of the world's people...while working in harmony with the environment."

However, many forthcoming trials appear relatively 'safe'. They involve genes which are naturally occurring (albeit in a different host), are conducted with hosts unlikely to have vigorous crossing capacity either within or across species, or they involve the removal of genes rather than the addition of foreign ones. Permission has now been given in the USA for field trials of 'low risk' genetically engineered organisms, and decentralised regulation of trials is likely. The situation in Europe is more confused: West Germany and the Scandinavian countries have severely restricted field trials, although several have been conducted in Britain, and Italy appears to have no restrictive legislation. Efforts are now being made to design a coordinated European approach to field testing.

Gene banks

The incorporation of new genetic traits into plants or animals may reduce the need to maintain genetic diversity in the field. Indeed, genetic erosion has accelerated with the Green Revolution: in south-east Asia, for example, a single rice variety (IR 36) now covers 60% of the rice area. This may increase vulnerability to pests and diseases, recalling the stem rust which destroyed almost 50% of the USA and Canadian wheat crop in 1950-54. However, the prospects of introducing 'foreign' genes remains so poor for many crops and traits that naturally-occurring germplasm still provides breeders with a more useful set of building blocks.

Scientists accept that diversity must be maintained, but it does not follow that the entire range of species has to be grown in the field. In areas where agroecological conditions vary widely, farmers maintain diversity through their need for several different strains to cope with varied conditions. In more uniform areas, the risks of relying on fewer varieties are now much reduced. Breeders incorporate resistance to pests and diseases that does not rely on a single gene and is therefore not prone to sudden breakdown. The characteristics of the wide range of genetic material now held at the IARCs have been classified and new sources of resistance can be bred quickly into commercial crops if some breakdown is threatened. Additionally, techniques such as **protoplast** fusion are generating new resistant germplasm, for example through crosses between sexually incompatible wild and cultivated varieties.

Developing countries and biotechnology

Research and development

Conventional plant breeding in developing countries presents a varied picture, with some Asian countries well-advanced, and, in Africa particularly, some countries making hardly any progress. This range is important as conventional and biotechnology-based methods of plant breeding are highly complementary. Tissue culture makes it easier both to compile germplasm collections and to supply disease-free material of known characteristics. Gene insertion techniques broaden the range of genetic variation from which breeders can make crosses. But the search for genetic diversity is the less difficult component of plant breeding. The selection of

Box 2: International Agriculture Research Centres with particular crop or animal production mandates

CIAT — International Centre for Tropical Agriculture: beans, cassava, rice, tropical pastures.
CIMMYT — International Maize and Wheat Improvement Centre: wheat, maize, triticale.
CIP — International Potato Centre: potatoes and sweet potatoes.
ICARDA — International Centre for Agricultural Research in the Dry Areas: barley, lentils, faba beans.
ICRISAT — International Centre for Research in the Semi-Arid Tropics: millet, sorghum, groundnut, chickpea, pigeonpea.
IITA — International Institute of Tropical Agriculture: roots and tubers, cowpea, soya.
ILCA — International Livestock Centre for Africa: cattle, small ruminants, camels.
ILRAD — International Laboratory for Research on Animal Diseases: trypanosomiasis, East Coast fever.
IRRI — International Rice Research Institute: rice.
WARDA — West African Rice Development Association: rice.

The IARCs are intended to capture the economies of scale in research which are unlikely to be available to the smaller ldcs. They hold major germplasm collections for particular crops, and are responsible for the distribution of breeders' material to ldcs. Substantial emphasis is therefore placed on biotechnologies relevant to the production or screening of clonal material derived through *in vitro* micropropagation. These include:

(i) *rapid clonal propagation:* proved successful with banana, tubers and oil palm, and shows promise in fruit, medicinal plants, and forest trees. Its particular advantages include: rapid and disease-free multiplication; the ability to propagate species which are difficult to reproduce vegetatively, and production of plant material on a year-round basis.

(ii) *in vitro conservation:* used extensively with cassava, potato, sweet potato and banana. These techniques offer an alternative to the maintenance of field collections, but problems arise from the genetic instability of crop-specific cultures of somaclonal variants.

(iii) *disease-free plant production:* virus-free tissue can be obtained from over 50 species of plants important to ldcs through the use of chemo- and thermotherapy and antibiotics. Germplasm derived from these is distributed to ldcs to form the basis of their breeding programmes.

(iv) *molecular diagnostics:* faster and more accurate virus detection techniques used on rice, and small grains.

The IARCs are also using the more advanced techniques to facilitate production of germplasm *in vitro:*

(i) *embryo rescue:* facilitates incorporation of genetic material from beyond the primary gene pool into crop improvement programmes. Following sexually-induced hybridization, the embryo is nursed by tissue culture techniques through the early cell divisions until it regenerates as a plant. Using ovule and embryo rescue, together with hormone treatment, scientists have incorporated disease resistance into plants (e.g. rice, groundnut and potato) by crossing wild and cultivated varieties which are sexually incompatible.

(ii) ***somaclonal variation:*** somaclones are screened for tolerance to salt and other environmental stresses. This may prove a useful addition to the variation available to breeders from existing gene pools, providing that *in vitro*-induced variation proves stable in field trials.

(iii) **anther** *culture:* deriving cultures from pollen cells can shorten breeding cycles and increase selection efficiency. Conventional breeding cycle periods can be cut by more than half, tolerance to cold, drought and salinity can be bred and plant regeneration efficiencies from tissue cultures can be improved.

(iv) *experimental techniques:* more sophisticated and costly techniques include the development of markers designed to identify the large blocks of DNA or **chromosome** segments that contribute to qualitative characters such as yield. These may assist the breeder in systematically testing and assembling the building blocks of the **genomes** sought, augmenting the empirical procedures currently used.

useful characters from the available diversity is more time consuming, and, since knowledge of the types of trait produced by particular genes is far from complete, plants which are modified either by genetic engineering or conventional crossing still have to be grown out to maturity in successive cycles of breeding-in desirable characteristics and breeding-out undesirable ones.

Many of the smaller and poorer countries lack the facilities even for conventional plant breeding, and certainly could not undertake tissue culture or genetic engineering. India, however, has a National Bureau for Plant Genetic Resources where substantial progress has been made with germplasm conservation through tissue culture techniques, and where research is being conducted on *in vitro* conservation.

Agricultural conditions tend to vary considerably in most ldcs, so that a wide range of produce is grown, and the internal market for each tends to be limited. Private sector biotechnology R & D has therefore been limited to certain crops, processes and countries, mainly with a view to potential export markets, and has generally been undertaken by multinationals. Reproduction of oil-palm by tissue culture is a well-known example for which large-scale field trials are under way, although its economic viability has not yet been established.

By 1983 in Brazil there were already 600 research scientists in biotechnology-related activities, with strong private sector involvement in tobacco research and the production of hormones, inoculants and vaccines through fermentation. The expansion of private sector research, however, faces obstacles such as the impossibility of patenting seeds, and import restrictions urged by a protectionist domestic equipment industry.

Most biotechnology research in ldcs will continue to be publicly funded, and the majority of these countries will require external support — from the IARCs in particular (see Box 2) — for their agricultural research efforts if they are to capitalise on biotechnology. There have also been efforts to establish a new multilateral publicly-funded institution, the UNIDO International Centre for Genetic Engineering and Biotechnology (ICGEB); but despite its potential importance as a research centre, its future remains uncertain.

The impact of biotechnology

Synthetic substitutes: Attempts have been made for decades in the North to synthesise substitutes for products generally imported from ldcs, but biotechnology-based substitutes have so far been modest in scope. High fructose corn syrup is the exception, the success of which in capturing some 40% of the US sweetener market is attributable to a combination of improved enzyme technology, other improvements in the wet milling of maize and long-standing subsidies to and protection of the US maize industry (although US sugar beet is also subsidised). The high costs of plant cell culture, and the limited scope for cost reductions mean that synthesis is unlikely to produce anything other than high value ($100/kg), low volume substitutes in the next decade. Claims have been made, however, that work in progress will reduce the costs of culturing vanilla from its present $2000/kg to $50/kg, which would make it price-competitive with the conventionally-grown product.

Fermentation: An important development in the fermentation industry is the capacity to use an increasing range of agricultural products (or by-products) as raw material for extraction of specific chemicals, switching from one to another as market conditions change. Some markets (e.g. for vegetable oils) may consequently become more volatile, increasing the disadvantage faced by producing countries which do not have easy and rapid routes to world markets or which are highly dependent on a narrow range of products for their export earnings.

However, the scope for improvements to fermentation processes through genetic engineering is limited to a few higher value products such as vitamins and antibiotics. This is partly because processing accounts for only a small proportion of total costs and partly because conversion to the final product is already very efficient in bulk processes (e.g. for citric acid, monosodium glutamate, penicillin and riboflavin).

Trade: Protectionist policies for major food commodities cause distortions to trade between the West and ldcs at a net current cost to ldcs of about $700 million per year.* According to recent official US figures, industrialised countries' agricultural exports have risen to 63% of world agricultural trade in 1988, from 42% in the early 1960s. The main reason for such an increase is the level of subsidies and concomitant protection; such policies are likely to outweigh the effects on prices and trade of better productivity arising from biotechnology during the next 10-15 years, both in aggregate and in major traded crops. Such effects as may be felt in ldcs will depend on whether they are importers or exporters of the commodity in question.

The main, foreseeable, impact of agricultural biotechnology on developing countries' trade will be chiefly in low-volume, high value products. This could threaten countries relying heavily on traditional methods for production of such crops. But the biotechnological innovations currently being developed represent only a small fraction of the potential, and the rate of innovation is likely to accelerate in the next century, so that no country will remain immune to trade or production effects.

* Assessments of the net costs to developing countries arising from the West's protectionist food and agricultural policies vary considerably. For details, see *The CAP and its Impact on the Third World*, ODI Briefing Paper, June 1986.

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