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BIOTECHNOLOGY - A Guide To The Implications Of This Set Of Technologies For Industrial Policy-Makers In Developing Countries

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I Introduction: The Major Themes Of The Present Paper

It is worth at the outset summarising the major themes that are presented in the present paper. These are the following:

1. Biotechnology is best thought of as a set of old and new technologies which together are having pervasive effects in and on both developed and developing countries. These effects are likely to accelerate as new biotechnologies and their applications are perfected. (In U.S. Congress Office of Technology Assessment (1984) a summary is presented of the main new biotechnologies.)

2. It is a mistake, however, to draw too close an analogy between biotechnology and information technology since there are significant differences between them with consequent important implications for policy-makers in developing countries. In Section 5 these differences are analysed.

3. Although the potential of biotechnology has been considerably enhanced by the development of the so-called new biotechnologies, it is likely to take a long time before biotechnogy makes a substantial impact.

4. At the present time, entry barriers into biotechnology production are relatively low. Many developing countries are able, with relative ease, to acquire the necessary 'upstream' scientific biocapabilities. However, the bottleneck in most developing countries lies in the 'downstream' bioprocessing side, including weaknesses in the infrastructure necessary for effective biotechnology production. Distribution and marketing networks constitute a further constraint. It is to these areas, therefore, that policy-makers in developing countries will have to pay significant attention. This is one of the more important current differences with information technology where the entry barriers are significantly greater and where, with the important exception of software engineering, most developing countries have not managed to make a successful entry.

5. In the *future*, however, as the product and related technology cycle advances, it is likely, at least in a significant number of application areas, that economies of scale, and other advantages of size, will increase and that barriers to entry will accordingly be more significant. Nevertheless, at the present time, for reasons that are considered in more detail in this paper, economies of scale are not yet very important in many areas of biotechnology. Evidence for this proposition comes from the large number of start-up for venture capital new biotechnology firms to be found in the United States and several European countries.

6. One of the great potentials of biotechnology lies in the ability to exploit substantial economies of scope. In other words, by acquiring a set of biocapabilities (including capabilities in the areas of recombinant DNA, cell fusion, cell culture, protein engineering, and bioprocessing) a developing country is able to apply these capabilities to a significant number of industries and products and processes within these industries. The successful reaping of economies of scope may substantially increase the returns derived from investment in these biocapabilities. This point will be illustrated later in connection with the case study on Cuba.

7. However, while the biotechnology revolution will provide new opportunities for developing countries, it will at the same time produce new constraints as developed country corporations, governments, and universities advance biotechnologies in ways which at times will have negative, even if sometimes unintended, effects for developing countries.

II The Technologies, Their Generation And Diffusion

In U.S. Congress Office of Technology Assessment (1984) a more detailed account is given of the main technologies involved in biotechnology. Here a brief summary is provided in order to go on to discuss the generation and diffusion of the biotechnologies.

A Biotechnology, Old And New

Biotechnology, defined as the use of biological organisms or their constitutents such as cells and DNA for the transformation of inputs into commercial outputs, is as old as human society as is evident from activities such as the fermentation of wine or soya and the brewing of beer. Bioprocessing, therefore, has a very long history. Similarly, before the advent of so-called new biotechnology, sophisticated methods had been developed for the manipulation of biological organisms in order to serve human purposes. Examples include screening and cross-breeding in order to enhance desired characteristics in biological organisms. The Green Revolution and the new plant varieties that it introduced, it is worth recalling, were made on the basis of 'old' biotechnology.

From around the mid-1970s, however, the potential of biotechnology was considerably enhanced by the introduction of a number of new powerful tools. These included the breakthroughs of Boyer and Cohen in 1973 in recombinant DNA and Milstein and Kohler in 1975 in

cell fusion. These techniques enabled new combinations of genes to be created in order to produce and subsequently separate and purify proteins that were otherwise difficult or expensive to obtain, or to modify the functions of biological organisms. At the same time, the sophistication of bioprocessing was increasing greatly as a result of improvements in automation and control facilitated in part by the application of information technology. Technologies such as these, referred to generically as 'new' biotechnology, greatly increased the potential power of biotechnology.

B The Stock Of Capabilities And Assets Necessary To Appropriate Economic Rent From Biotechnology

In order to take economic advantage of biotechnologies, it is necessary that a firm or country develop a stock of necessary and complementary biotechnology capabilities and assets. This stock includes the following:

a. Core scientific capabilities.

b. Complementary capabilities 1.

c. Complementary capabilities 2.

d. Complementary assets.

The contents of these capabilities and assets will now be elaborated upon.

C Core Scientific Capabilities

Biotechnology, and new biotechnology in particular, is science-based in the sense that it draws closely on a number of scientific disciplines. For example, in setting up its International Centre for Genetic Engineering and Biotechnology, UNIDO (1986) identifies a number of basic scientific capabilities that underlie the research programme to be undertaken in this Centre. These include molecular biology, chemistry, biochemical engineering, microbiology, cell biology, and informatics (information processing) (p15)

Expertise in these areas may be referred to as the core scientific capabilities which underlie biotechnology. These capabilities are drawn upon in the research and development of biotechnology-related products and processes. The source of these scientific capabilities is to be found in the universities. In building up these capabilities a developing country may draw on universities in developed countries, on universities in other developing countries,

as well as on local universities. One of the difficulties that most developing countries face in developing core scientific capabilities is the weakness of local universities in some of the scientific disciplines needed in biotechnology. For example, in searching for a developing country base for its International Centre For Genetic Engineering and Biotechnology, UNIDO carried out detailed investigations in the countries that were competing to become the location for this Centre. In a report on these investigations it was concluded that 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." [UNIDO (1986), p27] It was concluded that "In general, the genetic engineering and biotechnology research base, particularly in molecular genetics, at institutes and universities in each developing country visited by the Selected Committee [of UNIDO], was observed to be weak. In effect none of these countries presented substantial evidence of genetic engineering and biotechnology research being conducted at a competitive international level." (p15)

D Complementary Capabilities 1

However, even if a developing country has solved the problems involved in building the necessary core scientific capabilities, whether through the use of local or foreign universities, this will not be sufficient to begin appropriating economic rent from biotechnology. It will be necessary for the country also to develop other complementary capabilities which will enable it to apply the core scientific capabilities in producing new or modified products and processes. For example, it will be necessary to scale-up the production of products and processes and ensure efficient bioprocessing if the enterprise is to become commercially viable. The additional capabilities that are required *within the firm* to transform the fruits of the core scientific work into commercially viable output may be referred to generically as complementary capabilities 1. In general, these latter capabilities will be developed within firms rather than in the universities.

E Complementary Capabilities 2

However, it is still insufficient for the country to possess the necessary core scientific capabilities and complementary capabilities 1. It is also necessary for the country to be able to provide a conducive 'environment' surrounding the activities of the firm which will facilitate its transformation of core scientific

capabilities and complementary capabilities 1 into commercially viable output. These 'environmental' conditions may be referred to as complementary capabilities 2. They include infrastructure such as transportation facilities, electrical power supplies, repair facilities, availability of laboratory technicians, foreign exchange in order to import necessary inputs unavailable locally, etc.

A concrete example will make this clearer. As noted in UNIDO (1986),

> "Most enzyme 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." (p52/3)

This gives a flavour of some of the problems that scientists and biotechnologists in developing countries will have to grapple with, problems that their rich country colleagues can simply assume away. The importance of complementary capabilities 2 is dramatically indicated by the fact that Japanese companies, despite massive direct foreign investment in East and South-East Asia, have refused to locate fermentation-based biotechnology activities in these countries. The reason is not the absence of core scientific capabilities, complementary assets 1, and complementary assets (to be discussed in the following section) since the Japanese companies already possess these capabilities and assets and would bring them as part of their direct foreign investment package. Rather, it is the absence of complementary assets 2, the necessary infrastructure for the production and distribution of fermentation-based products, in these countries which has inhibited Japanese investment in these areas.

F Complementary Assets

In order to reap value from biotechnological capabilities there are a number of further conditions that must be met. These include access to distribution and financial 'assets'. It is insufficient to be able to efficiently produce biotechnology-related products and processes; these products and processes must also be distributed. Furthermore, access is often required to external sources of finance. The truth of this assertion is vividly demonstrated by the experience of the so-called new biotechnology firms, or start-up or venture capital firms in the developed

countries. These firms, which often begin as spin-offs from university research, usually have excellence in the area of core scientific capabilities. Often, however, they are much weaker in the areas of complementary capabilities 1 and complementary assets. Accordingly, the large majority of new biotechnology firms have had to establish alliances of one form or another with large companies that possess the necessary 'downstream' processing capabilities (complementary capabilities 1), the distribution networks, and perhaps the financial capabilities. Alternatively, finance has been obtained from financial institutions or venture capital markets.

6 The Biotechnology-Creating System

The present discussion of the stock of necessary capabilities and assets has a number of extremely important implications for the policy-oriented analysis of the generation and diffusion of biotechnology in developing countries. The main point here is that the capabilities and assets frequently exist in *different* organisations. This point has already been made in connection with the discussion of new biotechnology firms. To take this discussion further, the necessary core scientific capabilities usually exist in universities (it was stressed earlier that biotechnology is science-based) and sometimes in relatively small new biotechnology firms. Complementary capabilities 1, however, often exist in different firms with expertise and experience in 'downstream' processing. Complementary capabilities 2, on the other hand, exist in and are influenced by a large number of other organisations, such as the transportation and the electrical power authorities etc. Complementary assets, such as distribution and financial assets, are frequently available in still other organisations such as banks, whether in the private or public sector, and enterprises specialising in distribution.

Since it is necessary to bring these necessary capabilities and assets together in order to reap economic rent from biotechnology, *it is illuminating to develop a conceptualisation of a biotechnology-creating system of interdependent organisations and institutions which together influence the generation, application and diffusion of biotechnology. It is the functioning of this system which should be the focus of attention for policy-makers interested in deriving economic benefits from biotechnology.* This concept will be further developed and applied in the rest of this paper.

II The Diffusion Of Biotechnology

A further implication of the present discussion is that it is necessary to take care in defining 'diffusion'. To begin with, diffusion may be defined in the conventional way to refer to the adoption of biotechnology-related products and their associated processes. Examples which will be analysed in more detail shortly include the diffusion of immobilised enzyme technology and microbial technology in order to produce sugar substituting sweetners, the diffusion of tissue culture technologies to produce productivity enhancing oil palm clones which lower the costs of producing vegetable oils, the diffusion of genetic engineering technology to produce bovine growth hormones which significantly increase milk productivity, and the diffusion of tissue culture techniques to produce more economically in developed countries economically useful plant varieties previously grown in developing countries. All of these examples of diffusion have had significant consequences in developing and developed countries.

However, in analysing the diffusion of biotechnology it is also valid to be concerned with broader aspects. To the extent that our concern is with the *diffusion of the ability to put biotechnological knowledge to economic use*, then, as the concept of a biotechnology-creating systems emphasises, *it is necessary to examine the diffusion of a complexely related set of capabilities and assets*. This makes the analysis of diffusion more complex than is usually acknowledged. This point will be further elaborated upon in this paper.

1. The Diffusion Of Biotechnology-Related Products And Their Associated Processes

In a number of cases biotechnology-based products have begun to penetrate markets with important consequences for both developing and developed countries. The following serve as examples:

a. Sugar-Substituting Sweetners

More than 50 million people are employed in the sugar industry in developing countries. Their income from this source is currently undergoing significant change as a result of the introduction of sugar-substituting sweetners. For example, high-fructose corn syrup (HFCS) which substitutes for sugar has been produced with the use of immobilised enzymes, a technique that has been developed in the biotechnology industry. Similarly, aspartame, a microbially produced sweetner, has also been substituted for sugar.

A substantial rise in the consumption of non-sugar sweetners relative to sugar in the main industrialised countries has resulted in a major decrease in the world price of sugar. Since 1982 this

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price has been below the cost of production. The decrease in the price of sugar has had a major negative impact in Third World sugar exporting countries. For example, in the Philippines revenues from sugar exports decreased from $624 million in 1980 to $246 million in 1984, and resulted in the relocation of some 500,000 field labourers. (Fransman (1986), Ruivenkamp (1986), Bijman et al (1986), and Joffe and Greeley (1987).)

b. Increasing the Productivity of Vegetable Oil Sources

The two most important sources of vegetable oils and fats are soya and oil palm. The productivity of the latter has been increased by 30 percent (oil yield per tree) as a result of the cloning of oil palm plants. The greater profitability of oil palm production relative to rubber production in Malaysia has meant that plantations previously producing rubber have switched to oil palm. Since rubber production is more labour-intensive, the jobs of Malaysian and migrant Indonesian workers on rubber plantations are threatened. Furthermore, in the future the greater productivity of oil palms could lead to a reduction in the world market price of vegetable oil prices generally which would reduce the incomes of other producers of vegetable oils such as coconut farmers, many of whom are small and lack the resources to switch to oil palm production. In addition, less efficient oil palm producers, such as a number of African countries, may see their share of world markets dwindle. (Fransman (1986), Bijman (1986),)

c. Producing New Productivity-Increasing Inputs - The Case of Bovine Growth Hormones (bGH)

Milk productivity (output of milk per cow) has been rising since the 1960s as a result of traditional techniques. These include improved management and feeding practices together with conventional methods of improving the quality of herds such as selection. These techniques have in the United States resulted in "an average annual compounded increase in milk production of more than one percent per cow since the 1960s". (Kalter et al (1985), Fransman (1986).)

Biotechnology, however, promises to substantially raise the rate of increase of productivity by providing a method based on genetic engineering of producing in a cost-effective way bovine growth hormone (bGH). The "daily injection of bGH beginning about the 90th day of lactation has been found to increase output by up to 40 percent. That level corresponds to a 25 percenbt increase over the entire lactation cycle.... While the capacity...to stimulate milk production was recognized in the 1930s, it has been only since the advent of biotechnology that the compound [that is, the bGH] could be produced at a level and cost making it economical for farm use." (ibid p71)

In the study by Kalter et al a calculation of the cost and benefit of adopting bGH was made. The cost of adoption included the price of bGH, the administration costs associated with the use of bGH, and the cost of the additional consumption of feed by cows receiving the hormone. On the other hand, the benefit to the farmer was calculated taking account of the productivity increasing effect of the bGH together with assumptions about milk prices. The increase in the farmer's rate of return as a result of adopting the bGH was then computed. The resulting information was then given to farmers in the form of a questionnaire survey in order to calculate diffusion rates. "Farmers expressed an acute awareness of the potential of increased milk output to further depress milk prices.

Some...farmers questioned the desirability of bGH being made available given market conditions [that is, the low price of milk] one farmer writing, 'it should be outlawed'. Others noted that if other farmers used bGH they would, practically, have no option but to adopt as well." (ibid, p81)

Kalter et al therefore concluded that bGH will be widely adopted when introduced (with the diffusion path following the usual sigmoid pattern but with a high rate of early adoption); that adoption will lead to a significant increase in milk output in the United States; that in the absence of government price support, the price of milk will fall; and that this will lead to a substantial reduction in both the number of dairy farms and dairy cattle (the precise numbers depending on the various assumptions made). (Kalter et al (1985), Fransman (1986).)

d <u>Producing In Developed Countries Plants That Were Produced In Developing Countries</u>

One area of application of biotechnology involves the production in developed countries of plants that were grown in developing countries, thus undermining the natural comparative advantage of the latter. One example is the plant *shikonin* which has medicinal properties and sells for about $4,500 per kilo. This plant, which takes a long time and is extremely difficult to grow, was produced mainly in China and Korea. It is now being produced in bulk with the use of tissue culture techniques in Japan by Mitsui Petrochemical.

Other examples include the growth in developed countries by means of tissue culture of other plants with pharmaceutical uses such as pyrethin, codeine, and quinine. Since tissue culture involves the use of industrial processes, land, soil quality, and climate are no longer necessary conditions for the growth of plants. The comparative economics of industry-based and land-based production, however, is the major determinant of which production method will be chosen. Accordingly, it is high value industrially produced in developed countries.

However, genetic engineering is also being used to develop new plant varieties that are more suited to the temperate climates of the developed countries. One well-known example is the development

of so-called ice-minus organisms. These organisms in their natural state populate tomatoes and produce crystals in cold weather which spoil the tomatoes. By altering the genetic structure of these organisms, however, it is possible to circumvent the production of crystals thus possibly facilitating the production of tomatoes in temperate climates. To the extent that plants hitherto grown in developing countries can viably be grown in developed countries as a result of developments such as these, and to the extent that developed countries enjoy circumstances which give them a comparative advantage vis-a-vis developing countries (such as superior distribution systems, lower costs as a result of proximity to large markets, etc) the competitiveness of developing countries will tend to be undermined.

Furthermore, it is difficult for developing countries to derive significant benefit from one of their main sources of comparative advantage, namely their possession of varieties of germplasm which contain genes that can be used to improve the yield performance of other plants. For example, the germplasm from a wild Turkish wheat plant has been used to significantly improve the yield of a commercial variety of wheat by giving it resistance to particular diseases. Germplasm from developing countries is important because most of the world's major crops had their origin in these areas. However, despite the additional value added to commercial seeds and crops as a result of the use of germplasm from developing countries it is difficult for developing countries to ensure that they receive a share of this extra value. Ideally developing countries would be able to control the supply of germplasm and by so doing ensure that, as with any commodity in inelastic supply, they earn an economic rent from its sale. The price paid for germplasm by seed companies and other buyers would then reflect the added value that these purchasers expect to receive from the sale of the final improved varieties. In practice, however, it has been difficult for developing countries to control the supply of germplasm. One reason is that once bought a plant from a developing country can be infinitely reproduced through the use of tissue culture. This undermines the ability of developing countries to control the supply of germplasm in order to earn an economic rent.

IIIa Constraints On The Diffusion Of Biotechnology

As the examples in the previous section make clear, biotechnology, both old and new, has begun to diffuse and have effects on both developed and developing countries. However, as pointed out in section II H, if we are concerned with the diffusion of the ability to put biotechnological knowledge to economic use, then it is necessary to examine the diffusion of the complexly related set of capabilities and assets contained in the biotechnology-creating system. This issue will be analysed in the present section, paying particular attention to the diffusion of the biotechnology-creating system in developing countries.

Constraints on the Diffusion of Biotechnology to Enterprises

a. Firm Size

At the present time *economies of scale* in production tend not to create substantial barriers to the entry of firms into biotechnology The main reason is that the scaling-up of bioprocesses does not always guarantee scale-related cost advantages as a result of the complex interactions of the biological systems existing in bioreactors. Further indirect evidence in support of the contention that economies of scale tend not at the moment to be important constraints comes from the large number of small new biotechnology firms that have emerged particularly in the United States and Europe.

Supporting this point Kenney and Buttel (1985) note that "biotechnology is more knowledge-intensive than it is capital-intensive. For example, Nelson Schneider...a vice-president of E.F. Hutton, has estimated that the critical mass of scientists needed to start a biotechnology firm would be at least 25 PhDs and approximately 10 - 12 million dollars would be needed in initial investment capital." (p77/8) However, down-stream processing, involving scale-up, is more expensive. Nevertheless, "even Eli Lilly's recombinant DNA insulin plants cost only $40 million each" and a "monoclonal antibody research endeavour would probably cost from $3.5 million dollars to $4 million over three years. If the objective was eventually to produce usable monoclonal antibody based products, the total cost would be from $20 to 40 million over three years." (p78) Kenney and Buttel note that "these costs, of course, may seem large, yet when compared to the outlays and subsidies committed to the building of luxury car assembly plants or importation of weapons, the costs...are not unreasonable." (p78)

Accordingly, they conclude that "biotechnology still provides a sufficiently open and fluid structure such that successful entry need not be limited to a mere handful of multinational corporations." (p79/80) This stands in strong contrast to the microelectronics and information technology field where few Third World countries, apart from the largest and sophisticated industrially like South Korea, are able to produce products like semiconductors, computers and digital telecommunications switches, although more are able to provide simpler peripheral equipment and still more are able to use these technologies imaginatively.

However, although economies of scale *in production* may not be particularly important as a barrier to entry at the present time, there are a number of other advantages of size. In this connection particular mention may be made of economies of scale *in marketing and distribution*. Marketing and distribution were included earlier in the *complementary assets* that are a necessary part of the package of capabilities and assets necessary to transform

biotechnological knowledge into value. Having produced biotechnolgy-related products, it is necessary to sell them and in so doing it is possible that there are advantages of scale. It is for this reason that new biotechnology firms frequently enter into agreements with larger companies for the marketing and distribution of their biotechnology-based products. To the extent that economies of scale in marketing and distribution exist, this will tend to be a barrier from the point of view of the ability of an entrant to reap value from biotechnological knowledge.

b Technological and Skill Capabilities

It was seen above that according to one estimate a minimum of 25 PhDs are necessary to create a new biotechnology firm. Insofar as *core scientific capabilities* are concerned, there are no significant barriers to the acquisition of these capabilities. In general it is relatively easy for developing countries, if their own universities do not provide the necessary training in the required disciplines, to send trainees to developed countries for further study. In this way, for example, China has managed in a very short space of time to catch-up rapidly in terms of core scientific capabilities in the biotechnology area. The same is true for Cuba, as will be seen in the case study below, despite the severe political constraints that have limited its biotechnologists from studying in several Western countries, particularly the United States.

However, the constraints imposed by the necessity for *complementary capabilities 1* are far more serious. The main reason is that it is more difficult to acquire the knowledge needed for the effective implementation of bioreactor and bioprocessing technologies. In the case of core scientific capabilities access to the public knowledge available in universities is relatively easy and the cost is not particularly high. However, bioreactor and bioprocessing technologies are usually developed in private companies. On the one hand these companies frequently tend for commercial reasons to keep this knowledge private; on the other hand there is often a significant degree of *tacitness* inherent in this knowledge with the result that it cannot readily and at reasonable cost be made explicit and conveyed to outsiders. Accordingly, the acquisition of complementary capabilities 1 may constitute an important barrier to the entry of developing country enterprises into the biotechnology area.

c. Financial Requirements

Start-up biotechnology enterprises will require access to external sources of finance. This is usually particularly important in the early stages after start-up until the enterprise begins generating sufficient revenue to cover its costs. Government has a

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potentially important role to play in the provision of finance. The reason is that maket-based transactions might face inherent difficulties which prevent the enterprise receiving sufficient finance. These difficulties are likely to be particularly severe in developing countries where the absence or newness of venture capital companies imply the lack of experience in dealing with new technology ventures.

The difficulties referred to result from what Williamson (1985) refers to as *information impactedness* and the potential under these conditions for *opportunism*. More specifically, the new biotechnology enterprise might have more information about the biotechnologies that it will use, and about the market prospects for the products that it will be selling than the provider of capital. In this sense information is 'impacted' or unequally distributed between the parties to the transaction. Under these conditions it is possible that the enterprise might behave opportunistically, in this case, for example, exaggerate the potential returns that might be earned from its activities. Without the necessary information, private venture capital companies might be unable to assess the likely rates of return. While in developed countries venture capital companies have built up their own expertise in order to make assessments of returns, for example by employing their own technical and marketing personnel or by using outside consultants, such possibilities may be more constrained in developing countries. Under such conditions the costs of making a market transaction, in this case concluding a contract for the supply of capital and reaching agreement for the associated terms, might be high. It is therefore possible that the market might 'fail' to allocate sufficient capital to such new biotechnology enterprises.

Under these circumstances, the government in developing countries might have an important role to play. To begin with, the government may (but not necessarily) be in a better position to reduce the degree of information impactedness by drawing on government expertise (for example, the scientific and technical expertise in government laboratories and universities). (It is likely, however, that the government will find it more difficult to assess the market potential of the biotechnology-related products to be developed by the enterprise.) More importantly, however, since government has the power to tax to finance its operations, and since industrial development including the development of new technology enterprises is usually one of the objectives of government, it is likely that government will be in a better position to ensure adequate access to *complementary financial assets* than profit-motivated venture capital companies.

d. Regulation

The aim of official regulation is the control of action. The *regime of regulation* is therefore an important constraint on the

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activities not only of biotechnology enterprises but also of biotechnology research laboratories, whether in universities or government laboratories.

The issue of regulation is probably more important in the area of biotechnology than in most other industrial areas. The reason is that biological organisms, which lie at the heart of biotechnology, interact in complex ways with the biological ecosystems of which they form part. Accordingly, care must be taken to ensure that biotechnology-related activities do not have negative external effects. This is an important consideration when, for example, there is a risk that genetically-engineered organisms might accidentally be released into the wider environment or when there is deliberate release of such organisms. As a result of such dangers a complex web of regulations has evolved in developed countries, both domestically and through the activities of international organisations such as the OECD and the European Commission. In order to avoid the impact of negative externalities nationally and internationally it is extremely important that developing countries take the issue of regulation seriously and interface effectively with the ongoing attempts to coordinate internationally the regulation of biotechnology. This also raises the issue of *risk assessment* which must be undertaken in developing countries in order to make the decision regarding the boundary line between activities that are acceptable and those which are not. For a useful introduction to the issues involved in risk assessment, see Alexander (1985).

It is worth pointing out, however, that since regulation imposes important constraints, as it is intended to do, and since sectional interests are differentially affected by such constraints, there is usually significant *conflict of interest* surrounding the issues for the form that regulation should take. Typically, therefore, private enterprises argue that they are being unnecessarily over-regulated and that this will have negative effects on the economic benefits generated by biotechnology enterprises including their competitiveness (although there are sometimes exceptions). A similar stance is sometimes taken by researchers seeking minimal externally-imposed constraints on their activities. At the other end of the argument are to be found environmentalists and others who have a different view of the risks involved and a different weighting of the importance of the likely effects. This issue is exceedingly complex particularly since government, which is not above the political process but rather part of it, is unable to take a neutral or impartial stand on the regulation question. For this reason it is important that a wide section of interests be involved in the development of regulations for biotechnology.

e. Intellectual Property Rights

Intellectual property rights also provide a constraint on the

activities of biotechnology enterprises in developing countries. A particularly important issue here is the extension of patentability through measures such as the Plant Variety Protection Act 1970, Diamond v Chakrabarty 1980, and Ex parte Hibberd 1985, in the United States, to newly-created plants and other biological organisms (See Fransman (1986) for a more detailed discussion and analysis.)

On the one hand, the extension of patentability in this way is intended to secure intellectual property rights and in so doing increase the appropriability of returns from investment in the creation of such organisms, therefore increasing the total amount of investment in this kind of innovation. It is not yet clear, however, whether the legislation is having this desired effect. After hearings on amendments to the Plant Variety Protection Act (PVPA) in 1980 the Agriculture Committee of the US Senate requested the US Department of Agriculture to analyse the economic impacts of the PVPA. In the study that was done, Butler and Marion (1985) conclude that there "is no evidence that PVPA has triggered massive investments in R&D" (p1-3) However, they also concluded that "there is little evidence of substantial public costs from PVPA. Increases in prices, market concentration and advertising, and declines in information exchange and public plant breeding - the feared costs of PVPA - have either been nil or modest in nature". Accordingly, they concluded that "at the present time" the Act "has resulted in modest private and public benefits at modest public and private costs." (p1-3)

While this conclusion regarding the state of affairs in the United States is encouraging, it is by no means clear that it summarises accurately the situation confronting developing countries. Frequently lacking the range of alternatives of their counterparts in the developed countries, it is possible that developing country users of new and improved seeds and other biological organisms may have to pay the cost, which could be substantial, of creating incentives for innovation in this area. To the extent that patents over seeds and biological organisms limits competition, and this is the inherent aim of patent legislation, and to the extent that developing countries lack viable alternatives, they and their enterprises may be significantly constrainted by this extension of property rights.

f. Complementary Capabilities 2

As was noted earlier, the lack of complentary capabilities 2 can significantly constrain the abil: of enterprises to develop biotechnology-related skills and to apply them effectively The interdependencies of the transportation system, refrigeration facilities, and the delivery of enzymes such as the important restriction enzymes used in recombinant DNA were noted as one

example. This serves to emphasise again the importance of conceiving of a *socio-technical system* which extends far beyond the boundaries of the individual enterprise and which has a significant bearing on the ability of the enterprise to benefit from the diffusion of biotechnology and its ability to transform biotechnology knowledge into value.

IIIb Impact Of Biotechnology At The Company Level

Having examined the constraints on the diffusion of biotechnology to enterprises, attention will now be focussed on the impact of biotechnology on enterprises. Since biotechnology will also have significant effects on the agricultural sector, for present purposes both farms and firms will be treated as enterprises.

a. Inputs and Outputs

The application of biotechnology might in some cases affect both the inputs and outputs of enterprises. Here it is worth distinguishing a) new ways of producing existing products with the use of new inputs from b) new ways of producing new products. Examples of the former include the production of gasoline from ethanol which in turn is produced from sugar, the production of insulin using recombinant DNA technology, the production of the Hepatitis B vaccine using recombinant DNA technology, and the extraction of copper using mineral leaching bacteria. The alternative inputs are oil for gasoline, porcine pancreases for insulin, human blood (with some risk of AIDS infection) for the Hepatitis vaccine, and conventional mining techniques for copper. Examples of the latter include possible medicinal substances which are produced in minute quantity in the human body and which cannot be synthesised such as insulin, interleukin, or tissue plasmonigen activator (TPA).

In the former case the biotechnology-based inputs may be analysed as competing with the other alternative techniques and as in the case of any choice of technique it is ultimately the economics of the different options that will determine the optimal choice. It is by no means clear that the biotechnology-based option will always or usually be preferable. For example, although the oil crises of 1973/4 and 1979/80 induced a good deal of interest in biotechnology-based methods, the subsequent drop in the price of oil meant oil-based alternatives often continued to be preferable.

In the latter case it is the demand for the new product that will be the decisive factor in determining the derived demand and use of the biotechnology-based inputs. In this connection it is significant that public expectation about the future demand for

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biotechnology-based products, as reflected for example in the price of the shares of major biotechnology companies, often diverges significantly from realised demand. When Genentech shares were first sold on Wall Street in 1980 they set the record for the fastest price increase, rising from 35 to 89 dollars in 20 minutes. In 1988, however, Genentech was beginning to benefit from its first major biotechnology product, namely tissue plasmonigen activator (TPA), used for the dissolving of blood clots. Even then sales, although substantial and rapidly rising, were below forecast as a result of the high selling price of TPA.

b. Economies of Scope

In some cases biotechnology has increased the possibilities of deriving benefits from economies of scope. Examples are the move by agrochemical companies into the area of seeds, or the move of fermentation-based companies in areas such as food and alcoholic beverages into new biotechnology-based products such as pharmaceuticals. The possibility of producing new plant varieties that are herbicide-resistant creates new commercial possibilities for herbicide-seed packages. In an attempt to reap the returns from this new potential, large agrochemical companies have been involved in acquiring or setting up seed companies, previously a vertically disintegrated activity. Similarly, the possibility of developing pest-resistent plants has significant implications for the development of pesticides thus providing another rationale for the merging of agrochemical and seed research, production, and sales activities.

These economies of scope increase the returns to investment in the underlying capabilities and assets. At the same time, industry boundaries, when looked at from the point of view of the activities of the companies involved in the industry or the technologies which underly the industry, are being re-defined. From this point of view, for example, the food, alcoholic beverages, and pharmaceutical industries, previously largely comprising distinct companies and technologies, are merging. In Japan, for instance, companies from these three industries, such as Ajinomoto from the food industry, Suntory and Kyowa Hakko from the alcoholic beverages industry, and Takeda from the pharmaceutical industry have all developed capabilities in new biotechnology and begun developing and producing pharmaceutical products.

In turn this raises the issue of *appropriate industrial classification*. In contrast to the conventional ISIC categorisation, to the extent that the objective is to trace the effects of emerging and merging technologies on companies and industrial structure, it may be more appropriate to re-classify industries according to the underlying technologies.

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c. Research and Development

As a result of the advent and widespread applicability of new biotechnology, many companies have made the strategic decision to enter this area. In general, the new entrants are of two types. The first are companies whose product markets are likely to be affected by new biotechnology. The second type are companies whose existing technologies are closely related to new biotechnology. An example of the second type are companies which already have a basis in fermentation technology and wish to extend their bioprocessing capabilities into the area of new biotechnology. Some companies fall simultaneously into both categories.

The decision to enter new biotechnology has meant that new research capabilities have had to be developed. A number of different modes of acquiring these research capabilities have been used. First, new researchers with the necessary *core scientific capabilities* have been recruited. Secondly, existing researchers have been sent for training. Thirdly, some of the larger companies have resorted to take-over or merger in order to acquire the necessary capabilities in the company. Fourthly, some companies have entered into joint venture agreements, with complementary companies, competing companies, universities, or other research institutions.

U The Case of Cuba (1)

The Cuban case illustrates dramatically what can be achieved when a firm commitment is made to the development of biotechnology capabilities and their application to a wide range of areas in accordance with the country's economic priorities. In this section we shall examine the Cuban case in greater detail, paying particular attention to the way in which this country entered the field of new biotechnology, the areas in which new biotechnology has been applied, and the institutional changes that have been brought about in order to facilitate the development of biotechnology. Finally, based on this case study, conclusions will be drawn regarding the lessons for other developing countries.

A Cuban Entry into New Biotechnology

In terms of Cuba's scientific and technological development the crucial watershed occurred with the success of the Cuban Revolution in 1959. Until this time Cuba depended primarily on its agricultural activities, which excluded sophisticated processing and research and development, and on tourism. In this way the foreign exchange was earned which financed imports of manufactured products, largely from the United States. With the success of the Cuban Revolution a new set of priorities was established. Most important from the point of view of the development of the biological sciences in general, and biotechnology in particular, was the emphasis that was given to the importance of science and to the development of the national health service. Frequent reference is made by Cuban scientists to the conviction of Fidel Castro that the future development of Cuba was inextricably bound up with the future development of science in the country. Castro's slogan, which hangs in many Cuban laboratories, was that "The future of our country must of necessity be the future of men of science". It was this conviction that inspired a rapid growth in the school and higher education system. At the same time, an important result of the revolution was the expansion and extended delivery of medical services to all sections of the population. This meant that within a short period of time Cuba was able to develop a relatively sophisticated medical system which included training and research facilities in universities and other national institutions. It was this medical system which was later responsible for Cuba's rapid and successful entry into new biotechnology.

However, new areas of science and research do not emerge automatically; their emergence depends on new groups of scientists and researchers, committed to the new fields of study and devoted to the institutional changes that are required to realise the new scientific research. From this point of view it is significant to observe that the new institutions which evolved in Cuba to develop the biological sciences and biotechology emerged in a *pluralistic* rather than a linear way.

At the apex of Cuba's scientific planning establishment is the Cuban Academy of Sciences which was originally established in 1861 but which was substantially restructured after the revolution. The Academy contains the Superior Scientific Council which consists of about 77 distinguished scientists elected from the Academy's various institutes, from the Ministry of Higher Education, and from industry. The Academy also contains a number of other smaller but influential advisory groups. However, it is significant that the Academy does not totally dominate or control the scientific establishment. For example, only about 10 percent of the total number of Cuban scientists and engineers work in Academy institutes.

The Ministry of Higher Education, with some degree of autonomy from the Academy, has also played an important role in the establishment of scientific institutions. From the point of view of the development of Cuban biotechnology, an important example is the establishment of the National Centre for Scientific Research (CENIC) which was the major biomedical and chemical research centre and was set up in 1965 in order to stimulate research in new areas. CENIC has a staff of approximately 1,000 and is divided into four main divisions: biomedicine, chemistry, bioengineering, and electronics. CENIC has played a significant role in research and in training scientists who subsequently have become involved in other spin-off institutes.

An important example is the Centre for Biological Research (CIB) which was established in January 1982. The establishment of CIB is of particular interest as a result of its innovative and unbureaucratic origins. In 1981 a 'Biological Front' was established essentially outside the existing bureaucratic framework. The Front consists of scientists and policy makers with an interest in extending and developing biological research in various directions. The Front, under the leadership of Dr Rosa Simeon, President of the Academy of Sciences, served to coordinate and articulate the interests of those in the different ministries and institutes who wished to strengthen Cuban involvement in biotechnology. While the leaders of the existing scientific establishment were closely involved with the activities of the Biological Front, as is indicated by the role played by Dr Simeon, the Front was set up as a high-level policy-making body with relative autonomy from the Academy and the various Ministries involved in the biological sciences and their areas of application. From this position the Front supervised the establishment of CIB and later the Centre for Genetic Engineering and Biotechnology, CIGB. By helping to give birth to CIB and CIGB the Biological Front served to increase pluralism in the Cuban scientific system. While biotechnology could be developed in existing institutions, such as those under the control of the Academy of Sciences and in CENIC, this new set of technologies could also be advanced through new institutions such as CIB and CIGB.

CIB began with a staff of six researchers in a small laboratory with Dr Manuel Limonta as its Director. Its major initial mission was the production of interferon for use as an anti-viral agent.

In part the interest in interferon resulted from the outbreak in late 1980 of dengue hemorrhagic fever which affected approximately 300,000 people and resulted in 158 deaths. However, as we shall shortly see, in addition to this pragmatic goal, CIB also aimed to use interferon as a 'model' for the development of the wider range of capabilities and assets analysed in Section II above. In other words, interferon would be used as a springboard for the development of a Biotechnology-Creating System with expertise in the areas of genetic engineering and bioprocessing. CIB grew rapidly and by 1986 was divided into four laboratories: genetic engineering, immunology, chemistry, and fermentation. In addition to the production of interferon, CIB produces its own restriction enzymes and its research also involves the synthesis of oligonucleotides, the cloning and expression of a number of other genes, and the production of monoclonal antibodies for diagnostic purposes. Although recombinant DNA research was also done in a number of other institutes, notably CENIC and to a lesser extent the Cuban Institute for Research on Sugarcane Derivatives (ICIDCA) which was established in 1963, CIB became in the early 1980s the major location in Cuba for the development of capabilities in new biotechnology.

When CIB opened in January 1982 it began to produce human leukocyte alpha interferon using a method (which did not involve genetic engineering) developed by Kari Cantell of the Central Public Health Laboratory in Helsinki. Cantell gave assistance by transferring his method to CIB and was surprised at the speed with which the Cubans mastered the method. Having mastered this conventional method for producing interferon, CIB embarked on recombinant DNA-based techniques for producing various kinds of interferon. In this latter task a central role was played by scientists such as Dr Luis Herrera who was Vice-Director of CIB. Herrera's background is particularly interesting because it illustrates personally the way in which Cuba was able to enter the field of new biotechnology. In 1969 Herrera studied molecular genetics (working on yeast) at Orsy University in Paris. The following year he took up a post as researcher at CENIC where he started a laboratory dealing with the genetics of yeast. Yeast was of interest in Cuba because it was used in order to convert sugarcane derivatives into single cell proteins which were used as animal feed, thus substituting for imported soya feeds, the Cuban climate not being suitable for the growing of soya. Research on yeast was partly aimed at improving yeast strains in order to increase the nutritional value of the single cell proteins by eliminating some of the undesirable nucleic acids. Under the auspices of ICIDCA there were in total 10 plants each producing 12,000 tons per annum of single cell protein for animal consumption. In developing their work researchers in this laboratory became interested in new biotechnology. In 1979 Herrera returned to France to study molecular biology and genetic engineering. With the formation of the Biological Front and the establishment of CIB in 1982 he joined this institute as its Vice-Director. In 1983 he once again went to France where he spent time at the Pasteur Institute. Representing a new breed of young, post-revolution scientists who were quickly able to master the latest international research techniques, Herrera was awarded Cuba's highest honour, Hero of Labour. He has since established an international reputation for his research in new biotechnology.

Although in the case of Dr Herrera entry into new biotechnology involved access to European institutes, Cuban biotechnology and CIB in particular have also benefitted from Soviet science. A notable example is the group of chemists working in CIB and mostly trained in the USSR. With a strong background in organic chemistry some of these scientists moved on to the synthesis on oligonucleotides and the synthesis of DNA. These skills and the self-reliance they afforded have been important in view of the difficulties that Cuba has faced in acquiring automated DNA synthesising machines as a result of the boycott imposed by the United States. Other groups in CIB are involved in immunology, including immunochemistry and protein purification, and fermentation.

There is widespread agreement that the Cuban mastery of new biotechnology has been impressive. One example is the conclusion arrived at by a team of UNIDO experts appointed to find a Third World location for the new International Centre for Genetic Engineering and Biotechnology. This team visited the major Third World countries involved in biotechnology and concluded that the Cuban biotechnology programme was one of the best they had seen. Another example are the assessments made by distinguished foreign visitors to Cuba. While acknowledging that the Cubans are not attempting to do world frontier basic research, many of these visitors have been impressed with the level of achievement of Cuban biotechnologists. An example is Roald Hoffmann of Cornell University and a 1981 Nobel Laureate in chemistry who visited Cuba in early 1985 and attended the second congress of the Cuban Chemical Society. "Overall", he concluded, "I came away with a mixed but optimistic impression of the chemistry being done in Cuba." (Chemical and Engineering News, May 12, 1986, p32)

A further example is the result of *in vitro* gene manipulation work done in CIB laboratories. Some of these results were reported at the Second Cuban Seminar on Interferon and the First Cuban Seminar on Biotechnology held in Cuba in February 1986. The following extract is a report from the journal *Bio/Technology*:

> M. Quintana (CIB) has already cloned the interleukin-2 gene, and is engineering it for expression in *E. coli*. Other *in vitro* gene manipulation projects are equally impressive. Herrera and Quintana's group have cloned alpha-2, beta, and gamma interferons for expression in *E. coli* and yeast cells. Clinical trials with the bacterially expressed gamma interferon are about to begin, and the production levels of alpha-2 interferon are formidable. Yeast constructions containing the alpha-factor signal peptide, and driven by a glyceraldehyde 3-phosphate promoter, process and secrete 10 I.U./liter of 98-percent pure interferon. More recent clones are able to secrete upwards of 10 I.U./liter in an immobilised-cell reactor. The latter product is still only 80-percent pure, says Herrera, although they expect to have material of sufficient purity for toxicity studies within a month or two. As Patrick Gray (who reported Genentech's recent results [at the Cuban conference] showing synergy between tumor necrosis factor and gamma interferon) remarked: "These are considerably higher secretion levels than we have been able to obtain." (*Bio/Technology*, Vol 4, April, p265.)

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B Interferon as a 'Model'

Further comment is necessary on the use by the CIB of interferon as a 'model' for the development of new biotechnology capabilities.

The first point to be made is that the development of core scientific capabilities in the area of new biotechnology in CIB drew on the *already well-developed science base* that existed in Cuba by the time the CIB was set up in 1982. Mention was made in the last section, for example, of the earlier research done in CENIC on the molecular genetics of yeast. In entering new biotechnology, therefore, Cuba was not starting *ab initio*. In this way, Cuban entry into new biotechnology was facilitated by a pre-existing stock of substantial scientific capabilities. Clearly, many developing countries are not in as fortunate a position.

The second point is that interferon was an appropriate choice for Cuba largely as a result of the country's well-developed health sector. This meant that the development of interferon with the use of genetic engineering techniques was not simply a 'pure' research activity, but was an example of scientific work being closely linked to the production of useful output, namely the delivery of medical services, a high priority in post-revolutionary Cuba. *This link established a unity between 'science push' and 'demand pull' determinants of technical change, which in turn ensured that this part of the science system was not 'alienated' from the needs of the rest of the socioeconomy.* Interestingly, interferon has also been used as a 'model' by many Japanese companies entering the field of new biotechnology. In their case, however, the need determined from the corporation's point of view was for a way of acquiring new biotechnology capabilities at the same time as producing a commercialisable product. Interferon, it was believed, provided an example of one of the first new biotechnology-based commercial products. For other developing countries, however, a more appropriate 'road' for the development of new biotechnology may exist, depending on the circumstances and priorities of the country. For Brazil, for example, the ethanol from sugar project may have provided an appropriate road. In other Latin American countries the development of mineral-leaching bacteria for the purposes of mineral extraction may provide an appropriate way of entering new biotechnology.

Thirdly, the possibility of using interferon as a 'model' for the development of other applications and products illustrates the pervasiveness of new biotechnology. This point is further supported in the Cuban case by the history of the Centre for Genetic Engineering and Biotechnology (CIGB).

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C Realising Economies of Scope: The CIGB and the Pervasive Applicability of New Biotechnology

Encouraged by the success of CIB in developing new biotechnology capabilities and impressed with the potential of this set of technologies, the Biological Front recommended the establishment of a new and larger institute which would carry on and extend the work of CIB. Accordingly, on June 1, 1986 the Centre for Genetic Engineering and Biotechnology (CIGB) was established on a new site near CIB with Drs Limonta and Herrera, formerly from CIB, as its Director and Vice-Director.

CIGB was structured in terms of the following five groups, each dealing with a specific problem area:

1. Proteins and hormones. The aim of this group is the production of proteins using recombinant DNA techniques for applications in the areas of human medicine and veternary science. This group continues the work done in CIB on the chemical synthesis of oligonucleotides and DNA.

2. Vaccines and medical diagnosis. The aim of this group is to develop vaccines against diseases prevalent in Cuba and other tropical and subtropical areas through the cloning of the surface proteins of viruses, parasites, or bacteria. The group also works on developing monoclonal and polyclonal antibodies and DNA probes for the purpose of detecting and diagnosing various illnesses.

3. Energy and biomass. The research of this group involves the transformation of various kinds of biomass via the use of chemical methods and enzymes. For example, research is done on yeasts and fungi which transform the sugar by-products molasses and bagasse into proteins for animal consumption. A new strain of the yeast *candida* has been developed which increases the production of an amino acid important for both human and animal nutrition. In this way CIGB will extend research in this area done in ICIDCA and CENIC.

4. Plantbreeding and engineering. This group does research on improved plant varieties using genetic engineering and other biotechnologies such as cell culture. Nitrogen fixation is one area singled out for study.

5. The genetics of mammalian eukaryotic cells. This group uses the cells of higher organisms for the cloning of genes and the production of proteins.

Thus by using interferon as a 'model' first CIB and then CIGB have been able to develop core scientific capabilities in the area of new biotechnology and apply them to a wide range of areas consistent with Cuban development priorities. However, the research of CIGB has also been defined to include an emphasis on *complementary capabilities 1*, namely downstream bioprocessing. This has been done by making provision for a pilot bioprocessing plant in CIGB.

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D The Importance of Downstream Bioprocessing

As noted earlier in this paper, the development of an effective biotechnology-creating system involves more than the mastery of the core scientific capabilities. One feature of such a system is the possession of the necessary downstream bioprocessing capabilities. In order to develop the latter kinds of capabilities CIGB has established a pilot plant. Two groups work with this plant, the one specialising in the fermentation process and doing research on the optimisation of productivity and the other working on questions of purification. Both of these groups are involved with the difficulties that are confronted in scaling-up the bioprocessing with the use of larger bioreactors. A major problem confronted by both groups is that there is little experience in Cuba regarding bioprocessing and scale-up. Furthermore, unlike in the case of many of the core scientific capabilities where research is done in universities and where the results are usually made public, a good deal of research on bioprocessing is done in private companies with the findings kept commercially secret. Bioprocessing, requiring sophisticated engineering skills and specialised inputs, frequently constitutes more of a constraint in developing countries than the mastery of the core scientific capabilities. The same point was made to the present author by senior officials involved in the planning of biotechnology in the Peoples Republic of China during a visit in 1987. In the Chinese case, in strong contrast to the Cuban example, the core scientific capabilities were rapidly acquired largely as a result of scientific interchanges with the United States. However, major constraints exist in China on the downstream bioprocessing side which depends on the capabilities of Chinese industrial and engineering enterprises.

V International Dimensions

A Is Biotechnology as Pervasive in its Effects as Information and Communication Technology?

A number of points may be made in answering this complex and controversial question

1. There is no doubt that biotechnology, as an interrelated set of technologies, is having, and will continue to have, pervasive effects on a large number of industrial sectors. It is perhaps best to analyse biotechnology as a set of process technologies with application to a large number of product areas. The process technologies include classical methods of selection, recombinant DNA techniques, cell fusion, tissue culture, protein engineering, and bioprocessing. Combinations of these technologies may be applied to the research and development of a large number of products. Examples referred to in the present paper include pharmaceuticals (such as insulin, interferon, and vaccines), industrial chemicals (such as enzymes and other proteins, ethanol etc), and new plant varieties.

2. One implication of the pervasive effects of biotechnology is that important economies of scope may be reaped. In other words, investment in the capabilities and assets that are necessary for the creation of an effective biotechnology-creating system may be rewarded with high rates of return as a result of the widespread applicability of biotechnology. This possibility emerged clearly from the Cuban case study where the capabilities and assets built up in CIB and later CIGB were being applied across a wide range of areas, all of which contributed directly to Cuban development goals and priorities.

3. For the reason mentioned in the last paragraph, there would appear to be ample justification for establishing biotechnology programmes in developing countries. (Care however, will have to be paid to the particular circumstance of each country in order to understand the limitations and constraints confronting any such programme, a point that is examined in more detail in Section VI.)

4. There are a number of important differences between biotechnology (BT) and information and communication technology (ICT). For example, the link between process technology, product technology, and product characteristics is much closer in the case of ICT than in the case of BT. Furthermore, there are much stronger *integrative tendencies* in the case of ICT. For instance, the convergence of computing and communication technologies as a result of the digital 'common currency' has meant that ICT products tend relatively easily to become part of broader integrated systems. An example is the integration of personal computers, minicomputers, mainframes, robots, computer controlled machinery, and local and even national communication systems into a broader

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technological system. The same integrative tendencies are not apparent in the case of BT.

5. At the same time there is an important process of *convergence* between BT and ICT. On the one hand ICT is having a significant impact on the development of biotechnology process and product technologies. Examples are the use of microprocessors and computers in automated controls for bioreactors and DNA synthesisers, and in other areas such as sequencing. On the other hand, BT is beginning to have an effect on ICT although this effect is not yet as great as the other way round. For instance, one area of application for protein engineering is in the field of biosensors and biochips where integrated circuit technology is fused with protein engineering technology.

6. It is worth stressing that the entry barriers into BT are at the present time significantly lower than those into ICT, a point that has been stressed earlier in the present paper. Very few developing countries will be able to become significant producers of ICT products such as semiconductors, smaller computers, and communication-related products such as optical fibre or PBXs, although these kinds of products are being produced by countries such as Korea, India, and Brazil. Most developing countries will be *users* rather than *producers* of ICTs. However, many more developing countries will be able to make a successful entry into the field of biotechnology. The qualifications surrounding the possibility for successful entry are examined in more detail in Section VI below. From a policy point of view, therefore, little significance attaches to whether the pervasiveness of ICT is greater than that of BT. The policy question ultimately boils down to an analysis of the social returns that may be derived from investing in generating a biotechnology-creating system, given the circumstances and constraints of the country concerned.

B The Effects of Industrial Applications of Biotechnology in Global Perspective

Production, Trade and Investment

Two major points must be made. The first is that biotechnology is already having an important impact on global production, trade and investment. One example, that was discussed earlier on page 7, is the production of sugar-substituting sweetners. These sweeners have had an important impact on the price of sugar and therefore have had significant implications for those developing countries involved in investment, production, and international trade in sugar. Similarly, biotechnology is influencing the productivity of oil palm and other developing country agricultural exports.

However, the second point to be made is that up to the present time discussions of the impact of biotechnology on economic variables

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such as output, incomes, production, trade, and investment have remained anecdotal and partial, relying on the documentation of particular instances of the effects of biotechnology. Attempts have sometimes then been made to 'add up' these effects in order to arrive at more general conclusions regarding the impact of biotechnology. These attempts are inherently unsatisfactory because they ignore the interdependencies that exist in the global socioeconomic system in which biotechnology evolves and has its effects.

In order to illustrate this important point let us take the case of oil palm which was discussed earlier in this paper. As a result of advances made in the cloning of oil palm plants, the productivity of oil palm trees (oil yield per tree) has increased by some 30 percent. In the shorter run, with the world price of oil palm, a major source of vegetable oil, holding up, this has increased the profitability of oil palm production and has therefore tended to increase investment in such production. This has happened in the case of Malaysia, for example, where many plantations which have produced rubber have switched investment to oil palm thereby decreasing their investment in rubber trees. In turn, this has had important effects on employment and incomes since rubber production is more labour-intensive than oil palm production with the rubber tapped from the tree being collected by hand. The result is that the jobs and incomes of Malaysian and migrant Indonesian rubber workers have been threatened.

However, this account of the effect of biotechnology (in this case the cloning of oil palm plants) on investment, production, trade, employment, and incomes has not dealt sufficiently rigorously with many of the interdependencies involved. For example, there are 'Keynesian effects' that should be considered. As a result of the increase in profitability of oil palm production, it is possible that total investment increases. This in turn results in a multiplied increase in incomes as those whose incomes rise as a result of the increase in investment spend these incomes. This may mean that expenditure on consumption goods increases which consequently leads to an increase in the production of consumption goods and therefore to increased employment in the consumption goods industries. In this way the employment of former rubber workers may be increased. These Keynesian effects deal with the consequences of changes in investment on changes in expenditure and the 'knock-on' effects on other economic variables. But account should also be taken of 'Leontief effects', namely the intersectoral input-output effects. For example, as the output of oil palm increases, so the demand for inputs into the oil palm industry increases, such as the demand for agricultural implements, fertilizers etc. In turn, as the demand for these items increases, so the demand for the inputs which they require will increase. This will have implications for production, investment, employment, and incomes in these industries. However, the analysis of Keynesian and Leontief effects has ignored the 'General Equilibrium effects' on prices and the consequence of changing relative prices.

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For example, as the output of oil palm increases as a result of the biotechnology innovation, there may be a fall in the price of oil palm depending on the demand and supply curves for this commodity. In turn, a reduction in the price of oil palm might reduce the profitability of oil palm production with further consequences for the inter-sectoral distribution of investment, etc.

However, the 'general equilibrium' price effects discussed so far are not nearly general enough. In a truly general approach account must also be taken of other biotechnology-induced effects occurring elsewhere in the global socioeconomic system. For example, soya together with oil palm are the two most important sources of vegetable oils and fats. The productivity of soya production and the conditions under which soya beans can be produced are also being influenced by biotechnology with important implications for the substitutability of soya and oil palm in vegetable oil and fat production. Account must therefore also be taken of the soya market in a general equilibrium approach.

An important limitation of the approaches that have been considered so far is that they treat *technical change as an exogenously determined phenomenon that then has effects on the economic system.* However, a more satisfactory general approach that goes beyond a concern with the interdependence of markets based on price effects would take account of the determinants which shape the evolution of biotechnologies themselves. In other words, rather than taking biotechnologies and their applications as *given* and proceeding to examine the effects, it is important to understand how these technologies themselves are shaped. From this point of view, technical change is an inherent part of the socioeconomic system and not something external to it and 'given'. An understanding of the interrelationship between the socioeconomic system and the process of biotechnological change would enable us to appreciate more clearly the priorities and resources that are influencing the evolution of biotechnologies and their applications.

Furthermore, a general approach should also take account of the environmental effects and feedbacks. For example, while the development of high-productivity plants through the use of tissue culture may raise productivity in the short run, it also may increase the vulnerability of the plants to particular diseases and pests. The greater degree of genetic diversity in a 'conventional' set of plants might serve naturally to limit such vulnerability. Environmental effects such as these should also be included in any attempt to model the general effects of biotechnology.

To conclude, the main aim of the present discussion is to draw attention to the inherent complexity in any attempt to rigorously examine the effects of biotechnology. This difficulty follows from the complex nature of the system, both social and natural, in which biotechnology develops and has effects. However, despite the complexity it is essential that rigorous attempts be made to understand the system as a whole since such an understanding is needed to inform policy-making in important areas such international investment, production, trade, and structural adjustment.

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VI Policy Issues

A The Importance of Country Differences

In view of the enormous diversity both between developing countries in different income categories (that is, high-, middle- and low-income countries) and between the countries in each category, it is necessary to be cautious in attempting to derive policy implications from an analysis of biotechnology and its potential effects. In order to structure the present discussion, reference will be made to the stock of four necessary capabilities and assets analysed in Section IIB to F above.

The first point to make is that one crucial determinant of a developing country's ability to enter the field of biotechnology and benefit from its potential applications is the strength of its existing science system, particularly in those disciplinary areas that are most closely related to biotechnology. The Cuban case study clearly illustrated the importance of the strength of the science system in entering and applying biotechnology. In many other developing countries, for any number of reasons, the science system does not have the same strength. This does not, however, mean that the constraint on entering biotechnology is absolute. The Japanese case, for example, illustrates very well how foreign university systems can be used as a viable mode of entry and in this respect the Chinese case is similar. An important country difference, therefore, lies in the existing strength of their respective science systems.

However, although the science system does constitute a constraint on the ability to enter and apply biotechnology, the development of the necessary core scientific capabilities, as argued earlier, does not usually pose the major difficulties. More important is the strength of complementary capabilities 1 and 2, namely the downstream processing capabilities within the enterprises on the one hand, and the 'environmental' capabilities on the other such as effective power generating and transportation systems. Underdevelopment is practically synonymous with weaknesses in areas such as these which, as we have seen, are crucial to the ability of the biotechnology-creating system to operate effectively. While it is a relatively easy matter to train a bright group of science graduates in the areas relating to biotechnology, both within the national educational system and abroad, it is far more difficult to ensure the necessary quality in the areas of complementary capabilities 1 and 2. A crucial country difference, therefore, in terms of the ability of different countries to enter and apply biotechnology relates to the strength of their complementary capabilities.

The discussion so far has dealt primarily with the 'supply side' of the question. Equally important is the 'demand side'. A number of

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points are important here. The first is that the size of the domestic market will have obvious implications for the extent and kind of production activities that can viably be undertaken. The Cuban example illustrates that a relatively small domestic market does not need to be a significant constraint on biotechnology activities. Far larger countries, with much bigger markets, will have additional options resulting from the ability to establish biotechnology-related production on a larger scale. There are important implications here too for the question of appropriate foreign trade regime. For example, under what circumstances will it be advisable for a developing country to protect the domestic market through policies which restrict foreign trade in order to create an incentive for enterprises to enter the biotechnology area and produce biotechnology-related products? Here the issues are similar to the well-rehersed arguments relating to the advantages and disadvantages of domestic-market oriented and export-oriented production. (See, for example, Fransman (1986) for a more detailed discussion.)

The question of the 'demand side' also raises the issue of complementary assets, also considered earlier. Here it should be recalled that one of the conditions necessary for transforming biotechnology knowledge into commercial output is the possession of distribution and marketing 'assets'. Once again countries will differ in terms of the quality of their distribution and marketing capabilities.

B Modes of Technology Acquisition

A further set of policy questions relates to the most efficient modes of acquiring biotechnology capabilities. For example, what weight should be given to indigenous development of these capabilities, and how much emphasis should be given to other alternatives such as licensing and other technology agreements and direct foreign investment? The latter also raises the question of the advantages and disadvantages of involvement by transnational corporations. Since, however, these policy questions are essentially the same for biotechnology as they are for the case of other technologies, they will not be pursued further here and the reader is referred to the wider literature in this area. (For a survey of much of this literature and for further references, see Fransman (1986).)

C Reassessing Industrial Strategies in Developing Countries in the Light of Advances in Biotechnology

The advent of biotechnology requires that in a number of areas industrial strategies should be reassessed. The main reason is that since biotechnology is applicable over a wide range of industrial and product areas, a redrawing of industrial boundaries and interdependencies is implied. For example, in Japan companies from a wide range of industries have entered the field of new biotechnology. These include the chemical, pharmaceutical, food, and alcoholic beverages sectors. A large number of these companies have begun to develop and market biotechnology-related pharmaceutical products since this is the first area in which biotechnology is beginning to have a significant commercial impact. This has important implications for issues such as industrial structure, competition and competition policy, and technology policy.

In developing countries a similar redefining of industrial boundaries and interdependencies will require the development of new industrial strategies. For example, in the area of agroindustry account will have to be taken in formulating industrial strategy not only of the agricultural enterprises that produce the inputs for industrial processing, but also of the biotechnology-related enterprises and research institutes that may impact agroindustrial activities at various points in the food and related industrial chain.

VII Cooperation Among Developing Countries

The following is a list of some of the issues that might form the basis of cooperation among developing countries:

1. Cooperation in the development of products particularly suited to developing country conditions. One example is the development of vaccines and diagnostics for ailments that are particularly prevalent in developing countries. These kinds of products, sometimes of great importance to developing countries, tend to be neglected by developed countries and their corporations where significant markets are perceived not to exist.

2 Cooperation in training for biotechnology. Since biotechnology is, as we have been, science-based, it is necessary for training to be provided in the associated scientific disciplines. Expertise in these disciplines takes time and resources to develop. In some cases it may be that regional international cooperation will allow for a process of specialisation among developing countries in

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particular disciplines with an exchange of students providing the means of acquiring the necessary core scientific capabilities.

3. Cooperation in the acquisition of complementary capabilities 1 and 2 and complementary assets. It has been stressed in this paper that the acquisition of these capabilities and assets usually constitutes the most significant constraint confronting the attempt of developing countries to develop efficient biotechnology-creating systems. As in other technology areas, developing countries will be required to make *incremental innovations*, modifying and adapting imported technologies and introducing new innovations in order to increase the efficiency of the biotechnology-creating system. These incremental innovations will have a significant effect on the system's overall efficiency. Accordingly, one area for potentially fruitful developing country cooperation will involve sharing information on the ways in which particular problems have been dealt with and perhaps establishing working groups to devise solutions to others within the context of developing country conditions. (For a more general analysis of the importance of incremental innovation in developing countries, see Fransman (1986).)

4. International cooperation regarding the regulation of biotechnology. As mentioned earlier, the need to regulate biotechnology is particularly important in view of the potential ecological risks. On the one hand, cooperation with other international efforts to establish and enforce codes of practice is essential. On the other hand, there are developing country-specific issues involved here which could profitably form the basis of inter-developing country cooperation. For example, in view of an often weaker supporting infrastructure for biotechnology in developing countries, a new dimension is sometimes added to questions of safety. Discussion is also needed on ways of enforcing codes of practice among developing country scientists involved in biotechnology. Developed countries have established committees which supervise events such as the deliberate release of genetically-engineered organisms into the environment. In view of these developing country-specific conditions and issues, there are strong grounds for developing country cooperation in this area.

5. Developing country cooperation over the question of intellectual property rights. Developing countries are being affected by legislation in the developed countries which allows for the patenting of new organisms, including new plant varieties. As was seen earlier, for example, developing countries are often the source of the germplasm which is used as a source of genetic material to produce new plant varieties. While germplasm itself cannot be patented, it makes an important contribution to the rent that is ultimately reaped by the patenters of new plant varieties. Furthermore, the existence of patents means that developing countries will have to pay higher prices for improved seeds than they would have done in the absence of patents. In addition, the extension of property rights in this area has produced a tendency for the privatisation of knowledge that previously was in the international public domain. For example, whereas previously

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universities and public research institutes tended to rapidly publish and disseminate the results of their research, there are now restrictions on the flow of this knowledge as a result of the possibility of applying for intellectual property rights. To the extent that this has happened, developing countries have been deprived of an important source of information which is a significant input into biotechnology research. In areas such as this there may well be developing country interests at stake which could profitably be articulated and represented through developing country cooperation.

VIII Conclusion

As we have seen, biotechnology, virtually as old as the human race, has had its potential power significantly enhanced by the advent of new biotechnology which has provided substantially increased control over the fundamentals of life. New biotechnology indisputably constitutes a fundamental revolution. No longer are human beings pawns in the evolutionary game; they have acquired the ability to control the game itself, or at least aspects of it. The fruits of this revolution are gradually feeding into new technologies which in turn are beginning to impact a large number of commercial areas. However, as with other technological revolutions, the effects of the biotechnological revolution are both *gradual* and *uneven*. The incorrectness of both the high hopes and the frustrations regarding the potential impact of biotechnology has been dramatically illustrated by the ups and downs of the shares of the major biotechnology-based companies on developed country stock exchanges. In reality the biorevolution will be slow in coming and its introduction will be patchy. But there can be litle doubt that a revolution is in the making and that developing countries can ill-afford to ignore it. This paper has attempted to outline the main contours of the emerging biotechnology revolution, paying particular attention to the implications for developing countries and the ways in which they might begin to prepare themselves to make use of the new potential which biotechnology has provided. If it has increased awareness of both the hopes as well as the limitations provided by biotechnology, it will have served its purpose.

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