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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

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INDUSTRIAL BIOTECHNOLOGY POLICY: GUIDELINES FOR SEMI-INDUSTRIAL COUNTRIES

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TABLE OF CONTENTS

Industrial Biotechnology Policy: Guidelines for Semi-Industrial Countries[1]

1. Introduction

Entry into biotechnology (BT) manufacturing does not follow entry into BT research as naturally as is sometimes assumed. The transition is not an easy one even for firms engaged in *commercial production* of BT-based R&D services. Entry into BT production, marketing and distribution means having to cope with things such as the paucity of off-the-shelve technological and manufacturing solutions and fierce competition from established firms trying to retain their market shares.

Save a few exceptions, like that of *in vitro* diagnostic kits, the customary reference to low barriers to entry into BT in the literature should be taken with a grain of salt since it applies to pre-competitive entry only. The passage from the lab to the industrial arena is less trivial than many enthusiasts admit.

Furthermore, entry into BT as an industrial activity cannot be dealt with as a purely firm-specific phenomenon. For an emerging, generic technology-based industry, it also refers to a whole set of interacting agents, which calls for the often neglected systemic aspects of entry.

Particularly in developing countries (DCs), the accumulation of basic BT knowledge does not trickle down easily into the economic sphere. This diminishes its potential for wealth creation. The passage from the realm of the scientifically possible through that of the technically feasible on to that of the economically profitable is much smoother in the industrial countries (ICs), where for this reason, bio-policy often entails industrial policy, although it may not be called so.

But in order for a workable transition from scientific effort to the market to occur, a wide variety of capabilities and institutions have to be in place, such as a reasonably well articulated risk capital market; an enterprise sector permeable to the scientific culture; a scientific sector permeable to the enterprise culture; and corresponding sets of institutions and legal codes.

Although policy interventions are justified on grounds of indivisible investments in R&D, uncertainties and non-appropriabilities, clearly they cannot substitute for an efficient interface between the scientific and the industrial systems, the availability of entrepreneurial and management skills or the necessary interactions among the agents of innovation. In DCs, external diseconomies lead to mis-allocation of resources, e.g. by deterring outsourcing, thus detracting from the effectiveness of the innovative process.

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[1] For an in-depth treatment of many of the points made in this paper, see (Sercovich, F. and Leopold, M., 1990).

Actually, not even in the ICs the trickle down effect is taken for granted. Market failures (and national rivalries) lead to active government promotional and stimulatory involvement. Although market failure is nowhere as pervasive as in DCs, in most of them the industrial policy content of BT policies is not very readily identifiable, to say the least.

DCs have a lot at stake on the issue of what standards are set to define entry into BT. After so many short-lived incursions into industrialization, they cannot afford taking false steps into such a critical cluster of generic technologies by adhering to loose guidelines. This refers not just to scientific quality. It concerns especially industrial, engineering, organizational and entrepreneurial standards. These can in no way be satisfied if due attention is not paid to a set of key dimensions such as gaps in technological mastery, polyvalent engineering skills and scale-up-related issues. Perhaps, too much voluntarism has been one of the most outstanding features of advocations for BT in DCs. Meanwhile, precious time is being wasted.

In principle, there is nothing wrong with a science-push entry, particularly in a science-driven industry like BT, provided that the incentives, markets, capabilities and institutions are in place and work effectively so as to meet social needs and reach consumers competitively. However, the existence of externalities, indivisibilities, and like market failures involve the need for industrial policy. But industrial policy cannot do without the necessary capabilities and conducive institutions.

The main global trends in BT are discussed in section II. Then entry into BT is dealt with in section III. Section IV is devoted to various specific industrial policy issues focusing on the case of semi-industrial countries. The last section offers some closing remarks.

II. The global setting

Some of the most relevant global trends and factors affecting BT industrial policies in DCs will now be reviewed. They are: (a) Scientific and technological uncertainties; (b) relative competitiveness; (c) timing of introduction and rate of diffusion; (d) routinization of the basic techniques; (e) threshold barriers and shifting manufacturing frontier; (f) company strategy; (g) national policies; (h) trade reversals; (i) scope/scale trade-offs; (j) privatization of scientific knowledge; (k) industrial property regime; and, (l) need focusing.

(a) **Scientific and technological uncertainties**: BT's future is highly uncertain. Because the knowledge base is growing at a faster rate than the use of such knowledge in practical applications, the technological and industrial trajectory of BT is not yet quite clear, even within the not too distant future.

In the scientific sphere not enough is known yet about things such as the relationships between protein structure and functions, the mechanisms of pathogenicity in plants and drug delivery methods. However, if feasible technical solutions and profitable economic outlets are found, an ever increasing number of radical technological and commercial breakthroughs will certainly take place. This may lead, among other things, to a shift away from anti-cancer chemotherapies and agro-chemicals, thus bringing about major shifts in market structure. But this is highly unlikely to happen before the turn of the century.

(b) **Relative competitiveness**: Examples of BT's superiority abound. For instance, BT methods for protein manufacturing are far superior than those relying on extraction from vast amounts of animal tissue or the random screening of organic compounds. However, BT products' and processes' relative competitiveness still remains to be demonstrated, except in the few cases where it has given birth to entirely new products (like monocolonal antibodies-Mabs) or has overcome absolute physical and/or cost limits to input availability (to produce insulin, for instance). High costs related to research, stringent process and quality assurance requirements, handling, delivery systems, etc. so far offset BT's inherent advantages. Sharp changes in relative prices, may improve BT competitiveness in some applications and encourage efforts in areas such as energy and commodity chemicals. Technological mastery plus the diminishing quasi-monopoly power in established pharmaceuticals and agro-chemicals will gradually offset the initial handicap of BT products.

(c) **Timing of introduction and rate of diffusion**: These variables differ widely across sectors. The diffusion rate is the highest in drugs, followed by chemical and agricultural applications, with the rest far behind. Within drugs, the diagnostics sector is more advanced than therapeutics and therapeutics, in turn, is more advanced than preventive applications. These contrasts follow a complex and uncertain interplay among the state and evolution of the knowledge base, policy priorities, the role of the regulatory environment and public opinion, the relative competitiveness of BT processes and products, the inter-play of competitive forces and the status of industrial property rights.

Cross-industry diffusion rates depend much on industry-specific variables such as unit product value, R&D thresholds and payback periods. Drugs, a highly R&D intensive industry, will keep a headstart in BT as long as the efforts required for scientific breakthroughs and engineering constraints are not made trivial by technical progress. As for the rest of potential BT user industries, the key largely lies with technological mastery. The building of *savoir faire maison* is going to take long in most BT user industries while the basic techniques are routinized and intermediate supplier networks developed.

The timing of introduction and pace of diffusion are also influenced by the policy environment. Thus, for instance, in 1989 over $245 billion were poured by OECD countries into import quotas, acreage set-asides, export subsidies and other policies, making agriculture the most manipulated industry of all (*The Economist*, 1990). This affects the timing of introduction and pace of diffusion of BT innovations (like bGH), since these would deprive cosy subsidies of justification. US subsidies that encourage more research into sugar or petroleum substitutes than warranted by market prices work in the opposite direction (*Fortune*, 1990, p.57).

(d) **Routinization of the basic techniques; application-specificity of engineering and manufacturing know-how**: The routinization of the basic scientific techniques coupled with the growing application- specificity of BT engineering and manufacturing know-how, cause BT to be absorbed into the various user sectors rather than evolve as a readily identifiable industry--except for the intermediate input and instrument segments. The acquisition of core in-house R&D BT capabilities by large firms in many industries strengthens this trend (Toyota being the latest reported entrant) (*Bio-Technology*, 1990, p.802) As BT matures, so does the growing differentiation of entry barriers relating to sector-specific engineering, manufacturing, marketing, regulatory standards, routines and practices. As a result of this, the current science-led stage will give room to a more market-driven stage.

Over what remains of this century, the structure of the BT "industry" will probably become well defined. In the US, it is likely to take a multiple, application-sector focused and hub-like shape, centered around a rather limited number of large firms playing as nexus among hosts of research boutiques, research institutions and dedicated BT firms serving niche markets, through a complicated network of financial and technological arrangements. In the EC and Japan the structure will be less diversified.

(e) **Threshold barriers and shifting manufacturing frontier**: Because of competition from conventional products, scientific uncertainties, intense R&D rivalry and evolving manufacturing practices, reaching the market with a specific product does not guarantee the recovery of the substantial sunk R&D investments involved. This is why risk-sharing through subcontracting, partnerships or subsidies has become inescapable even for the largest players. Although it is true that BT has brought about a compression between the different stages that go from basic scientific discoveries to actual applications, exaggerating the existence of short-cuts and quick "fixes" pays lip service to the interests of DCs contemplating their entry into the industry.

(f) **Company strategy**: Strategic partnering with large multinational appears so far to be the only way how new entrants can hope to get into mainstream BT markets. In mutual partnerships, both startup companies and multinationals have valuable assets to offer. The former provide their ability to leverage knowledge from universities, hire university faculty on part-time basis and motivate contributions by scientists, entrepreneurs through stock ownership and other economic incentives. The latter contribute with their R&D financing muscle; regulation-related experience and resources; scale-up capacity; established marketing networks; and, diversity of product lines that make it possible to reap economies of scope. Often, startups have a high price to pay when they cannot afford but to get into this kind of arrangements, i.e. relinquishing control on their scientific and technological developments. Except in niche and highly specialized market segments, alternatives to this are becoming less and less feasible.

Although multinationals can strongly affect the timing of introduction and pace of diffusion of BTs, they cannot suppress them; nor are they likely to try to do so in order to protect their markets for conventional agro-chemical and pharmaceutical products. For one thing, a good deal of their patents protecting these products are expiring so that profit margings are diminishing. For another, public opinion and pressure groups are creating an atmosphere hardly conducive to keep relying on conventional products. Thus, although the intrinsic potential superiority of the BT route remains to be expressed in the economic arena, multinationals are definitely open to the prospect of using it to recreate their weakening quasi-monopoly power.

(g) **National policies**: ICs are explicitly applying infant industry policies in BT. For instance, the EC has recently lifted its opposition to proposed Belgian government subsidies to commercial R&D on recombinant products on grounds of the innovative nature of genetic engineering and associated risks. This is in addition to things such as the 3rd EC Framework Programme (1990/94) recently approved by the Council of Ministers that will provide $200 million for BT R&D. The US provides subsidies to (tax exempted) schemes such as Research and Development Limited Partnerships-RDLPs and tax preferences to patent royalty income.

ICs are also targeting support of scale-up efforts. The so-called "downstream processing club" in the UK involves two research institutes and various firms in search for improved separation and purification of products from bioreactors. Direct support to scale-up is considered one of the most relevant policy issues in the US. Japan paid attention to scale-up related problems very early in the development of its own BT industry.

(h) **Trade reversals**: Cases such as those of sugar and vanilla substitutes show that BT is aggravating the impact of trade reversals originated in the automation of labour intensive processes. Further examples: the plant *shikonin* (grown in China and Republic of Korea) which, thanks to its medical properties, sells at $4.500 per kilo, is now being produced in bulk through tissue culture techniques by Mitsui in Japan. Similar is the case with products such as pyrethin, codeine and quinine. However, industrial use of the knowledge base is often kept on tight hold due to economic and social uncertainties. This cushions the actual impact on DCs.

(i) **Scope/scale trade-offs**: BT poses the need to master skills such as the ability to manage multidisciplinary R&D teams and taking prompt advantage of synergies and cross-fertilization in scientific and technical knowledge in order to exploit spin-off potentials. Particularly when the time comes to scale-up BT processes, trade-offs arise between reaping economies of scope in R&D and exploiting economies of scale in specialized manufacturing. Few firms can have it both ways. In DCs, lack of markets and interactions induce the first route at the cost of delaying actual entry into the market. But this undermines the economic prospects of the ventures by preventing the timely recovery of R&D investments (see examples futher below).

(j) **Privatization of scientific knowledge**: Basic scientific knowledge is no longer flowing as freely as it used to. Nowadays, when scientists are on the verge of a breakthrough, the first thing they are advised to do is not to publish or disclose it in any way, but to reserve property rights through patenting. Their activity affects stock market quotations directly, which indicates the extreme sensitivity of BT business to shifts in the scientific frontier.

(k) **Industrial property regime**. The strengthening of industrial property rights is intended to offset diminishing imitation time-lags. There is a conflict of interest between IC-based enterprises that want to maximize global returns accruing to their R&D investments and DC firms trying to gain breathing space for their imitative activities. To make things worse, only very few hold indisputable or undisputed rights on BT patents. But the key to entry into BT resides ever less in getting access to basic knowledge and ever more in knowing how to apply it industrially. Herein lies the main challenge ahead for DCs.

(l) **Need focusing**: BT's trajectory has so far been focused on the needs of OECD country populations and, within this, on the highest value added products. Two thirds of drug R&D in the US go to applications catering the needs of the oldest segment of the population while less than 3% goes to tropical disease prevention or cure. Meanwhile, the rate of infant mortality in DCs is assessed at 20%, while hundreds of millions are infected by parasitic organisms.

III. Developing countries' market entry

In discussing DCs' entry into BT and related policy issues, the first thing that comes to mind is market failure. Acute imperfections in the markets for factors and information prevent BT developments from reaching those market segments where they are needed most. This poses formidable challenges to policy-makers.

To date most BT developments are sharply at odds with views that suggest that BT is particularly suitable to DCs--because of what it promises, its allegedly low entry barriers, and its assumed appropriateness or amenability to be used for leapfrogging. However, while BT's birth is still being laboured, basic techniques are being routinized, the technological trajectory is becoming increasingly user-specific and imitation costs and time lags are being shortened. All this may facilitate DCs' market entry, provided that scaling-up and downstream processing problems are addressed appropriately. DCs genetic endowment is a purely static advantage. It will be irremediably lost unless its value is enhanced through S&T efforts. Not even the shrewdest protective legal devices will do in their place.

Although most DCs' (like ICs') entries into BT are supply-led, there are variations. Sometimes the push from science is stronger than the pull coming from industry or vice versa, while strong market driven elements can be identified in some cases.

Cuba is a good example of a science-driven entry into--largely health-oriented--BT, mainly at the R&D stage. Although some production capacity was developed, it cannot reach world markets because of allegedly deficient quality assurance guarantees (so far Cuba is only serving some third world markets based on concessionary assistance and science and technology co-operation deals). Its cost competitiveness is unknown. The Centre for Biological Research (CIB), set up in 1982, produces its own restriction enzymes and does research on the synthesis of oligonucleotides, the cloning and expression of a number of other genes, and the production of Mabs for diagnostic purposes.

Cuba's entry into BT pursued social ends; i.e., the interest in interferon was prompted by the outbreak of dengue hemorrhagic fever affecting some 300,000 people in late 1980s. But there also was a science-push drive: first rate bioscientists were available and it was thought that BT suits Cuba because of its research-intensive nature (which applies to entry into research rather than into manufacturing). If Cuba is to take steps to get closer to the world market, substantive efforts will have to be made to set up cost-efficient and world quality process, product, and production engineering standards as well as marketing and distribution channels.

Argentina's entry into BT shows strong industry-push elements. It is based on a small though rather dynamic industrial BT establishment drawing on the remainders of a world class biology science base. There are a few BT firms working in the field of diagnostics, vaccines and micro-propagation led by two small pioneer firms mainly active in human health. The predicament facing one of these firms is typical of a DC milieu (i.e., external diseconomies and the need for expensive in-house efforts).

In order to enter the rDNA route, a series of related techniques such as cell culture, protein purification, Mab production, fermentation, etc. had to be learned. But their mastery would not have made sense in order to produce just one product: a steady drive towards exploiting scope economies plus a lack of out-sourcing networks led to a steady growth in the size of an initially modest project. Size escalations and start-up delays followed. What first looked like "shortcuts" drawing on imitation and extensive use of freely available information later turned into unexpected bottlenecks and difficulties requiring a good deal of unforeseen experimental work and innovative efforts to learn a wide range of basic techniques and to apply them effectively. The start-up of the lab, isolation of the gene, its expression and optimization, added upto 6 years previous to commercial production. The initial budget grew ten times [Katz and Bercovich (1988)]. Little time was saved compared to what it takes a dedicated BT firm in an IC, although the investment was significantly lower because it relied on reproducing a process already known. Although the project was technically feasible, its economic rationale remains to be demonstrated. No industrial policy framework was available to support this effort.

Much stronger and effective demand-pull elements are found in Brazil. The elements behind the rationale for the Alcohol Programme were energy dependency, a very high level of photosynthetic efficiency, and an expected price of a barrel of petroleum over $40. Brazil's headstart in the field of ethanol from sugar-cane relied on natural advantages and upon the mastery of all skills and capabilities needed to turn out complete package deals, including project design, execution and start-up, process know-how, machinery construction, training, technical assistance and planning of integrated agro-industrial operations. The Programme sought to control natural processes rather than to engineer them. Hence, it relied largely on known fermentation-related process control engineering, scaling-up and mass production rather than on the manipulation of genetic information. However, the Programme (which is now re-entering a more favorable phase), along with the exploitation of a variety biomass sources, created a large and avid market for BT breakthroughs (Sercovich, 1986).

Brazil's headstart in traditional BT has spun-off what has now become an incipient and dynamic development of frontier BT. These efforts are being led largely by academic research scientists and by increasing numbers of innovative start-ups. University-industry links are being forged through initiatives like Bio-Rio, a science park that will offer an incubator facility, central labs for sequencing and synthesis of nucleotides, rDNA experiments and scale-up, administrative support and technical services.

While in Latin American the weak link usually is industry, in developing South East Asian countries it is the domestic science base. The Republic of Korea, Singapore, Taiwan Province of China and Thailand show comparatively stronger market-driven orientations. They also have more explicit and focused industrial policies towards BT, including supply of credits, grants, risk capital and support for skill formation and process and product development. Thailand pays relatively more attention to agricultural and the other countries to health-related applications. In Singapore, Taiwan Province of China and Thailand start-ups play an important role. The Republic of Korea relies much on chaebols, i.e. large conglomerates that devote substantial resources to BT R&D. South East Asian countries offset the relative weakness of their science base by drawing directly on ICs' scientific establishment through their expatriates and by setting up BT research firms there--the Republic of Korea's Samsung and Lucky-Goldstar have done so in the US (Yuan 1988). And the circuit goes both ways. Glaxo is setting up a $50 million research joint-venture with Singapore's Institute of Molecular and Cellular Biology (IMCB). Not accidentally, all three senior scientists involved in the IMCB are, or have been, associated with major research institutions in the US and Europe (*Genetic Engineering News*, 1989, p.26).

In conclusion: (a) demand-driven elements appear to have a stronger presence in South East Asia than in Latin America, where supply-led elements tend to prevail; (b) within the supply-led experiences, science-push forces are particularly strong, most of the action taking place at university research centers or in research-oriented firms; and, (c) there is a pervasive lack of skills and capabilities to bring scientific output into industrial use. The scope for LDC firms to continue to take advantage of shortening imitation time and cost lags is at stake in bilateral and multilateral TRIP (GATT)-related negotiations currently underway. A weak of industrial policy content is particularly noticeable in the Latin American experience.

IV. Industrial Policy Issues

BT poses plenty of room for controversy and doubts, for it challenges a good deal of the conventional wisdom regarding issues such as the role of basic science in industrial progress, the economics and management of R&D efforts, the locus and focus of technical change, industrial property rights and biosafety-related issues. However, all this ought not to delay industrial policy action anymore.

The science-push drive fails to work in some cases, like in vaccines, where price competition allegedly discourages leading firms to engage into development and manufacturing. This case illustrates dramatically the critical importance of threshold barriers to DCs entry. Plainly, as long as technological and manufacturing barriers are not overcome, a number of vaccines that can be produced today on the basis of existing scientific knowledge just will not reach those who need them. Because IC markets do not justify their commercial development, they remain expensive and because they are expensive they are beyond the reach of those who need them most.

The progressive routinization of the basic techniques makes it easier for user industries to appropriate the know-how concerned. DCs have the possibility to undertake such appropriation directly in connection with applications most relevant to them (be it in agriculture, food, health care, mining, waste disposal or whatever).

This prospect is not favored at all by the increasing privatization of scientific knowledge in ICs. However, this problem concerns particularly the very cutting edge of the scientific frontier. Short of it, DCs have a lot of room to take advantage of the already routinized breakthroughs (like gene splicing engineering).

One of the main promises BT brings with it is that of letting DCs wean themselves from economic dependence on commodity prices. Australia has focused on this problem as the main target of its policy in BT. From this angle, Australia's approach is relevant to most DCs (Freeman, 1989, p.14). However, such a promise must be looked at with a great deal of caution. The route to it may be hazardous.

DCs remain relatively backward, despite all their potential for catching up, because they lack many or all of the ingredients that concur in forming the social capability required to realise such potential. There should be no illusions as to BT being an exception in this regard. Many DCs can put together a group of first rate scientists and even endow them, at the cost of great sacrifices, with the resources necessary to undertake high quality research. But to expect to be able to reach the world market **on this basis** is an illusion. As Japan, and then the Republic of Korea, Hong Kong, Singapore and Taiwan Province of China have shown, the key to effectively exploiting the leapfrogging potential does not just lie in the mastery of the scientific underpinnings of a technology, but rather, in the mastery of the engineering, industrial and commercial skills and capabilities that make it possible to reach the market competitively. Although less successful, Brazil and Mexico have been trying to apply the same lesson. Science-intensiveness does not make matters any easier--rather the opposite.

The case of idiosyncratic, DC-specific, needs for which BT applications may be sought, as well as all those instances where the market fails to operate efficiently (like in vaccines or in bGH), merit a special consideration of the scope for government intervention.

But, no matter how much or how little the government intervenes, the fact still remains that entry into BT cannot be seriously considered if enough attention is not paid to things such as skills to be mastered, resources to be commanded, products to be manufactured, organizational modes and manufacturing standards to be adopted and markets to be served right from the lab throughout all stages up to the distribution to the final consumer.

The above does not mean--particularly after allowing for differences among countries--that DCs should focus on "low-end" applications, most of which are still to be developed. It simply indicates the need for paying enough attention to bottlenecks and constraints to the "high-end" applications which are sometimes recommended.

Entry into high level BT research can render extremely valuable services because, among other things, it makes it possible to keep an eye on what is going on in the scientific frontier and, eventually, take advantage of it as a possible quick follower. However, entry into the research stage without having much chance to proceed forward along the innovative chain, entails the risk of having the results industrialized elsewhere and, what is even worse, of subsidizing ICs' research endeavors.

Over and above the need to bridge the gaps between scientific breakthroughs and technological design, between technological design and engineering development and between engineering development and manufacturing practice, there are also requisites regarding the necessary interaction among the diverse agents of the innovative process. The Brazilian experience in ethanol is a good illustration of the role of the systemic and synergistic aspects in BT development. But only a few DCs can afford engaging in an effort at such a comprehensive scale.

Some 20 to 30 years will elapse before BT becomes a widely utilized technology affecting many industrial sectors. How can DCs take better advantage of it over this period?

The intensity of current international competitive rivalry and the fact that the US, the leading country in the field, is on the defensive and trying to offset its eroding competitive power, is a rather unfortunate coincidence for DCs endeavoring to enter BT. Conditions for access to technological know-how are now harder than they used to be when a lot of knowledge and information regarding manufacturing processes was transferred on a commercial basis. Today, this kind of transfers to DCs has become rare. The rapidly shifting scientific, technological and industrial frontiers in BT accentuates the risks and uncertainties linked to DC moves.

For instance, initial price quotations for BT products are very high since the firms concerned intend to recover R&D costs as quickly as possible. But prices may go down substantially any time. This makes it rather tricky for DC firms considering whether to get into the BT business to undertake a realistic assessment of future returns (even though their own R&D costs may be substantially lower thanks to imitator's advantages). Another difficulty lies in the sparsity of engineering cost estimates, since most relevant equipment for advanced BT applications is currently being made to order.

Potential success of attempts at entering BT depend, among other things, on the previous experience profile at the firm and country levels; inter-organizational synergies within the private sector and between it and the public sector; availability of risk capital; innovation financing; linkages between industry and the scientific and technological system; and, application-sector specific scale-up skills and capabilities.

Although DCs may have little chances of entering directly into high value added product lines involving heavy R&D expenses, they do have certain indirect strategic routes for taking effective economic and social advantage of advanced BT and building up the experience necessary to enter increasingly higher value added products. Such routes include applications regarding: (i) plagues and idiosyncratic diseases; (ii) improvement in the competitiveness of traditional industrial sectors (agriculture, biomass, food and drinks, forestry, textiles, mining, etc.) by enhancing existing product quality and process efficiency; and (iii) developing new products based on traditional industrial sectors aimed at niche markets.

But it would be absolutely illusory to attempt entering commercial BT without paying enough attention to the mastery of effective downstream processing technologies through joint work between chemical engineers and biochemists. The lack of bioprocess engineering skills may effectively block scale-up efforts, particularly at the purification stage (the major cost item). The ability to undertake effective scale-up is a major entry barrier into most commercial BT segments. Substantial lead times are involved. Genetic engineering has permitted mass production of proteins and lower fermentation costs for products such as enzymes and amino-acids. But it does not substitute for more traditional engineering disciplines. The choice of techniques (e.g. regarding the optimum expression medium) is still another important challenge to engineering developments involved in scale-up efforts.

The rich variety of agents of BT change in the world market provides plenty of room for identifying and resorting to sources of international scientific and technical co-operation. Many IC-based BT start-ups are eager to engage into technology transfer agreements with DC-based firms. However, it is necessary to proceed with caution since, in most cases, their technologies are still at an experimental stage. On the other hand, examples of DCs' excellence in BT research abound. There are also many instances of successful applications of the outputs of such research (like Zimbabwe's DNA probes for salmonella, Argentina's diagnostic test for the Chagas disease and Colombia's malaria vaccines) (Eisner, 1988).

As pointed out, Singapore along with other South Asian countries and Spain pursued a shrewd strategy that consists of taking advantage of expatriate scientists and engaging in joint-research ventures in ICs. Zimbabwe, for instance, takes advantage of expatriate scientists working in France in the area of DNA probes for salmonella. This work is of global interest as the disease causes 3.5 million deaths each year in children with diarrhea (*The Economist*, 1990.a, p.81).

But joint-research ventures do not necessarily work to DC's advantage. Some agreements may allow IC-based corporations to use DCs research skills and capabilities as a source of cheap inventive labour whose output is subsequently processed industrially and commercially back in the IC (Thayer, 1989, p.7.) and (*Chemical and Engineering News*, 1989, p.14). The Chinese are involved in this kind of joint-research venture while acquiring, at the same time, turn-key, pre-fabricated BT facilities from a major multinational to manufacture recombinant hepatitis B vaccines. This black box-type transfer includes highly sophisticated hardware items (such as ultra-centrifugation process equipment that brings into play forces hundreds of thousands of times as powerful as gravity) (*The Wall Street Journal*, 1989).

V. Concluding remarks

One of the basic dilemmas DC face in BT is how to enter it at the right time, and how to avoid pursuing wrong leads and dead ends. Getting into BT at a point too far removed from the market or too dependent on price sensitive products in highly competitive and risky markets may not be a sensible approach.

DCs need to understand the dynamics of BT change in DCs in order to identify technology and market trends and valid interlocutors (universities, research boutiques, dedicated BT firms, or multinational corporations) according to specific needs. This, in turn, requires a clear assessment of the nature of these different actors, their relationship to each other, and their respective strategies and likely trajectories.

It is also essential for DCs to understand the nature of the most important factors that affect the timing of introduction and rate of diffusion of BT, such as company strategies, scientific, technological and engineering bottlenecks and uncertainties, barriers to entry and threshold factors and the relative competitiveness of BT products and processes.

To bridge the gap between the rapid development of the scientific frontier and the lagging evolution of the technological and manufacturing frontiers will take a great deal of time and resources. An increasing number of entrants at the R&D stage can be anticipated. But it is not so certain that the state of the art in manufacturing will catch up any time soon with the acquisition of applied scientific skills at the enterprise level. Herein lies a vital breathing space for DCs.

However, the inability to supply products and services at competitive prices (net of infant industry learning-related costs and external diseconomies) downgrades the capacity to generate wealth. No matter how creative the efforts involved might be, this kind of situation is likely to lead to a dead end. High value added products make it possible to pass on high costs of research, but for now they do not appear to be the solution for DCs attempting to enter BT commerically.

The 1970s have witnessed the birth of BT industrial applications. During the 1980s MNCs have cautiously followed events, becoming more and more involved and thus getting ready to fully enter it. During the 1990s they are likely to impress their particular mark upon future developments.

Once the basic BT techniques become routinized, one of the main questions to be addressed is what to do with them (new proteins or life forms can be created without a clear purpose). The answer to this question can not be pre-fabricated. It can only result from a learning process whereby the accumulation of scientific, technological and manufacturing skills and capabilities interacts with social needs and market realities.

Among other things, this process entails, on the one hand, the carrying out of basic and applied research on a continuous basis and, on the other, setting up the engineering capability that is needed to translate the resulting insights into competitive products. This process will be more and more influenced by the increasing absorption of BT by user industries, whereby its trajectory will progressively assimilated by that of those industries.

The above is precisely what, once again, the Japanese appear to have understood very early. In their two-tier strategy, the first stage (1981-88) consisted of achieving the mastery of the scientific underpinnings and practical use of the basic techniques of BT. For this, they have taken full advantage of research links with the best centers of excellence in the world. The second stage (1988-onwards), which started while the first was still in progress, consists of acquiring the necessary manufacturing experience through licenses--and then starting to enter the real game as innovators, forging ahead both at the scientific, technological and commercial levels (Masuda, 1989).

International technical co-operation has an important catalytic role to play. This includes, first, supporting the setting up of information networks. In the second place, it concerns the building up and strengthening of domestic scientific and technological capabilities. This comprises areas such as bioprocess engineering skill formation, experimental development and scale-up efforts, setting up and upgrading standards of manufacturing, quality and process and product safety and working out of industrial policy guidelines. Thirdly, assisting in the transfer and adaptation of technology. And, fourthly, supporting the development of new products and process.

Initiatives such as PRATAB--Programme of Policy Research and Technical Assistance in Biotechnolgy, (see Sercovich and Leopold, 1990), would help tackling an urgent need to avoid duplications, create synergies and improve the use of resources.

PRATAB is intended to perform as a scanning and early warning system for the benefit of DCs through the execution and support of technical assistance and policy research in BT, based on the articulation of the so far scattered efforts made by governments and international organizations. A network of data banks would be set up and consulting services to DC government and organizations would be provided. PRATAB's sponsorship is to come from governments and international sponsoring agencies. The programme would establish a network of researchers and policy makers from both DCs and ICs so as to facilitate their reciprocal consultations on a periodical basis. Its financing would result from sums granted by the different sponsoring agencies to specific research, consultant and technical assistance tasks in the context of their on-going activities so that overheads would be kept at a bare minimum.

Bibliography

Bio/Technology (1990). Vol 8., September, p. 802;

Chemical and Engineering News. (1989). "Cell Technology in Chinese Joint Venture", April 3;

Eisner, R. (1988). *Genetic Engineering News* . July/August

Fortune (1990), Oct 8.

Freeman, K. (1989), "Aussies in US". *Genetic Engineering News*. February

Genetic Engineering News (1989). June

Katz, J. and Bercovich, N. (1988) Biotecnologia e Industria Farmacéutica, CEPAL, Buenos Aires

Masuda, M. (1989), "Bio-Industry Policy Reviewed in Mid-Term". *Business JAPAN*. July

Sercovich, F. (1986). "The political economy of biomass in Brazil--the case of ethanol", in Jacobsson et at. The Biotechnological Challenge. Cambridge University Press, Cambridge, UK

Sercovich, F. and Leopold, M. (1990), Developing Countries and the "New" Biotechnology: Market Entry and Related Industrial Policy Issues, Manuscript Series, IDRC, Ottawa

Thayer, A. M. (1989), "US firm, Chinese set up biotech venture". *Chemical and Engineering News*, March 20

The Economist (1990). Special Report on World Trade, September 22

The Economist (1990.a), "The slow march of technology", January 13, p. 81.

Yuan, R.T. (1988). Biotechnology in South Korea, Singapore and Taiwan, International Trade Administration, Washington, D.C.