

# An Overview of Health-related Industrial Biotechnology in Latin America and the Caribbean<sup>1</sup>

MARÍLIA BERNARDES MARQUES<sup>2</sup>



*There is some uncertainty about the extent to which Latin America and the Caribbean have participated in the advances of health-related industrial biotechnology. This article reviews the available literature and seeks to provide an overview of the prevailing situation.*

*In general, national governments and multinational agencies have provided most of the health-related biotechnology investments within this region. Efforts to achieve technology transfers, a subject of prime concern, have been developed by a number of programs including the WHO Special Program for Research and Training in Tropical Diseases, the UNDP/LINESCO/UNIDO Regional Biotechnology Program for Latin America and the Caribbean; PAHO's Program for the Regional Development of Biotechnology as Applied to Health; The PAHO/WHO Expanded Program on Immunization (EPI); and PAHO's Regional System of Vaccines (SIREVA).*

*Regarding current production capacity, some successful efforts have been made to produce a variety of therapeutic products including recombinant and natural interferons, interleukins, insulin, and recombinant streptokinase; but in general the region's current potential in this area is at best incipient and uncertain. However, the region does have a limited ability to make diagnostic products and a well-established capacity for vaccine development. Overall, this picture suggests that the region has the potential to play a small but significant role in health-related biotechnology.*

Health-related industrial biotechnology depends on an important set of technologic innovations currently emerging in the chemical/pharmaceutical sector. Disciplines normally found within this area in-

clude scientific research, technologic development, and industrial production of both recombinant and other biologic substances applicable to medicine; i.e., products of therapeutic, diagnostic, or immunologic value (1).

Internationally, it is widely recognized that the market demands of developed nations have been the principal driving force behind the generation of new, high-value-added biotechnologic products and processes applicable to the health field (2-5).

The extent to which Latin America and the Caribbean have participated in this process is not entirely clear. Homma (6) points to considerable technologic advances this century in the area of biologic products, as shown by production of vaccines against

<sup>1</sup> Reprint requests and other correspondence should be addressed to Marília Bernardes Marques, Núcleo de Estudos em Ciência e Tecnologia do Centro de Informações Científicas e Tecnológicas, Fundação Oswaldo Cruz, Av. Brasil 4036, 7 andar, 21040-361 Rio de Janeiro, Brazil (tel. 55 021 2605979, fax 55 021 2609944). This article will also be published in Spanish in the *Boletín de la Oficina Sanitaria Panamericana*, Vol. 121, No. 3, September 1996.

<sup>2</sup> Studies in Science and Technology Group, Center for Scientific and Technologic Information, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil.

serotype B meningococcal meningitis, hepatitis B (via recombinant DNA), and Argentine hemorrhagic fever. Regarding Latin American and Caribbean participation in actual generation of these and other technologic innovations, however, the available information is scanty (7, 8).

In contrast to such positive accounts as the three cited above, most descriptive studies conclude indirectly—based on low numbers of patents, articles, and citations with Latin American or Caribbean origins referred to in indexed reviews—that the area's contribution to the advancement of modern industrial biotechnology as applied to health is negligible (9). It should be noted, however, that these descriptive studies are restricted in their scope to health or medical research, and therefore lack access to all of the relevant empirical information about health-related industrial biotechnology that would be needed to substantiate such a conclusion (10).

Some authors emphasize that, despite the small budgets allocated to science, technology, and health in the area, efforts made since the early 1980s have strengthened scientific activity in the health field, significantly increasing a number of countries' scientific productivity. For example, Argentina, Brazil, Cuba, Mexico, and Venezuela approximately doubled the number of their scientific publications between 1976 and 1983. (Nevertheless, the number of such publications in the area remains small, being estimated by several studies at 1–2% of all such publications in the world—11–14.)

For Pellegrini (15), the only clear conclusion to be drawn from five recent country studies (in Argentina, Brazil, Cuba, Mexico, and Venezuela) on the status of health-related scientific activity was that the information and statistical systems for health science and technology in the area remain weak. In that author's opinion, such weakness is consistent with the area's pattern of scientific development, one where science

and society remain largely alienated from each other—the main reason why no need is seen to assess such things as the relevance, quality, and impact of scientific production vis-à-vis social demands.

To the scarcity of information must be added the known limitations of scientific activity assessments based exclusively on scientometric surveys. In fact, such assessments do not measure the degree of integration achieved endogenously between scientific activity, technologic development, and industrial production; nor do they make it possible to evaluate the extent of linkages between those activities and socioeconomic demands of the various countries (16).

Within this context, it appears that an initial integrated assessment of the general panorama of health-related industrial biotechnology in the countries of Latin America and the Caribbean, even though incomplete, would provide a useful starting point, one perhaps capable of encouraging more comprehensive assessments based on appropriately designed and implemented surveys. It is with such expectations that the following observations are presented. The reader should be advised, however, that these observations are preliminary and that little use has been made of privileged information sources—such as documents pertaining to international cooperation projects. Such limited use appears justified by the difficulties involved in gaining access to such sources, which are not normally included in the holdings of scientific libraries.

By and large, the information used was obtained from more widely disseminated sources—such as catalogs, brochures, newsletters, scientific articles, and other publications—collected by the author in recent years. The rest of this information was obtained from a number of specialists who have participated in discussions on the evolution of health-related industrial biotechnology in the Americas.

## REGIONAL TRAINING AND COOPERATION SINCE 1980

As Orrego (17) has pointed out, in the 1980s local production of restriction enzymes, marked nucleotides, and tissue-culture media was under way in Brazil; Mexico dominated the technical process of synthesizing oligonucleotides; Colombia was producing Petri-dish media; and Argentina had developed the capacity to manufacture  $-70^{\circ}\text{C}$  refrigeration chambers. This author, who noted that at least 16 international organizations were actively involved in developing biotechnology in Latin America and the Caribbean, stressed that all of these products could come to be manufactured at a cost lower than that of similar imported products. More generally, despite the economic downturn, during the 1980s various countries—Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Mexico, Uruguay, and Venezuela—introduced national initiatives and programs stimulated by expectations justly roused through application of modern biotechnologies in the fields of agriculture and health (18–20).

According to Peter Commandeur, “the creation of national biotechnology programs was a first step in defining policies for the development of (modern) biotechnology capabilities in almost all Latin American countries. With these programs, governments aimed to coordinate R&D institutions and projects, to stimulate linkages to industry, to channel international cooperation and, in some cases, to finance projects” (19, p. 4).

Regional investments in R&D and industrial production have mostly been the responsibility of national governments and multilateral agencies. The various initiatives and programs thus introduced have led to measures promoting ties between university and government research activities and the demands of industry and the health services.

Within this context, transfer of technologies applicable to the field of health from developed countries to the countries of the region has been a prime concern. Strategies for achieving such transfer, involving integrated actions of international agencies and national governments, have included incentives to promote cooperation between the universities of developed and developing countries. Beginning in the 1980s, a number of programs and initiatives came to demonstrate their relevance to the area. They included the WHO Special Program for Research and Training in Tropical Diseases (Tropical Disease Research—TDR); the UNDP/UNESCO/UNIDO Regional Biotechnology Program for Latin America and the Caribbean; PAHO’s Program for the Regional Development of Biotechnology as Applied to Health; the PAHO/WHO Expanded Program on Immunization (EPI); and PAHO’s Regional System of Vaccines (SIREVA).

(a) The WHO Tropical Diseases Program (TDR), an initiative cofinanced by the World Bank and the United Nations Development Program (UNDP), was conceived within the framework of the 1974 World Health Assembly and the Alma Ata Declaration. Key TDR elements have included strengthening the capacity to conduct research on leading tropical diseases (malaria, schistosomiasis, filariasis, African trypanosomiasis, Chagas’ disease, leishmaniasis, and leprosy) in endemic countries and development of appropriate health technologies.

When TDR project financing was distributed to the different WHO geographic regions in 1975–1988, a large share of the resources (34.5%) was allocated to the Americas. About two-thirds of this (20.6%) was channeled to the United States and Canada (21), a distribution compatible with those countries’ growing participation in molecular biology and basic drug development projects concentrated in the industrialized countries. In 1987 new measures,

including one known as the Initiative for Implementation of Biotechnology, sought increased developing country participation in the program.

Initially, the TDR's primary aim was to attract the most advanced scientific expertise available in immunology, pharmacology, and epidemiology to the field of tropical diseases. The program was subsequently redirected to also attract expertise in molecular biology and biotechnology, and to guide it toward field research on applications aimed at controlling the target diseases.

An implicit TDR premise was that by attracting modern biotechnology to address the diseases targeted, it would be possible to identify new targets for pharmaceuticals and protective antigens and in this manner to pave the way for developing new drugs and vaccines. The effort to develop products, ranging from basic research to the stage at which a disease is actually controlled in the field, thus characterized the incentive provided by the TDR.

At the end of the 1980s, however, the pharmaceutical industry's lack of interest in the developments achieved with TDR investments in drugs and vaccines was becoming evident (22). One example concerned research on an anti-malaria drug already in the clinical testing phase. Derived from mugwort, a medicinal plant discovered and introduced by the Chinese, this drug was considered promising. However, the pharmaceutical industry showed no significant interest in its manufacture and marketing.

The difficulties and obstacles encountered by the TDR led to acknowledgment that social incorporation of scientific and technologic findings in the field of health is determined not only by an epidemiologic rationale but also by the political will to satisfy health needs. Political decisions made outside the health sector, together with pursuit of a variety of commercial interests, can either constrain or facilitate achievement of epidemiologic goals.

(b) The UNDP/UNESCO/UNIDO Regional Biotechnology Program for Latin America and the Caribbean, a US\$ 5 million initiative, was formally launched in 1987, when the First Meeting of the Regional Committee was hosted in Mexico City. In all, 13 countries participated (20).<sup>3</sup> During its first phase (1987–1991), the program guided international technical cooperation in the field of biotechnology by encouraging integrated actions by countries and participating groups. The program focused on transfer of research results to the point of laboratory development, strengthening of education in the basic sciences, identification and evaluation of appropriate technologies, and development of those technologies on a pilot scale with a view to future industrial application.

In the health field the program supported projects aimed at developing systems for diagnosing trypanosomiasis and leishmaniasis in endemic parts of the Americas and developing markers for diagnostic probes of enteric infections, hepatitis, and malaria. Support was also provided to two projects that demonstrated commercial potential: industrial production of penicillinase and its use to obtain 6-aminopenicillamic acid (6-APA); and an integrated project directed at mass production of monoclonal antibodies in Latin America.

National biotechnology commissions were set up to coordinate activities in each participating country. In 1992 the program's second phase was launched. This had as its prime aim the strengthening of basic structures developed in the preceding phase and the training of high-level human resources through promotion of advanced courses with an emphasis on both academic study and technology.

<sup>3</sup> Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, Guatemala, Mexico, Peru, Uruguay, and Venezuela.

(c) The Program for Regional Development of Biotechnology as Applied to Health, a PAHO initiative announced in 1987 at the 26th Annual Meeting of the Advisory Committee for Health Research held in Rio de Janeiro (23), sought to strengthen existing facilities, increase their capacity to produce biomedical products on an industrial scale, and link such efforts initially in six countries: Argentina, Brazil, Costa Rica, Cuba, Mexico, and Venezuela. The program thereafter provided support to 12 research projects—on malaria, HIV, and hepatitis B—and to 11 institutions in four countries (20). Significant biotechnologic results were obtained—including production of monoclonal antibodies and sera and establishment of banks of well-characterized strains of HIV in Mexico, Brazil, and Argentina. Starting in 1991, the program began to prioritize human resource training—emphasizing such matters as quality control, ethics, and biosafety as well as the disciplines of molecular epidemiology and molecular entomology and a multicentered project aimed at developing a “kit” for diagnosis of HIV infections.

(d) The Expanded Program on Immunization (EPI) was proposed at the 1974 World Health Assembly and ratified in 1977 by PAHO’s Directing Council. The EPI has achieved distinction for extending basic vaccination coverage in the Americas (24). The linkage implicit here between the EPI and health policies appears to have made the program one of the most important indirect mechanisms stimulating industrial production and quality control of vaccines in Latin America and the Caribbean. Among other things, the EPI’s efforts have dealt with vaccines against poliomyelitis (trivalent oral vaccine); diphtheria, tetanus, and whooping cough (DPT vaccine); tuberculosis (BCG vaccine); and measles—as well as the time-honored yellow fever vaccine, tetanus toxoid, and more recently developed vaccines such as that directed against hepatitis B.

(e) The PAHO Regional System of Vaccines (*Sistema Regional de Vacunas—SIREVA*) was established to promote ties between research, development, industrial production, and human resource training in the Region. Recent studies suggest it is succeeding in promoting the transfer of modern technologies for producing certain vaccines, such as DPT (6).

In addition to these programs, there have been various bilateral initiatives: in 1985 the Argentina/Brazil Biotechnology Center (*Centro Argentina/Brasil de Biotecnología—CABBIO*) was created, permitting a variety of partnerships between public research institutions and private firms. CABBIO’s funding for the first five years totalled US\$ 20 million and constituted the first direct subsidy to a private research and development initiative granted in the two countries (19). In 1986 Venezuela and Colombia signed a cooperative agreement, and in the early 1990s the signing of free trade treaties began to assume increasing importance.

From a trade standpoint, three basic political changes were observed in the Region: privatization of state-owned companies, deregulation of national economies, and opening of geographic borders to international trade. It seems apparent that these policies have had and will continue to have major implications for projects and programs dealing with industrial biotechnology in the health field. To date, however, assessment of these implications has been rendered difficult by lack of the empirical information needed to make a reasonably objective, as opposed to a merely ideological, evaluation.

Thus, the negotiations conducted within the framework of the North American Free Trade Agreement (NAFTA) initially generated expectations that endogenous training in industrial biotechnology would be strengthened. However, these expectations were partly frustrated by Mexico’s economic crisis of 1995, a crisis that also pro-

duced significant consequences for other Latin American countries, including Argentina and Brazil.

In 1991, signature of the Treaty of Asunción formalized creation of the Southern Cone Common Market (MERCOSUR) including Argentina, Brazil, Paraguay, Uruguay, and later Chile. Expectations for MERCOSUR in this area of South America are currently high, with new technology cooperation initiatives involving the academic and entrepreneurial sectors of health-related biotechnology being expected (25).

The 1992 Bolívar Program for Regional Technologic Integration and Promotion of Industrial Competitiveness has established country bureaus and has joined forces with an Inter-American Development Bank (IDB) initiative in promoting the establishment of joint ventures between companies and research centers from two or more countries. Its principal aims are to achieve internationally uniform quality standards and to strengthen each participating country's production capacity through generation of new products, processes, and services (19).

It should also be noted that in 1992 the European Community (EC) and the Latin American Economic System (LAES) finalized a proposal to establish a joint program lasting at least four years to stimulate trade between Europe and Latin America. This program may eventually have positive impacts on Latin American development of industrial biotechnology.

## **CURRENT HEALTH-RELATED INDUSTRIAL BIOTECHNOLOGY**

### **Therapeutic Products**

Successful efforts have already been made to produce some pharmaceutical products for therapeutic use from a biotechnologic base at the local level. These

products include recombinant and natural interferons, interleukins, insulin, and recombinant streptokinase. Cuba has obtained the first patent on the latter substance, which has aroused considerable interest because of uncertainty regarding the therapeutic advantages of the activating factor of tissular plasminogen, tPA, over streptokinase. Besides production of these substances, other biologicals including amino acids, nucleotides, steroids, enzymes, hormones, specific hyperimmune sera, conjugated antibodies, and monoclonal antibodies are being purified and synthesized (26); and computer-aided sequence analysis of nucleotides and proteins has been introduced into Latin America and the Caribbean (27).

Given the current state of the art worldwide, it appears that monoclonal antibodies may come to be used for various therapeutic purposes—such as direct passive immunotherapy against toxins, endotoxins, or infectious agents (as in the case of Gram-negative septicemia). Indeed, while representing only a part of the available arsenal, in the future monoclonal antibodies seem likely to head up a new and important class of therapeutic products. For this reason, a number of biotechnology companies operating in developed countries are attempting to introduce this approach to address a broad range of viral diseases—such as hepatitis B, cytomegalovirus, human immunodeficiency virus (HIV), herpes simplex, respiratory syncytial virus, rhinovirus, and parainfluenza virus.

Considering that monoclonal antibodies are commonly used for diagnostic purposes in the region, it seems clear that this cumulative experience may be useful in the future for developing therapeutic innovations in some of the countries with appropriate industrial capacity—such as Argentina, Brazil, Cuba, and Mexico. However, it is not currently possible to predict whether the development of health-related industrial biotechnology in Latin America and the

Caribbean will achieve a significant share of specific therapeutic markets, such as the market for medications derived from medicinal plants, for example, despite the rich available flora (28). Such future evolution will obviously depend on the priority accorded by national governments to the specific policies and programs required.

Rodolfo Quintero, Director of the UNIDO/UNESCO/UNDP Regional Biotechnology Program for Latin America and the Caribbean, feels that Latin America and the Caribbean can already be considered outside the market for therapeutic products obtained through biotechnology (29). He envisages the market as having a volume of hundreds and perhaps thousands of millions of dollars by the late 1990s, when some 300 new active principles will be available; and he emphasizes the considerable distance that separates the size of private industrial investments and government expenditures by the United States, Japan, and some European countries on the one hand from similar expenditures in Latin America and the Caribbean on the other.

However, not all analysts share this pessimistic view. In particular, the entrepreneurial dynamics and excellent qualifications of various research groups in the area constitute positive factors that can make increased participation in this field viable, at least for some countries, when combined with the national government's appropriate political will and adequate levels of financing (30).

## **Diagnostic Products**

The diagnostic products sector offers the best opportunities for private investment, as it has none of the difficulties associated with large-scale industrial production. Also, with regard to technology transfer, the present trend is toward strategic alliances and other forms of association between large pharmaceutical companies and the so-called new biotechnology firms. It seems

likely that this trend will exert considerable influence over future development of industrial biotechnology within this sector in Latin America and the Caribbean.

The tradition of biomedical research found in some countries of the area, together with reasonable endogenous capacity to make diagnostic products, has permitted rapid incorporation over the past decade of modern biotechnologic tools (monoclonal antibodies and recombinant DNA). These same circumstances are currently providing the basis for developing a promising generation of new products with high sensitivity and specificity, particularly for the diagnosis of infectious and parasitic diseases prevalent in the area (31–33).

The Latin American and Caribbean countries' present scientific and technologic capacity in the biomedical area suggests that within the diagnostic products sector this capacity may be the key to success of local entrepreneurial endeavors. Here the identification of strategic diagnostic products, directed toward specific priorities defined in health policies, will be of fundamental importance. Since the area's primary deficiency involves the marketing phase, the strategic associations that are eventually established with companies in the United States, Europe, and Japan will set the stage for overcoming this obstacle. Such associations may also spur the introduction of international quality control and safety standards, compatible to a large extent with those of the United States Food and Drug Administration, in the search for competitive advantage.

## **Vaccines**

According to PAHO (24), Mexico is the only country in the region with the industrial production capacity to meet the demands of the EPI, being currently able to satisfy 60% of total national requirements. Various South American countries have commercial vaccine production capacity,

but less than 50% of their requirements are satisfied by this capacity; while in Central America and the Caribbean, with the exception of Cuba, industrial production of vaccines simply does not exist.

PAHO's data also indicate that the availability of high-quality vaccines is limited and that those vaccines produced locally are more expensive than those imported. In 1989, supplies of viral vaccines for the EPI were produced in only two Latin American countries, Brazil and Mexico. And although both countries produce measles vaccine, only Mexico produces oral polio vaccine, while Brazil packages polio vaccines imported in bulk from Europe.

There is a generally unsubstantiated but frequently stated notion that the money needed to bring a single vaccine to market can be as high as US\$ 200 million. Because the financial returns on vaccine development investments tend to be poor, major private manufacturers have shown little interest in developing vaccines, especially ones directed against diseases that strike the populations of poor countries—diseases such as yellow fever, malaria, shigellosis, salmonellosis, leishmaniasis, dengue, Chagas disease, and others. The new biotechnologic tools therefore offer promising potential for obtaining new and better vaccines against infectious and parasitic diseases.

In addition to the research being conducted on vaccines for AIDS, herpes, malaria, rheumatoid arthritis, cancer, and lupus (34), vaccines for a number of other diseases are currently on the horizon in various developed countries, especially the United States. These diseases include chicken pox; rotavirus disease; shigellosis; cholera; diseases caused by certain types of *Escherichia coli*; otitis media; infectious respiratory diseases, both acute and chronic, such as pneumoniae caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* type B (Hib); parainfluenza; and disease caused by respiratory syncytial virus (35). One should also note efforts being made at

the international level to develop combined vaccines for diphtheria, tetanus, whooping cough, disease caused by *Haemophilus influenzae* type B, hepatitis B, and polio.

Supplementing these efforts are initiatives directed at improving the currently available polio and measles vaccines, which constitute critically important goals for developing countries, and the research now being conducted in South America on a combined Venezuelan leprosy vaccine (*Mycobacterium leprae* and live BCG), a Colombian malaria vaccine, and a Brazilian leishmaniasis vaccine (36).

All of the foregoing diseases are responsible for significant morbidity and mortality in Latin America and the Caribbean. Accordingly, from a regional standpoint, vaccines conferring effective protection against them would be highly desirable.

There is also an important policy issue in this sector, one that can be summed up by the following question: How can future new vaccines, of improved quality but expensive and technologically complex to manufacture (such as a possible HIV/AIDS vaccine), be made available to the people of poor countries? For Latin America and the Caribbean, the answer to this question is rooted in the quest for scientific and technologic training and for self-sufficiency in vaccine production. This is an important reason why efforts are being made to ensure greater regional competitiveness in this sector by increasing current levels of productivity and quality.

## CONCLUSIONS

To sum up, current Latin American and Caribbean participation in the therapeutic products sector is at best incipient and of uncertain potential. However, the region has a small strategic capacity for making diagnostic products, together with a tradition and vocation in the vaccine field that has been amply demonstrated by a number of major technologic advances.



This general picture, though incomplete, does not support the view of those who assume that the region's capacity for manufacturing certain essential health products and supplies is unimportant. On the contrary, it suggests that the region has the potential to play a small but significant role in health-related industrial biotechnology.

We know that in developed countries most health-related industrial biotechnology occurs in the private sector, being conducted by highly specialized small to medium-sized firms in combination with large corporations operating in the chemical-pharmaceuticals sector. This contrasts with the situation currently observed in Latin America and the Caribbean, where investment in R&D and manufacture of health-related biotechnology products is dominated by government agencies. This naturally leads one to ask whether the present international trend toward hegemony on the part of private industrial R&D will be forced upon our region.

This question has no ready answer. However, it seems likely that despite the current predominance of government involvement, the future composition of the government/private sector mix as well as the size of the private sector will depend on the availability of adequate budgets and on the timely introduction of well-articulated public policies emphasizing the need for ties between health policies on the one hand and scientific, technologic, and industrial policies on the other. Various specific strategic plans will also prove relevant, as will improvements in the legal framework—including those arising from various new regulatory challenges posed by modern biotechnology in the areas of bioethics, biosafety, and intellectual property. Within Latin America and the Caribbean, such improvements could have a decisive influence in adjusting the development of industrial biotechnology to countries' economic and social needs.

## REFERENCES

1. Blumenthal D, Gluck M, Louis KS, Wise D. Industrial support of university research in biotechnology. *Science* 1986;231:242–246.
2. Dembo D, Dias CJ, Morehouse W. The vital nexus in biotechnology: the relationship between research and production and its implications for Latin America. *Interciencia* 1986;14(4):168–180.
3. Goldstein DJ. Implications of biotechnology in the Third World. *J Sci Ind Res* 1991;50:423–440.
4. Marques MB. Cooperação entre empresas e instituições de pesquisa no MERCOSUL: potencial das técnicas de engenharia genética de aplicação diagnóstica em medicina. *Anais do IV Seminário Internacional e I Congresso Brasileiro de Transferência de Tecnologia*. Rio de Janeiro: World Federation of Engineering Organizations—WFEO and Federação Brasileira de Associações de Engenheiros—FEBRAE; 1992:281–290.
5. Marques MB. *Limites ao desenvolvimento científico e tecnológico em saúde pública no Brasil*. Rio de Janeiro: Fundação Oswaldo Cruz; 1989. (Série política de saúde, publicação 9).
6. Homma A, Di Fabio JL, Miranda DP, Oliva OFP. Producción de vacuna DPT en las Américas. *Bol Oficina Sanit Panam* 1995;118(1):24–40.
7. Marques MB, Gadelha CG, Emerick MC. *Biotecnologia em saúde no Brasil: limitações e perspectivas*. Rio de Janeiro: Fundação Oswaldo Cruz; 1987. (Série política de saúde, publicação 3).
8. Solleiro JL. Biotechnology for developing countries: the Mexican case. In: Edwardson W, Graham M. *Biotechnology in developing countries: research advances and applications*. Ottawa: International Development Research Centre, Environment and Natural Resources Division; 1994:55–79.
9. Banco Interamericano de Desarrollo. Tema especial: ciencia y tecnología. In: IDB. *Progreso económico y social en América Latina: informe 1988*. Washington, DC: IDB; 1988. (Chapter 9).
10. Silva LC, Pino A, Miranda Z, Martínez V, Pérez C. Origen nacional de los artículos publicados o citados en el *Boletín de la OPS* de 1971 a 1990. *Bol Oficina Sanit Panam* 1994;116(4):331–337.
11. Martínez-Palomo A, Sepúlveda J. Biomed-

- cal research in Latin America: old and new challenges. In: Bloom BR, Cerami A. Biomedical science and the Third World: under the volcano. *Ann New York Acad Sci* 1989;569:36–44.
12. Pellegrini Filho A. La investigación en salud en cinco países de América Latina. *Bol Oficina Sanit Panam* 1993;114(2):142–157.
  13. Cordeiro H, Marques MB, Possas C, Buss PM. *Prioridades nacionais, pesquisa essencial e desenvolvimento em saúde*. Rio de Janeiro: Fundação Oswaldo Cruz; 1990. (Série política de saúde, publicação 10).
  14. Polanco X. *Naissance et développement de la science-monde: production et reproduction des communautés scientifiques en Europe et en Amérique Latine*. Paris: UNESCO, Conseil de l'Europe, Éditions La Découverte; 1990.
  15. Pellegrini Filho A. Análisis comparativo. In: Organización Panamericana de la Salud. *La investigación en salud en América Latina: estudio de países seleccionados*. Washington, DC: PAHO; 1993:137–163. (Scientific publication 543).
  16. Marques MB. *Ciência, tecnologia, saúde e desenvolvimento sustentado*. Rio de Janeiro: Fundação Oswaldo Cruz; 1991. (Série política de saúde, publicação 11).
  17. Orrego C. Opciones para un programa regional de biotecnología: informe para el Departamento de Asuntos Científicos y Tecnológicos de la Organización de los Estados Americanos (basado en una gira por siete países de América Latina). Berkeley, California: 1987. (Mimeographed).
  18. Correa CM. Políticas de desarrollo biotecnológico en América Latina. In: Jaffé W, Zaldívar ME. *Formulación de políticas para el desarrollo de la biotecnología en América Latina y el Caribe*. San José, Costa Rica: Instituto Interamericano de Cooperación para la Agricultura, Programa de Generación y Transferencia de Tecnología; 1992:123–146.
  19. Commandeur P. Latin America commences to "biotechnologize" its industry. *Biotechnol Dev Monit* 1993;(4):3–5.
  20. Costa Rica, Consejo Nacional para Investigaciones Científicas y Tecnológicas (CONICIT). *Bol Biotechnol* (San José, Costa Rica) 1993;10(2). (Special 10th anniversary issue).
  21. World Health Organization. *Tropical diseases: progress in international research, 1987–1988; ninth programme report of the United Nations Development Programme/World Bank/World Health Organization Special Programme for Research and Training in Tropical Diseases (TDR)*. Geneva: WHO; 1989.
  22. Godal T. The roles of the World Health Organization in tropical diseases research. In: Bloom BR, Cerami A. Biomedical science and the Third World: under the volcano. *Ann New York Acad Sci* 1989;569:318–324.
  23. Organización Panamericana de la Salud. Vigésimo-sexta Reunión del Comité Asesor de Investigaciones en Salud. Rio de Janeiro: OPS; August 1987. (Document OPS/CAIS/26/87.1–13).
  24. Organización Panamericana de la Salud. *Las condiciones de salud en las Américas* (volume 1). Washington, DC: OPS; 1990:303–304. (Publicación científica 524).
  25. Marques MB. *Patenting life: foundations of the Brazil-United States controversy*. Rio de Janeiro: Oswaldo Cruz Foundation; 1992. (Série política de saúde, publicação 13).
  26. Robinson C. Biotechnology in Cuba: tackling Third-World problems with front-line technology. *TIBTECH* 1993;11:80–84. (Meeting report).
  27. Arriete LFM. Biotecnología en Cuba como una ventana de oportunidad. *Interciencia* 1993;18(6):295–299.
  28. Gottlieb O, Kaplan MA. Das plantas medicinais aos fármacos naturais. *Ciênc Hoje* 1993;15(89):51–54.
  29. Quintero R. Brasil está fora do mercado de medicamentos. *Gazeta Mercantil*. Rio de Janeiro, Brazil: 1991.
  30. Correa CM. The pharmaceutical industry and biotechnology: opportunities and constraints for developing countries. *World Competition* 1991;15(2):43–63.
  31. Marques MB, Possas CA, Gadelha CAG, Emerick MC, Bortoletto ME. Oferta tecnológica para o desenvolvimento em saúde: o caso da FIOCRUZ. *Cad Saúde Pública* 1988;1(4):9–32.
  32. Programa das Nações Unidas para o Desenvolvimento, Bio-Rio. *La biotecnología industrial en América Latina y el Caribe*. Rio de Janeiro: Bernardo Sorj (org); 1990.
  33. Schatzmayr HG, Marques MB. Industrial biotechnology in public health: perspectives for Latin America and the Caribbean. *Interciencia* 1994;19(1):7–13.
  34. Cohen J. Childhood vaccines: the R&D factor. *Science* 1993;259:1528–1529.

35. Robbins A, Freeman P. Obstacles to developing vaccines for the Third World. *Sci Amer* 1988;90-95.
36. Bloom BR, Jacobs WE jr. New strategies for leprosy and tuberculosis and for development of Bacillus Calmette-Guérin into a multivaccine vehicle. In: Bloom BR, Cerami A. Biomedical science and the Third World:

under the volcano. *Ann New York Acad Sci* 1989;569:155-173.

Manuscript submitted on 8 December 1994. Accepted for publication in the *Boletín de la Oficina Sanitaria Panamericana* (following revision) on 18 July 1995. Accepted for publication in the *Bulletin of the Pan American Health Organization* on 28 July 1995.



## *Maternal Mortality Estimates*

A major new study carried out by WHO and UNICEF indicates that maternal mortality has been substantially underestimated for some areas of the world. About 99% of pregnancy-related deaths occur in developing countries.

Maternal mortality is a particularly sensitive indicator of inequity among countries and regions and offers a litmus test of the status of women, their access to health care, and the adequacy of the health care system in responding to their needs. However, maternal mortality is extremely difficult to assess at the national level, since few civil registration systems systematically note pregnancy status on the death form. The new estimates were developed with a methodology that involved adjusting the available data for underreporting and using a simple model to generate estimates where reliable data were lacking.

The new figures represent a revision of the previously issued estimates for 1990, not changes over time. The estimates increased considerably for Africa and to a lesser extent for Asia. In the Americas, the estimates showed a slight decline in all subregions except the Caribbean. The tremendous disparity between developed and developing countries is illustrated by the rates for this Region: the new 1990 estimate of the maternal death rate in Latin America and the Caribbean is 190 per 100 000 live births, while the figure for North America is 11 per 100 000.

The new estimates should be taken as indicative of orders of magnitude rather than precise figures. They should be used as a guide for action—the most fundamental one being expansion of access to quality care for all women during pregnancy and childbirth.

Source: World Health Organization. New estimates of maternal mortality, part I. *Wkly Epidemiol Rec* 1996;71(13):97-100.