



**Pan American  
Health  
Organization**



*Regional Office of the  
World Health Organization*

**Technical Series No. 1  
Essential Medicines, Access, and Innovation**

# **Access to High-Cost Medicines in the Americas: Situation, Challenges and Perspectives**

Pan American Health Organization

**Area of Technology, Health Care and Research,  
Essential Medicines and Biologicals Unit (THR/EM)**

525 Twenty-third Street, N.W., Washington, D.C., 20037

September, 2010

**Edición original en español**

“El acceso a los medicamentos de alto costo en las Américas:  
contexto, desafíos y perspectivas”

Serie Técnica No. 1

© Organización Panamericana de la Salud

ISBN 978-92-75-33038-8

*PAHO HQ Library Cataloguing-in-Publication*

Pan American Health Organization

Technology, Health Care and Research Area,

Essential Medicines and Biologicals (THR/EM)

Access to High-Cost Medicines in the Americas: Situation, Challenges and Perspectives

Washington, D.C.: PAHO © 2010

(Technical Series No. 1 - Essential Medicine, Access, and Innovation)

ISBN: 978-92-75-13038-4

I. Title    II. (Series)

1. DRUGS COSTS – standards
2. NATIONAL DRUG POLICY
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4. PHARMACEUTICAL TRADE
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NLM W 74.DA1

Proofreading and Layout of texts:  
Clara Inés Rodríguez

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# ACRONYMS

|            |   |
|------------|---|
| ANVISA     | Brazilian Sanitary Surveillance Agency  |
| ARVs       | Antiretroviral medicines  |
| AUGE       | Chilean Universal Program of Explicit Guarantees in Health                                |
| BNDES      | Brazilian Development Bank  |
| CCSS/Caja  | Costa Rican Social Security Fund  |
| CENABAST   | Chilean Supply Center for the Ministry of Health  |
| CITEC      | Brazilian Commission for the Incorporation of New Technologies                            |
| CIPIH      | WHO Commission on Intellectual Property Rights, Innovation and Public Health              |
| DIGEMID    | Peruvian Bureau of Medicines, Medical Supplies, and Drugs                                 |
| GSPA       | Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property |
| IGWG       | Intergovernmental Working Group on Public Health, Innovation and Intellectual Property    |
| INN        | International Nonproprietary Names for Pharmaceutical Substances                          |
| IP         | Intellectual property   |
| NICE       | U.K. National Institute for Health and Clinical Excellence                                |
| MDGs       | Millennium Development Goals  |
| ORAS-CONHU | Andean Regional Health Organization /Hipólito Unánue Agreement                            |
| PAHO       | Pan American Health Organization  |
| PANDRH     | Pan American Network for Drug Regulatory Harmonization                                    |
| PROFARMA   | Support Program for Development of the Medical-Industrial Complex (Brazil)                |
| QALYs      | Quality-adjusted life years   |
| R&D        | Research and development  |
| PCDT       | Brazilian Clinical Protocols and Therapeutic Guidelines                                   |
| SGCAN      | General Secretariat of the Andean Community   |
| ST&I       | Science, Technology and Innovation  |
| TRIPS      | Agreement on Trade-Related Aspects of Intellectual Property Rights (WTO)                  |
| UCAMAE     | Centralized Procurement Unit for Medicines and Related Supplies (Uruguay)                 |
| UN         | United Nations  |

|        |  |
|--------|--|
| UNAIDS | Joint United Nations Program on HIV/AIDS |
| UNDP   | United Nations Development Program       |
| WHO    | World Health Organization                |
| WTO    | World Trade Organization                 |

# ACKNOWLEDGEMENTS

This is a publication of the Pan American Health Organization, Regional Office of the World Health Organization (PAHO/WHO), Technology, Health Care and Research Area, Essential Medicines and Biologicals Unit (THR/EM).

This publication draws on the conclusions of the First International Meeting on Access to High-Cost and Limited-Source Medicines (November 2008), organized by the Pan American Health Organization (PAHO) and the Brazilian Ministries of Health and Foreign Relations, with the participation of delegations from Argentina, Barbados, Brazil, Bolivia, Colombia, Costa Rica, Chile, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Jamaica, Mexico, Panama, Paraguay, Peru, Suriname, and Uruguay.

PAHO would like to thank the meeting's Organizing Committee and members of the above-mentioned delegations for their contributions to this publication.

We wish to acknowledge the following expert contributions: Juliana Vallini of the Brazilian Ministry of Health; Joan Rovira and Jaime Espin of the Andalusian School of Public Health (EASP); Miguel Cortés of the IFARMA Foundation, Colombia; and Federico Tobar of Argentina.

This publication was prepared under the direction and supervision of professionals in the Essential Medicines and Biologicals Unit at PAHO, with contributions from Jaume Vidal (PAHO headquarters), José Luis Castro (PAHO Representative Office, Argentina), and Christophe Rerat (PAHO Representative Office, Brazil).

The final version of this publication was edited by James Fitzgerald, Coordinator of the Essential Medicines and Biologicals Unit at PAHO, and Jaime Espin at the Andalusian School of Public Health (EASP).



# Chapter 1:

## Introduction



Access to medicines is a core element of any pharmaceutical policy and one of the main priorities of public health policy. There are a number of challenges that we face in ensuring access to medicines including artificially low target levels of coverage, financially-strapped health care systems, limitations associated with medicine supply networks, and problems relating to access to health care services for a significant portion of the population. The situation is worse in the case of high-cost medicines, principally because of additional complexities associated with ensuring access to products that retain market exclusivity guaranteed under the patent system and granted as a means to stimulate pharmaceutical research and development. The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) provides a set of flexibilities to assist governments to improve access to innovative therapies. Innovation for purposes of developing new health care technologies must be part of a broader framework within intersectoral efforts to improve health and development.<sup>1</sup>

A key component of access to medicines is affordability. The price of a medicine should not account for such a high percentage of income that consumers are either unable to afford the medicine or they are forced to sacrifice other basic needs to acquire them. In the case of medicines covered by social security systems which are either free or subsidized for users, cost is still relevant as it poses a threat to the financial sustainability of the health care system as a whole.

Asymmetries in information combined with the absence of market transparency represent other major obstacles to ensuring access. These problems must be addressed if we are to create the necessary conditions to improve access to new technologies within national health care systems in a manner that is rational, consistent with the evidence-based needs of health care.

In view of the above, it is now more critical than ever that countries in the Region of the Americas understand the need to implement coherent pharmaceutical policies. Moreover, policy implementation should be accompanied with impact assessments to ensure effective performance, bearing in mind key aspects such as innovation and management of intellectual property rights. The use of the evidence-based approach constitutes an important element for the formulation of sustainable public policies. Some of the new challenges discussed in this document have long been the focus of discussions at the international level; for example, the evaluation of health technologies and price regulation. It is now the time to review lessons learned with a view to implementing effective pharmaceutical policies in the countries of the Region, taking into consideration the recent Report of the Commission on Intellectual Property Rights, Innovation and Public Health of the World Health Organization (WHO).

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<sup>1</sup> World Health Organization. *Public Health, Innovation and Intellectual Property Rights: Report of the Commission on Intellectual Property Rights, Innovation and Public Health*. Geneva: WHO; 2006.

This document includes four chapters and two annexes. **Chapter 1** provides information on background to the publication and its objectives. **Chapter 2** discusses the issue of access to high-cost, limited-source medicines from the public health perspective and within the framework of some WHO/PAHO initiatives. **Chapter 3** describes the challenges that high-cost medicines pose for the Region, while **Chapter 4** puts forward a series of strategies to help improve access to these medicines. With regard to the annexes included in this publication, **Annex I** provides background information on the First International Meeting on Access to High-Cost and Limited-Source Medicines, while **Annex II** summarizes some of the presentations given at that event.

## 1.1 BACKGROUND

This document draws on the conclusions of the First International Meeting on Access to High-Cost and Limited-Source Medicines (November 2008; hereinafter “the meeting”), organized by the Pan American Health Organization (PAHO) and the Brazilian Ministries of Health and Foreign Relations, with the participation of delegations from Argentina, Barbados, Brazil, Bolivia, Colombia, Costa Rica, Chile, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Jamaica, Mexico, Panama, Paraguay, Peru, Suriname, and Uruguay.

In part, the meeting was organized to reflect on the Region’s experience in joint antiretroviral (ARV) price negotiations involving high-cost and/or limited-source products (for a brief history of these negotiations see Annex I), but also taking into account the significant costs associated with the proliferation and adoption of other new health care technologies in the Region which threaten the sustainability of public health care services. The meeting was also organized in response to the opportunity presented by the *Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property* (GSPA), adopted by the World Health Assembly in May 2008, through Resolution WHA61.21, whose implementation in the Region of the Americas is addressed in PAHO Directing Council Resolution No. CD48.R15 (**Box 1**).

In response to the specific challenges in the Region regarding access to high-cost and limited-source medicines, the meeting addressed: the importance of health technology innovation and evaluation as a determining factor in processes for the selection of new innovative and highly-complex medicines; the management of intellectual property rights within a context of respect for and promotion of public health; and the analysis of current options available for improving access to high-cost medicines. Some of the options put forward included the regulation and/or negotiation of medicine prices, as well as innovative methods of medicine financing, procurement, and manufacturing. As an outcome of the debate at the meeting, a set of recommendations were drafted with priorities set to guide the design, development, and implementation of government

strategies and policies to increase access to high-cost medicines within the framework of the implementation of the GSPA in the Region.

### **Box 1: Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property**

The Region of the Americas supported the process leading to the approval of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (WHA61.21) and the adoption of the regional perspective for the Americas within the framework of PAHO CD48.R15, which resulted from a number of preparatory meetings at the subregional level, including those held in La Paz, Rio de Janeiro, and Paramaribo, organized by the respective national authorities together with PAHO technical support. In addition, one regional-level preparatory meeting was held in Ottawa, cosponsored by PAHO and Health Canada.

In order to implement the GSPA, it is important to consider orientations presented in each of its eight chapters:

1. Prioritizing research and development needs;
2. Promoting research and development;
3. Building and improving innovative capacity;
4. Transfer of technology;
5. Application and management of intellectual property to contribute to innovation and promote public health;
6. Improving delivery and access;
7. Promoting sustainable financing mechanisms; and
8. Establishing monitoring and reporting systems.

Efforts are needed to adapt the Global Strategy to social and health conditions in the Region. In view of the Region's limited health research and development capacity, especially with respect to medicines, this will be no small task. Moreover, new regional tools and mechanisms are needed in the short and medium term to support health research and develop new health technologies based on a platform of equitable access.

## 1.2 OBJECTIVES

In view of the above, the objectives of this document are:

- To describe problems associated with high-cost and limited-source medicines and examine their underlying factors, especially incentives for innovation and the absence of competition in the pharmaceutical market; and
- To identify policies and strategies for promoting access to medicines, ensuring the conditions for developing innovative medicines for the countries of the Region within the context of the regional perspective of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property.

## Chapter 2:

# High-Cost and Limited-Source Medicines and the Public Policy Agenda



## 2.1 THE PROBLEM OF ACCESS TO HIGH-COST AND LIMITED-SOURCE MEDICINES IN LATIN AMERICA AND THE CARIBBEAN

The possibility—or impossibility—of ensuring access to a medicine is one of the most tangible indicators of disparities and inequities that may exist between countries of the Region, and among populations segments within the countries. The financial determinants of access to medicines, including the price of a medicine and its impact on household budgets and the financing of the health care system is becoming of considerable importance in the Region.

There are a number of barriers to ensuring access to medicines including:

1. **Problems of research and development.** Oftentimes there is a lack of pharmaceutical research and development to address the prevalent diseases affecting a given country or the Region as a whole, as is the case with several of the tropical diseases. Generally speaking, products are not being developed due to scant financial motivation or interest on the part of the pharmaceutical industry, and because governments of the Region provide little in the way of incentives for such research.
2. **Problems of availability.** Although a particular medicine has been developed and subjected to clinical trials to ensure its safety, quality, and efficacy, it may not be supplied to a country in sufficient quantities. In some instances, pharmaceutical manufacturers will remove products and/or discontinue sales in a given market over concerns that it may not be economically beneficial as a consequence of lower prices that greatly reduce profit margins. On the opposite end of the spectrum, some medicines are sold at very high prices. In this situation, the local supply of the product is affected because the product is unaffordable to the point that there is insufficient demand to make it an attractive market for producers and/or importers.
3. **Health care services limitations.** It can be argued that the same barriers hindering access to medicines also prevent access to health services. Geographic barriers may exist, that exclude people who happen to live too far from a health care center and/or a government-operated or retail pharmacy outlet. Secondly, cultural barriers come into play when the health care delivery model collides with the cultural traditions and belief system of users. Lastly, coverage and legal barriers arise when health protection systems lack sufficient resources to meet the health care needs of the target population or indeed do not include certain benefits within their basket of available services.

4. **Supply system limitations.** The ability to provide medical supplies is a core function of health systems. This work is performed by a subsystem of the health care system itself. Even under the best scenario of accessible and appropriate health care services, an effective system for pharmaceutical management must be implemented to support these services. This entails a full cycle of operations, beginning with medicine selection, procurement, warehousing, logistics and distribution, and finally, delivery to end-users—requiring a prescription for the medicine and a pharmacy to fill the order before medicines can be used by patients.
5. **Affordability limitations.** Affordability is one of the main barriers of access to medicines. This situation occurs when there is an imbalance between the available resources to fund medicines and the total cost of the medicine.

In the case of high-cost medicines the problems of access are compounded. While there is no one definition to fit every case, the characteristics of these medicines are determined by a variety of factors. In most cases, these medicines are the only treatment option for diseases with a profound social impact and/or a high risk of mortality (e.g., HIV/AIDS, certain cancers) or those used to treat conditions affecting only a minute portion of the population, such as the so-called “orphan” medicinal products for extremely rare diseases. Purchasing these medicines represents a significant financial burden for public health care systems and/or out-of-pocket expenditures of individuals and families.

Some countries in the Region have taken steps toward developing a conceptual definition of these medicines, primarily through qualitative indicators; such as medicines for diseases with a high risk of mortality; or quantitative indicators; such as establishing a fixed amount for each patient per year or treatment. Other expressions commonly used to refer to these types of medicines include “highly complex medicines”, which are often associated with those administering complex and costly therapies, such as those requiring frequent patient monitoring or that have to be administered under very specific conditions; and, “limited-source” medicines, a term which emphasizes partial market exclusivity and hence, high cost.

The notion of a “catastrophic disease” reflects a serious medical condition with associated high costs, in terms of drug therapy and health care services required, demanding significant financial resources on the part of those affected; whether for the individual who must pay out-of-pocket or for the public system when the cost of treatment is covered by public funding. For lack of a universal definition, all these elements—cost, exclusivity, novelty, and type of disease—converge to form the characteristics of these types of medicines, leading to serious challenges in access and for the sustainability of the health system.

## 2.2 PUBLIC HEALTH, INNOVATION AND INTELLECTUAL PROPERTY

For the most part, improving the efficacy of existing medicines and developing new pharmaceutical products for treating diseases for which no treatment currently exists depends on successful innovation programs. Policies aimed at encouraging innovation must be based on a clear, transparent, and operational definition of what is understood as “innovation” in the health care context. In addition to the inherent difficulty in defining the concept of innovation, there are already a number of different viewpoints on the subject, some of them complementary and others contradictory. Innovation is often looked on as “added value” in the context of new knowledge or a new product, although there is no consensus regarding how to measure or evaluate this value. In some cases, it is associated with the creation of business opportunities; the economic development derived from the competitive advantage the innovation in question makes possible. From a public health standpoint, innovation is associated with therapeutic benefits (e.g., health situation is improved over existing treatments) and/or economic benefits (e.g., lower cost treatments) emphasizing the idea of innovation as a social necessity or in service to health needs, as opposed to innovation seen solely for its ability to generate financial benefit. The scientific evidence derived through evaluation of health care technologies points to a real lack of therapeutic innovation for many of the medicines marketed in recent years, medicines which may technically constitute new chemical entities for pharmaceutical use but have no improved therapeutic benefits whatsoever (also known as *me-too* medicines<sup>2</sup>), although they do tend to have a considerably higher price tag. Data shared by a representative of Brazil’s medicine regulatory authority at the meeting revealed that of the medicines submitted for therapeutic evaluation, 80% were classified as “category II” or medicines offering no additional therapeutic benefits. In fact, the data suggest that some 70% of medicines offered in the global pharmaceutical market are *me-too* products, non-essential, or minor variations of an original pharmaceutical. It is therefore crucial, especially with regard to public regulation and financing, to define innovation in terms of a medicine’s therapeutic contribution and to make public financing contingent on this contribution.

The current situation of innovation and high-cost medicines is largely determined by the existing model used to promote research and development (R&D), where the market or “sufficient demand” sets the priorities. The success of this model relies heavily on market exclusivity associated with intellectual property rights awarded to the patent holder.

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<sup>2</sup> *Me-too* medicines are new chemical entities developed for pharmaceutical use that do not include any genuine therapeutic improvement. In: CORREA, Carlos María. “Ownership of knowledge: the role of patents in pharmaceutical R&D.” *Bull World Health Organ* [online]. 2004, v. 82, n. 10, p. 785. <http://www.scielosp.org/pdf/bwho/v82n10/v82n10a15.pdf>

The developments that took place, both at the global and national levels, following the debate and approval of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), and the inclusion for the first time on a global scale of products and pharmaceutical processes within the intellectual property protection regime, ushered in significant changes for pharmaceutical research, production, and marketing. Concern over the eventual impact of these events on access to essential medicines prompted renewed reflection on the part of all involved stakeholders—government, the private sector, academia, industry, and the scientific community—regarding the need to reconcile the interests of those conducting the research (eventual patent holders) and the needs of populations in developing countries in ensuring access to medicines developed through such research. The adoption by the United Nations of the Millennium Development Goals (MDGs)<sup>3</sup> in September 2000, and specifically the approval of the Doha Declaration on the TRIPS Agreement and Public Health<sup>4</sup> within the framework of the World Trade Organization (WTO) in November 2001, represent decisive points in this debate which, fueled by the impact of pandemics and inaccessibility to treatments, pit the needs of public health against the protection of intellectual property rights.<sup>5</sup>

Eager to address the innovation problem, WHO, with the support of its Member States, established the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) to study the situation relating to access to medicines, taking into account intellectual property protection requirements and current mechanisms for promoting innovation. The Commission reviewed the market-based R&D system from the perspective of health promotion and protection. The crux of the problem was identified: how do we go about encouraging innovation in the pharmaceutical sector while addressing the pressing need of ensuring access to medicines? Various factors were considered in the analysis, such as gaps in research on diseases that disproportionately affect the developing world (also known as “neglected diseases”), funding challenges for the sustainable development of medicines beyond merely any potential commercial returns or benefits, as well as traditional barriers of access to medicines (e.g., shortcomings of public health care systems,

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<sup>3</sup> The MDGs establish in Target 17 the need to provide access to affordable essential medicines in developing countries.

<sup>4</sup> Some countries have enacted “TRIPS-plus” legislation, which include additional measures such as extended protection periods for patents, exclusivity, test data, and a linkage between patent status and the concession of sanitary registration, among others.

<sup>5</sup> Pan American Health Organization. Report of the Working Group. *Trade Related Aspects of Intellectual Property Rights (TRIPS) and Access to Medicines: Focusing the Analysis in the Americas*. Managua, Nicaragua, 14-16 April 2004. [http://www.paho.org/english/ad/fch/ai/Trade\\_related\\_intellect\\_property\\_rights\(TRIPS\).pdf](http://www.paho.org/english/ad/fch/ai/Trade_related_intellect_property_rights(TRIPS).pdf) and

Pan American Health Organization. Report of the Working Group 2005. *Trade Related Aspects of Intellectual Property Rights (TRIPS) and Access to Medicines*. Santo Domingo, Dominican Republic, 4-6 April 2005. [http://www.paho.org/Spanish/AD/FCH/AI/Derechos\\_de\\_propiedad\\_intelectual\\_\(ADPIC\).pdf](http://www.paho.org/Spanish/AD/FCH/AI/Derechos_de_propiedad_intelectual_(ADPIC).pdf) AD/FCH/AI/

deficient distribution mechanisms, and the inherent difficulties in adapting treatments and product formulations for vulnerable groups).

The conclusions of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH) emphasized, inter alia, the need to establish an intergovernmental working group on public health, innovation and intellectual property to debate, negotiate, and formulate a global strategy and action plan to establish the basic structure for implementing CIPRH<sup>6</sup> recommendations, based on international consensus. This work laid the foundations for the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) which formulated, between December 2006 and May 2008<sup>7</sup>, the Global Strategy and Action Plan on Public Health, Innovation and Property Rights set forth in Resolution WHA61.21.<sup>8</sup> It is important to note that the Region played a significant role throughout the debates leading up to the adoption of the Global Strategy and Action Plan, and proved its effectiveness as a regional bloc in implementing the activities approved through Resolution WHA61.21 as well as Resolution CD48.R15 (which mandates PAHO to implement the Global Strategy in the Americas, in coordination with WHO).

Introducing new models for innovation, for instance national/international public financing of research or compensating innovation by means other than the patent system, such as prizes and other compensation systems,<sup>10</sup> may help improve access to medicines with respect to the current system of pharmaceutical innovation. Nevertheless, it is difficult to promote efficient research since it is impossible to determine beforehand the probability of success of a particular research project, or the costs and benefits of future innovations. One way to promote more efficient innovation is to establish a mix of public-private systems that would award a non-refundable fixed amount of compensation to a research entity upon selection of research projects, while the remainder would be contingent on fulfilling specific objectives. Accordingly, the evaluation of health technologies

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<sup>6</sup> World Health Organization. *Public Health Innovation, and Intellectual Property Rights: Report of the Commission on Intellectual Property Rights, Innovation and Public Health*. Geneva: WHO; 2006. <http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf>

<sup>7</sup> Relevant working sessions and background documents available at: <http://www.who.int/phi/documents/en/index.html>

<sup>8</sup> WHA61.21 Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property [http://apps.who.int/gb/ebwha/pdf\\_files/A61/A61\\_R21-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/A61/A61_R21-en.pdf)

<sup>9</sup> Of note in this regard was the approval of a draft subregional consensus document among a significant number of member countries, which, under the name Rio Document made a considerable contribution to clarifying the concerns and primary demands of the Region. In: [http://www.who.int/phi/public\\_hearings/second/regional\\_consultations/Sub-regional\\_Consensus\\_Document.pdf](http://www.who.int/phi/public_hearings/second/regional_consultations/Sub-regional_Consensus_Document.pdf)

<sup>10</sup> For examples of current financing systems, see the Report of the Commission on Intellectual Property Rights, Innovation and Public Health. WHO/CIPRH/2006/1. Op. cit. p.88. In: <http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf>

to promote the desired type of innovation could be applied in the research financing stage of the project, tying funding to specific objectives or diseases.

### **Box 2: PAHO/WHO Resolutions on Access to Essential Medicines, Innovation, and Intellectual Property**

- 2002** WHA55.14 on ensuring accessibility of essential medicines;
- 2003** WHA56.27 on intellectual property rights, innovation and public health;
- 2006** WHA59.24 on public health, innovation, essential health research, and intellectual property rights: towards a global strategy and plan of action;
- 2007** WHA60.30 on public health, innovation, and intellectual property;
- 2008** WHA61.21 on a global strategy and plan of action on public health, innovation, and intellectual property;
- 2004** CD45.R7 on access to medicines;
- 2004** CD45.R10 on scaling-up of treatment within a comprehensive response to HIV/AIDS;
- 2005** CD46.R15 on the PAHO Regional Strategic Plan for HIV/AIDS/STI, 2006-2015;
- 2006** CD47.R7 on public health, health research, production and access to essential medicines;
- 2008** CE142/INF/4 Intergovernmental Working Group on Public Health, Innovation and Intellectual Property: Current Status;
- 2008** CD48.R15 on public health, innovation, and intellectual property: a regional perspective.

## **2.3 STAKEHOLDERS AND RESPONSIBILITIES**

The various stakeholders are addressing the challenges of access to high-cost medicines from a variety of perspectives. Governments concerned over burgeoning expenditures for pharmaceuticals and the sustainability of the public health system, must develop strategic action plans to help them prepare for this new reality. Such plans must be based on health care needs, scientific evidence, expenditure and budgetary impact assessments. Some strategies to follow might include negotiations with the pharmaceutical industry on priorities for financing, awareness-raising campaigns and independent assessments among health care professionals and civil society groups regarding the therapeutic contribution of new medicines, and selective financing based on innovation and therapeutic added value.

In this regard, the pharmaceutical industry must become part of the solution to access instead of being part of the problem. Its interests in obtaining commercial benefits are compatible with the social objectives of innovation and access, and consequently, it has no reason to oppose

these objectives. The pharmaceutical industry has an important role to play and an undeniable responsibility to promote access to the products it develops and markets. However, its interest in maximizing benefits and profits cannot undermine its social responsibility within the public health promotion framework at the domestic and international levels. The establishment of tools such as closed-end pharmaceutical budgets (with refunds), where there is a fixed maximum contribution paid from public coffers with the rest being absorbed, either partially or completely, by the industry; or risk-sharing agreements, through which government and the industry agree on the compensation details of specific high-cost medicines subject to different variables (effectiveness, sales volume, and health outcomes for example), are all new mechanisms that underscore the unquestionable need for government and industry to negotiate and reach an understanding.

Health care professionals also play a key role in the dilemma of high-cost medicines, as the principal guarantors of tools for rational medicine use. Any lack of transparency or knowledge regarding issues such as medicine prices erodes their role as guarantors of rational medicine use. Consequently, tools such as evidence-based medicine, efficiency criteria, and knowledge of medicine prices must be applied in clinical and therapeutic decision-making.

In light of this situation, citizens also play a key role in the rational use of medicines and must therefore be aware of the related challenges facing health systems. Tools used to regulate demand in which citizens play a part, such as the different types of co-payments and educational and awareness-raising campaigns are essential to successfully addressing these challenges. Moreover, the increased visibility of the different types of civil society participation in this regard can help identify possible solutions, by promoting regulations and public policies to facilitate better conditions of access.



## **Chapter 3:**

# **Challenges in the Region of the Americas**



### 3.1 MOVING FORWARD THE AGENDA: FROM ACCESS OR INNOVATION TO ACCESS AND INNOVATION

Traditionally, pharmaceutical policies in the Region have been designed to ensure access to quality medicines that are used rationally within a cost containment framework, for example, through incentives geared toward the production and use of generic medicines. The most frequently used tools at the national level within the policy framework have been the development/updating of lists of essential medicines,<sup>11</sup> the promotion of the use of generic medicines, and the establishment of price control mechanisms. Nevertheless, the limited success achieved with regard to pharmaceutical policy objectives remains a cause for concern; for instance, the disappointing extent to which generic medicines are prescribed in the countries of the Region, such as Brazil where “generic medicines represent 14% of medicine revenues and 16% of total sales.<sup>12</sup>”

Over the last 20 years, circumstances have changed in the Region requiring adjustments in the implementation of pharmaceutical policies and, in some cases, changes in the objectives of such policies. For example, the rate of pharmaceutical innovation has declined worldwide; fewer new chemical entities have been developed and the relative therapeutic benefit of new medicines has been less significant than in years past, despite increased R&D investment. Also notable over this period has been the increased cost of newer medicines with detrimental consequences for financing of the public health system and the ability of the public and private sector alike to purchase such products. Against this backdrop, globalization continues within world markets and with it a de facto harmonization of intellectual property protection measures, resulting in patents of 15 to 20 years which can impact access to medicines. Demand is increasing from society for universal coverage and access to health care services, and with it political willingness on the part of a growing number of developing countries to promote biomedical and pharmaceutical innovation.

Due to the combination of the above-mentioned factors, many of the traditional policies and strategies implemented to regulate the financial aspects of pharmaceuticals have either lost their original effectiveness or seen it seriously diminish. We therefore must evaluate the impact of these policies in light of current circumstances and, once such evaluation is complete, either modify or substitute such policies and strategies if we are to ensure access and innovation in health demanded by our societies.

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<sup>11</sup> A summary of trends in pharmaceutical policies in the Region of the Americas and an analysis of specific cases at the country level can be found in the Spanish-language publication “Essential Medicines in the Region of the Americas: Accomplishments, Difficulties and Challenges” [Los Medicamentos Esenciales en la Región de las Américas: logros, dificultades y retos]. Edited by PAHO in 2007 and available at: <http://www.paho.org/spanish/ad/ths/ev/DocTecnico-Meds%20Esencs%20en%20laRegi%C3%B3n-2007.pdf>

<sup>12</sup> See “Access to High-Cost Medicines,” by Odete Gialdi in Annex II hereof.

## 3.2 COORDINATION AMONG THE HEALTH, SCIENCE AND TECHNOLOGY, AND PHARMACEUTICAL INDUSTRY SECTORS

In terms of public policy objectives, medicines are not simply of importance within the health field: pharmaceutical products, as industrially-produced commercial goods, also represent opportunities for the design of economic development and growth strategies. Moreover, the pharmaceutical market is a driving force behind innovation, which both generates and requires the use of knowledge and information. These three dimensions—industrial policy, science and technology policy, and health policy—represent the three strategic pillars which must be considered in the formulation of pharmaceutical policy at the national and regional levels.

In order to address newer determinants and factors affecting access and innovation within the public policy agenda, we must develop integrated strategies that consider the relationship and interdependence among access, industrial development, and innovation, which also includes access to innovation. In this regard it is important to engage, through dialogue and coordination, the pertinent stakeholders with decision-making authority in all arenas, both public and private: health systems professionals and managers, the pharmaceutical industry, intellectual property institutions, regulatory authorities, and other government agencies, academia, lawmakers, the courts, and civil society.

Some countries provide alternatives for promoting access to innovative and strategic medicines. For countries at the forefront of health research (e.g., the United States, the United Kingdom, Canada, and France) access is promoted through coordination among the government agencies responsible for sectoral policy, with the support of academic institutions<sup>13</sup> that view research as essential to their own development and prestige. The National Institutes of Health (NIH) of the United States is one such example. NIH is supported by significant public investment for basic health research, sometimes in collaboration with the private sector. Several countries of the Region are beginning to enter this field; for instance, Cuba has created a network of inter-related scientific institutions.<sup>14</sup>

Nonetheless, it should be noted that government agencies responsible for formulating policy for the sector are not yet involved to the degree necessary to influence the priorities for innovative research. However, some countries with a well-established industrial base are able to set priorities in a coordinated and integrated manner, consistent with real domestic and/or regional needs, instead of allowing priorities to be determined by external factors. The comparative advantages

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<sup>13</sup> According to the CIPIH, the University of California has the most DNA-related patents, followed by the United States Government, through the National Institutes of Health.

<sup>14</sup> See “The Cuban Experience in Pharmaceutical Innovation,” by Yera Alós in Annex II.

of a vertical science, technology and innovation model are inherent in that such a model makes it possible to balance the priorities of research with those of sectoral policy, thereby making it possible to mobilize new and more significant resources to promote research, development, and innovation.

### 3.3 THE MARKET AND THE RATIONAL USE OF MEDICINES

The inherent pressures associated with a wide variety of products being available in the pharmaceutical market means that countries must develop robust strategies and mechanisms to ensure independent decision-making in the selection and use of medicines in order to protect and promote health. Some of these strategies, which are well known and have been published in recommendations of official and academic documents, require a sustained political commitment, cooperation among involved stakeholders at the national level, as well as planning, monitoring, and the evaluation of results.

Since 1997, WHO, with technical support from a group of experts, has prepared and periodically updated a list of essential medicines. WHO recommends that countries adapt this list to their own specific health needs. By 1995, more than 120 countries had adopted national essential medicines lists. In the Region the concept has been effectively introduced in practically all countries.

In fact, whether or not a country has and periodically updates such lists of essential medicines is a key indicator of the rational use of medicines. Nonetheless the development of an essential medicines list lacks value in itself: it needs to be accompanied with a strategy to promote awareness, noting the participative approach in its development and its impact at the health service level. The implementation and management of criteria for developing an essential medicines list and dissemination of the concepts sustaining it should, like the list itself, be continually updated with the members of the health team. The task of developing an evidence-based strategy for selecting essential medicines is one that must take market considerations into account, but whose focus is first and foremost on the needs of priority diseases. This view stands in contrast to the belief promoted by the market—which holds sway not only among professionals but also society—that “newer and more expensive is better.”

There can be little doubt that in order to make headway in the rational use of medicines we must debate and arrive at a consensus regarding the key elements needed for revitalizing the undergraduate and post-graduate curricula of prescribers and pharmacists. As key actors within the health team, their education must be developed with a broader vision, with values and criteria that currently are either absent or insufficient, and by placing greater emphasis on the patient, his/her situation, and on problems such as the focus of care.

**Box 3: The Brazilian Experience: Science, Technology and Innovation Policy**

Recently, Brazil has made changes to its science, technology, and innovation policy (ST&I), including the creation of sectoral funds; the Innovation Act; the enactment of special tax incentives for innovation known as the “Good Law”; enactment of the regulations governing the National Fund for Scientific and Technological Development (FNDCT); and implementation of the PROFARMA I and II programs of the Brazilian Development Bank (BNDES). Consequently, a new health model is needed in Brazil—one that includes vertical programming, a sectoral focus, and emphasis on the promotion of technology and innovation. Examples of Brazilian successes based on this type of vertical model include the Brazilian Agricultural Research Corporation (EMBRAPA), the Brazilian Petroleum Corporation (PETROBAS), and the Ministry of Defense.

The Ministry of Health has implemented its own ST&I development model. This model views health as a right of citizenship, as well as a specialized field of development; one that is a source of income, investment, and employment; and a source of innovation and of strategic knowledge in the context of the “Third Technological Revolution.” The implementation of this model required some structural changes at the Ministry of Health to enable it to adapt to the development and modernization of the “medical-industrial complex.”

Between 2003 and 2006, the Secretariat of Science, Technology, and Strategic Supplies (SCTIE) was created. The SCTIE is composed of three departments: the Department of Pharmaceutical Assistance Services or “DAF,” with robust procurement power; the Department of Science and Technology or “DECIT,” which funds general science and basic research; and the Department of Health Economics or “DES.” In 2007, DES underwent a reorganization and was renamed the Department of the Medical-Industrial Complex and Innovation (DECIIS). In 2008, the Commission for the Incorporation of New Technologies (CITEC) was established, as was the Accelerated Growth Program (PAC), the Program to Support Scientific and Technological Development (PADCT), the Education Development Plan (PDE), and the “More Health” (*Mais Saúde*) and the Production Development Policy (PDP). In May 2008, efforts were made to integrate the work of the PAC in Science and Technology (PACC&T), the “More Health” program, and the PDP, resulting in broad institutional and political commitment within the sector to develop the medical-industrial complex. The objective is to reduce the medical-industrial-complex-related trade deficit from the current US\$ 5 billion to US\$ 4.4 billion by 2013, and to develop technology for local production of 20 strategic products for the Unified Health Care System (SUS) by 2013.

The challenges to address are: 1) to reduce the vulnerability of the National Health Policy; 2) to increase investment in innovation; 3) to increase and diversify exports; 4) to increase the density of the medical-industrial complex production chain and strengthen national businesses; 5) to strengthen, expand, and modernize management of the public pharmaceutical manufacturing network; and 6) to encourage high-tech companies from abroad to establish production and R&D centers in Brazil.

The tools needed to overcome these challenges include the use of government purchasing power to stimulate local production, funding to increase production capacity, expanding access to R&D resources in strategic areas, and the creation of support networks for technological and industrial development. All of these activities require the Ministry of Health to collaborate with other government agencies and the private sector. With a view to managing these objectives, the Executive Board of the Medical-Industrial Complex (CIS) was created in 2008 to promote specific measures and actions. The CIS strategic areas are as follows:

1. Ensure local production of blood derivatives (albumin and coagulation factors VIII and IX and globulins);
2. Develop vaccines for the National Immunization Program;
3. Produce health-related equipment and supplies in accordance with the National Health Policy;
4. Develop reagents and equipment used for blood monitoring based on modern biotechnologies;
5. Produce medicines and active ingredients; and
6. Produce biotechnology products for the health field.

To achieve these objectives, Brazil formed the Managing Committee of Cooperation Terms and Technical Assistance between the National Bank of Economic and Social Development and the Ministry of Health, which includes PROFARMA II (2008). The National Committee for Biotechnology and the Forum on Biotechnology Competitiveness (2007) were also created, promoting activities aimed at encouraging innovation within, and the strengthening of, the National Health System.

We must also promote the use of evidence combined with unbiased and independent information, and a critical assessment of the way medicines are marketed: the extent to which drug information is regulated is another variable that merits study. Perhaps what is needed is an approach that effectively emphasizes health; one that aims to strengthen the regulatory framework and in particular oversight, not only in marketing of medicines through the media but also in monitoring perverse incentives promoting the use of medicines. Access to independent information for decision-making is crucial in the field of health; consequently, such information is a critical component of any pharmaceutical strategy and policy at the country level.<sup>15</sup>

#### **Box 4: Essential Medicines: Costa Rican Social Security Fund<sup>16</sup>**

The Costa Rican Social Security Fund (CCSS/*Caja*) adopted the structure it considered appropriate for promoting and strengthening the national essential medicines policy, and also formulated two components that would simultaneously strengthen the rational use of medicines: the Scientific-Technical Component, comprising the selection, prescription, use, and education, administrated by the *Caja*'s Medical Management Division; and the Operative Component, comprising planning, budgeting, procurement, warehousing, quality assurance, and distribution of medicines, administered by the *Caja*'s Logistics Management Division.

These two components constantly share information to ensure that the population has access to the medicines when needed, and in the quantities required. According to the Medical Management Division, the selection of medicines is responsibility of the Office of Pharmacoepidemiology and the Central Committee on Medicine Therapy. The latter is made up of 13 physicians in specialized fields of medicine from national hospitals, as well as two pharmacists, whose primary objective is to ensure that all medicines are used rationally and made available to all segments of the population. The main criteria considered in the selection of medicines include the country's epidemiological profile, clinical/pharmacological criteria, and health system sustainability. A formulary system has been established, based on the ongoing evaluation and selection of medicines, for the purpose of updating the formulary, and to provide additional information in the development of the Official Medicines List.

With regard to medicine safety, pharmacovigilance systems are effective mechanisms for assessing behavior and evaluating use. However, such systems require a shift in focus toward a more selective—and perhaps more cost-effective—approach according to the priorities of specific therapeutic groups, including high-cost medicines or diseases.

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<sup>15</sup> Pan American Health Organization. "Essential Medicines in the Region of the Americas: Accomplishments, Difficulties and Challenges." Lima: PAHO; 2007. Page 18 available at: <http://www.paho.org/spanish/ad/ths/ev/DocTecnico-Meds%20Eseces%20en%20laRegi%C3%B3n-2007.pdf>

<sup>16</sup> For more information see "Medicine Selection Criteria and Treatment Protocol Development" by Albin Chavez in Annex II hereof.

Government regulation of the different processes, the role of formularies and treatment guidelines in determining financing, and systems promoting incentives for the rational use may play a decisive role in facilitating equity in access and rational medicine use. Governments play an important role in identifying which medicines are to be covered through collective financing mechanisms, both public and private. On the one hand, regulation can be used on the demand side when public funds are used to purchase only those medicines included on a given list and when health insurance providers, whether public or private, are required to purchase from such a list. Governments can therefore exert some degree of influence on the market by requiring institutions that provide financing to cover a specific set of medicines for each category of drug therapy. In other words, selection criteria are critical for guiding pharmaceutical coverage and financing.

A recent phenomenon associated with the issue of access to high-cost medicines has been the participation of the courts in deciding who should and should not receive such medicines: this has been dubbed the “judicialization of access”. In fact, the number of actions filed with the courts is on the rise as people unable to access medicines and drug therapies through regular channels of the health system turn to the courts. On the one hand, this strategy allows citizens to exercise their legal right to health as part of their basic human rights; on the other, systematic legal action may result in distortions of the system, jeopardizing the objectives of rational use and leading to inefficiencies in the use of limited health care resources. Moreover, such action may result in a set of judicially-valid and legally-binding decisions, yet unsustainable from the public expenditure standpoint. This is a national problem rooted in the constitutional interpretation of the right to health and access to medicines. In some cases decisions are not based on scientific evidence or cost-effectiveness criteria, putting the sustainability of health care systems at risk. It is important to differentiate those cases where a government is required to facilitate access to essential medicines in order to save lives and ensure human dignity, from those where a court requires a government to provide high-cost and patent protected medicines for a particular disease in the absence of evidence proving comparative therapeutic benefit. With respect to the latter category, it has been observed that outside actors, in furtherance of their own financial motives, become involved in advancing the demands of patients and family members.

## Chapter 4:

Strategies,  
Mechanisms and  
Tools for Promoting  
Access to High-  
Cost and Limited-  
Source Medicines



International guidelines on pharmaceutical policies establish the need to promote competition in the supply chain as an important strategy for improving access to medicines, and especially essential medicines.

However, pharmaceutical policies must increasingly distinguish between two different segments of the pharmaceutical market: medicines with market exclusivity achieved through patent protection; and their generic equivalents that become available once the patent protection period has expired. Differences in the degree of market exclusivity influence the types of policies, strategies, and instruments that are available to authorities in ensuring and regulating access. It is impossible to promote competition when there are no other suppliers in the marketplace or when products achieve monopoly through intellectual property rights protection. In other words, a policy framework that promotes competition cannot effectively address the problem of access to products that have a monopoly in the market. Therefore existing policies must be modified or combined with other types of policies and regulatory frameworks to ensure access under such conditions.

Generic medicine policies oftentimes include tax incentives to promote the manufacture and registration of competitor products, the use of comparative pricing data, and the strengthening of quality assurance norms in production. In addition, they promote the use of the International Nonproprietary Names for Pharmaceutical Substances (INN) at the various stages of marketing and, in particular, in prescribing; in information campaigns targeting physicians, consumers and/or pharmacists, with a view to improving acceptance of generics; and to encourage the filling of prescriptions with lower-cost generic medicines. Recently, the regulation of mandatory bioequivalence testing has also been considered as an important component of generic medicine policies.

In product markets where patent protection does not exist, it makes sense to pursue pro-competition strategies to promote access. Such strategies may include improved market transparency; the dissemination of objective information regarding efficacy, price and cost-effectiveness; and incentives for the rational prescribing of medicines on the basis of quality and cost. With respect to transparency and the dissemination of medicine pricing information, initiatives from the Region such as Brazil's Database for Health Purchases (BPS) can be used as a reference to raise awareness regarding the need to address information asymmetries in procurement of medicines.

A number of different strategies, mechanisms, and tools are available to promote and regulate access to high-cost and limited-source medicines (**Box 5**). However, it may not be possible to implement these tools with the same degree of ease in all countries of the Region since the context within each country varies depending on:

- relative size of the domestic pharmaceutical market;
- economical development, production capacity, and technological innovation;

- leadership capacity of health authorities and the development of competencies within regulatory agencies;
- degree of health system fragmentation;
- extent of health service centralization or decentralization and degree of regional autonomy in supplying medicines;
- levels of coverage and financing for those medicines for which access has been guaranteed for the population; and
- bilateral/multilateral cooperation and free trade agreements.

Each government needs to assess the national context, to identify those variables relevant to its particular circumstances with a view to determining its capacity to both carry out and sustain interventions, but most importantly to determine the potential impact that action might have on access to high-cost medicines for the population. Governments can then choose from among existing policy options and instruments that are most appropriate for its particular needs.

**Box 5: Summary of Strategies, Mechanisms and Instruments: High-Cost and Limited-Source Medicines**

1. Developing integrated policies to promote access and innovation;
2. Managing intellectual property to promote innovation and public health;
3. Evaluating innovation and incorporating new health technologies;
4. Promoting the selective financing of medicines;
5. Negotiating and regulating prices;
6. Managing public sector procurement;
7. Implementing the rational use of medicines; and
8. Developing tools for intervention.

## **4.1 DEVELOPING INTEGRATED POLICIES TO PROMOTE ACCESS AND INNOVATION**

It is important to bear in mind that not all countries have the same potential in the development of pharmaceutical production and innovation capacity for health technologies. However, the countries of the Region can move to promote greater integration of their pharmaceutical, science and technology, and industrial development policies in order to promote access to and innovation in—by promoting and funding research and development, production, and/or procurement—

those pharmaceutical products and health technologies required for the delivery of health care services.<sup>17</sup>

The system of scientific and technological innovation covers a whole spectrum of activities: from the creation and accumulation of knowledge to the production of goods and services; from research, technological, scientific and technical services development to the transfer of technology, marketing, and the use of modern managerial techniques.<sup>18</sup> The priorities of pharmaceutical policy to promote access are shared with the interests of industrial development policy in the promotion of competition and the development of products that are more affordable, and with the priorities of science and technology policy in the promotion of advances in drug therapy. In contrast to innovation in other areas, innovation in the health field is unfortunately often the result of uncoordinated interactions between the public sector and industry. And, although the production of scientific knowledge includes a very significant public component, the pharmaceutical industry takes advantage of information in the public domain to produce goods for its own financial gain and, ironically, at a high cost for public health systems.

The recommended objectives for public policies designed to promote access and innovation include facilitating increased production capacity, encouraging investment in research and development, providing incentives for increasing the supply of products, addressing the health needs of the population through the development and production of medicines for priority diseases and ensuring access to products through price regulation in accordance with the purchasing power of consumers. While in the short term these policies may not have much of an impact on access, over time they provide solid foundations for ensuring sustainable access. Implementing these policies will require political commitment and coordination among the different ministries, at minimum the ministries of Science and Technology, Industry, and Public Health; the allocation of sufficient funding to promote research and development of products so as to ensure an adequate supply of strategic products identified by government; and the development of production capacity for generic medicines. Moreover, the successful implementation of these policies will require a commitment from private-sector stakeholders with efforts to encourage mixed public-private production approaches. (See **Box 6**.)

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<sup>17</sup> The innovation cycle known as the 3 Ds “Discovery, Development, and Delivery” reproduce the close relationship between the different stages of discovery, development, and access that characterize medicine production. See the Report of the CIPIH, p. 23.

<sup>18</sup> See “The Cuban Experience in Pharmaceutical Innovation,” by Yera Alós in Annex II.

### **Box 6: Implementing Integrated Policies to Promote Access and Innovation**

Some countries in the Region have begun to progressively formulate and implement policies for promoting access to, and the innovation of, medicines and health technologies. On the one hand, these policies are facilitated by providing incentives for R&D and, on the other, through coordinating industrial development incentives, both for the substitution of imports and promotion of exports. Some interesting experiences in this regard have been observed in the Region, including those in Brazil, Argentina, and Cuba.

In 2003, the Brazilian Development Bank (BNDES) launched its Support Program for Development of the Medical-Industrial Complex (PROFARMA) mentioned in Box 3, with a view to providing funding and support for investment initiatives of companies located in Brazil involved in all stages of pharmaceutical production, including pharmaceutical chemicals and medicines. PROFARMA's projected budget expenditures through 31 July 2012 are on the order of R\$3 billion (approximately US\$ 1.333 billion based on an exchange rate of 2.25 Brazilian *reais* per U.S. dollar).

Argentina enacted its Biotechnology Law, which includes incentives for the development of biopharmaceuticals. Argentina's Agency for the Promotion of Science and Technology established its Science and Technological Research Fund (FONCyT) and the Argentine Technology Fund (FONTAR), which makes funding available to encourage development in science, specific technical fields, and technological innovation, including pharmaceuticals. Beginning in 2009, the Argentine Ministry of Economy and Public Finance initiated a series of studies to guide implementation of its Program to Strengthen the Pharmaceutical Industry (PROFAR) which may include measures such as refunding export taxes, accelerated depreciation on income tax, early value-added tax (VAT) refunds on purchases of capital goods, as well as converting 50 percent of total employer contributions to social security into tax credit bonds.

Meanwhile, Cuba's work to establish a network of interrelated scientific and research institutions has helped strengthen that country's scientific capacity, facilitate bioscience development, and foster growth of a Cuban pharmaceutical industry. This type of institutional coordination is credited with speeding up the pace of innovation in health so that innovative technologies can reach the patients who need them in a timely manner.

## **4.2 MANAGING INTELLECTUAL PROPERTY TO PROMOTE INNOVATION AND PUBLIC HEALTH**

There are a number of different strategies that can be effectively used to promote access to products with market exclusivity through the management of intellectual property that seeks to encourage innovation and promote public health while taking into consideration the need to improve the quality of patents that are granted. For example, the inclusion of instruments within legal and regulatory frameworks, such as compulsory licensing (Article 31); exceptions to rights conferred (Article 30); other key flexibilities contained in the TRIPS Agreement which have been endorsed by the

Doha Declaration; and the implementation of pro-competition policies to prevent the potential for monopolistic abuses through the artificial prolongation of patent rights known as “evergreening.” These measures must be implemented with other interventions to improve the efficiency of public-sector spending on health through improvements in transparency and the dissemination of unbiased information on product efficacy, pricing, and regulatory processes, and through the provision of incentives to increase demand for generic medicines.

Many proposals have been put forward to improve the patent system, especially with regard to how such a system should be applied. Some suggest focusing on improving the quality of patents by increasing protection standards. This is normally in the interest of the applicant and rights holder over the interest of other parties, and oftentimes it results in an actual decrease in patent quality particularly with regard to evidence requirements or degree of certainty that a patent makes a real contribution to innovation. True examples of policies designed to improve patent quality include the “prior approval” practice used by some countries in the Region, Brazil among them, in which representatives of the health sector participate in decisions on whether or not to approve pharmaceutical patents. Another such example is India’s new patent law (2005) which raised the “novelty” and “nonobvious” requirements. Furthermore, Section 3(d) of India’s patent law requires proof of greater efficacy in order to grant a patent for a new form of a known substance.<sup>19</sup> Other measures proposed to improve the effectiveness of the patent regime include amending the conditions and criteria for granting and applying for patents, presumed validity, transparency, and mechanisms to oppose the granting of patents, amongst others.<sup>20</sup>

The impact of changes in intellectual property rights on access to medicines can be evaluated through the use of models and studies developed for this purpose. Such models compare a basic scenario under a given condition with alternative scenarios that simulate market trends under different combinations of hypothetical variables related to intellectual property rights and market behavior.

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<sup>19</sup> In 2006, India’s Chennai Patent Office India rejected a patent application filed by the Novartis Pharmaceutical Corporation for a beta crystalline form of imatinib mesylate (Gleevec) because, inter alia, the Patent Office considered the product to be a new form of imatinib—a known substance—that had not been demonstrated to have improved efficacy. For more information on this case see:

MUELLER, J. JD Taking TRIPS to India—Novartis, Patent Law, and Access to Medicines. In: *New England Journal of Medicine*. Volume 356: 541-543. February 8, 2007. Number 6.

<sup>20</sup> Marketing authorization is a regulatory decision in the life cycle of a medicine that can be used to promote innovation. This assumes applying criteria for the relative efficacy or superiority of a medicine. This approach, under the name of the “necessity clause,” characterized the Norwegian medicine registry for many years in contrast to the habitual practice of most regulatory agencies of authorizing products proven to be “better than placebo” or “no worse than existing therapy.” However, a significant number of regulatory agencies will accord priority in the registry process for those products that a priori assume a relevant therapeutic improvement. However, it must also be borne in mind that failing to register products that are similar to an original product will, at least during the legal period of exclusivity, result in less competition on the supply side and, hence, less power among regulators and buyers to negotiate prices.

These models make it possible to measure, for a specific market of competing medicines, the future and past impact of changes in intellectual property rights resulting from the implementation of trade agreements and other policies. These models have been applied in a number of countries in the Region, including Costa Rica and the Dominican Republic.<sup>21</sup>

### 4.3 EVALUATING INNOVATION AND INCORPORATING NEW HEALTH TECHNOLOGIES

Health technology evaluation, and especially economic impact studies, is increasingly being used to support decision-making and allocate health resources in order to guarantee efficiency and efficacy in the use of technologies, but particularly with a view to incorporating new technologies into the therapeutic arsenal financed by health care systems. The manner in which economic assessments are used in the context of price regulation and selective financing varies from country to country, although some common features can be identified among countries that systematically employ the use of such assessments. In such countries a transparent regulatory process is applied to determine the products to be assessed, when, and who will implement the assessments and present outcomes; the adoption of a standard methodology to carry out comparable studies and identify an efficiency threshold (e.g. cost per quality-adjusted life years (QALYs)) as an essential feature of the decision-making process.

The evaluation of health technologies to promote a specific type of innovation can be carried out in the financing phase of research, in which case financing is tied to specific objectives and/or diseases. Accordingly, some factors to consider in establishing the priorities of research among diseases and public health problems include the disease burden (e.g., years of potential life lost), health gains (e.g., QALYs), or the cost of treatment. Most countries that use economic assessments to promote innovation geared toward attaining additional therapeutic benefits and to evaluate the cost ramifications of including a new medicine in their lists of essential medicines make these decisions in the context of price regulation and selective medicine financing. This form of regulation was originally introduced by Australia and subsequently adopted, in the specific regulatory context, by the United Kingdom through its National Institute for Health and Clinical Excellence (NICE), as well as by Canada, the Netherlands, Sweden, Portugal and—in a more discretionary and less transparent manner—by other countries.

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<sup>21</sup> See the presentation “Is it Possible to Measure the Impact of Intellectual Property on Access to Medicines?” by Miguel Cortés in Annex II. Also see “Evaluation of the Impact of the TRIPS Provisions” [*Evaluación del impacto de las disposiciones de ADPIC*]:

[http://new.paho.org/hq/index.php?option=com\\_content&task=view&id=1620&Itemid=1178](http://new.paho.org/hq/index.php?option=com_content&task=view&id=1620&Itemid=1178)

International experience in health technology evaluation is charting a new course in which the price and financing conditions of a given medicine will be determined through an evaluation that takes into account not only the added therapeutic benefits it may provide, but also the circumstances surrounding the innovation. Such circumstances include whether it fills a therapeutic void not previously filled; its budgetary impact; the needs of the population; and the seriousness of the disease for which the medicine in question is indicated. To this end, these new decision-making tools will help encourage the rational use of medicines through a series of measures such as conditional reimbursement that ensures that financing is contingent on whether a medicine is prescribed pursuant to the therapeutic indication(s) and its market authorization and not for some other purpose, thus curbing incentives for inefficient prescribing practices.

Introducing mechanisms to facilitate exhaustive evaluations of health technologies based on different criteria would effectively streamline the systematic inclusion of new technologies within the health systems of the Region. Conversely, the lack of such mechanisms intensifies and exacerbates the lack of coordination between the public and private sectors.<sup>22</sup>

#### 4.4 PROMOTING THE SELECTIVE FINANCING OF MEDICINES

Selective financing is one of the most traditional strategies used to promote access to medicines, although within the modern day context the traditional approach may require adjustment to address new challenges; for example, in the use of evaluation tools that appropriately compensate socially-necessary and therapeutically-proven innovation. Governments can regulate from the demand side, identifying those medicines to be covered by collective financing regimes and co-payment models, using selection criteria to guide medicine coverage and financing that not only takes into account product registration data providing evidence of safety, quality, and efficacy,<sup>23</sup> but also the cost-effectiveness of financing. Unfortunately, the use of essential medicine lists has been traditionally limited to public health care services; and where the lists have been extended to health insurance carriers, population coverage has remained low.

Whether or not to include a new medicine in the list of publicly-financed medicines is a critical decision. A variety of considerations must be taken into account, principally the therapeutic improvement of the new product. Inclusion in “positive” lists or formularies must be contingent on proven therapeutic and economic advantages when compared to other existing products, and as a means to counter the influence of pharmaceutical marketing strategies that lead to inappropriate drug prescribing practices and the inefficient use of public resources to finance technologies of questionable effectiveness.

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<sup>22</sup> See “Access to High-Cost Medicines” by Odete Gialdi in Annex II.

<sup>23</sup> Important in this regard is the Pan American Network on Medicine Regulatory Harmonization (PANDRH), a regional forum for the medicine regulatory authorities of the Americas, with a clear commitment to improving medicine safety, quality, and efficacy. See: [http://new.paho.org/hq/index.php?option=com\\_content&task=blogcategory&id=1156&Itemid=513&lang=en](http://new.paho.org/hq/index.php?option=com_content&task=blogcategory&id=1156&Itemid=513&lang=en).

A shared payment system, also known as “co-payment” or “co-financing,” is a mechanism in which the public health system covers a portion of the price and the consumer the other. It is based on the recognition of the health system’s role in financing supply, but also requires users to bear a share of the cost, for two main reasons. Firstly, to contribute to the financing of the system—co-payment—and secondly, to moderate and discourage unnecessary consumption and prevent what is referred to in health economics as “moral risk.” The inherent disadvantage of the co-payment system is that the amount each person must pay out-of-pocket is not proportional to their income but to health status and the price of the medicine. In other words, this mechanism discriminates against the very poor and the chronically ill. For these reasons, most health insurance plans set different levels of co-financing in accordance with the severity and costs associated with a given disease. In some countries of the Region, the government and/or social insurance agencies assume full responsibility for high-cost medicines. Nevertheless, some 50 percent of HIV/AIDS patients in the Region have no access to treatment despite the declining costs of these medicines in recent years. Providing coverage for these high-cost medicines takes a heavy toll on public finances and accounts for a much higher relative share of the budget when compared to other medicines such as those used in primary health care.<sup>24</sup> Because the individual still assumes two-thirds of the cost of medicines in the Region from out-of pocket expenditure, in some cases equivalent to 25 percent of total household expenditure, one of the most pressing challenges facing decision makers in the coming years will be how to increase both coverage and public financing for medicines, forging the necessary political consensus to ensure universal access.

## 4.5 NEGOTIATING AND REGULATING MEDICINE PRICES

For products subject to market exclusivity, price negotiation and regulation strategies should be implemented that draw on the regulatory power of the public sector. Some countries have begun to move forward in this area initially by strengthening the role of the State in the regulation of medicines use, by controlling expenditures, but also through price regulation. However, the degree to which price regulation is effective varies from country to country with differences in effectiveness being attributable to: a) the extent to which the price regulation strategy is linked with national pharmaceutical policy; b) the method of price regulation selected; and c) the makeup of the regulatory authority. Beyond simply the existence of a regulatory policy, there are a number of different factors that States must take into account that are critical to the success of regulation. For example, possible conflicting interests of the various stakeholders responsible for price regulation, institutional capacity, and the transparency of the regulatory and decision-making processes.

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<sup>24</sup> Pan American Health Organization. *Health in the Americas*. Washington, D.C.: PAHO; 2007. (PAHO, Scientific and Technical Publication No. 622). Volume I - Regional, p. 373.

As observed from the experiences of countries in the Region, a variety of criteria for direct regulation of medicine prices have been applied based on production cost, also known as “cost plus” (e.g., Colombia, Cuba, and Ecuador), therapeutic use (Cuba and Brazil), economic assessments (Brazil and Nicaragua), the cost of alternative treatments available on the market for the same diseases/conditions (Brazil and Cuba), and/or on international price comparisons (Brazil, Colombia, Cuba, Mexico, and Nicaragua). (See **Table 1**).<sup>25</sup>

Whereas direct medicine price regulation has been the traditional strategy applied to impact the price of medicines, international experience indicates that other effective alternatives are available. Indirect controls such as those in force in the United Kingdom may target areas other than price, such as placing a maximum cap on what a pharmaceutical company can invoice the public health system. Indirect controls can be effective by increasing the sustainability of public spending on medicines, and are compatible with encouraging innovation in the pharmaceutical industry. More sophisticated and complex indirect methods based on the premise of “value for the money” or paying in accordance with the value or utility of the product are also being applied. Another step forward in setting prices and conditions for the financing of high-cost medicines has been taken in some developed countries such as Australia, the United Kingdom, and Italy. This new strategy known generally as “risk-sharing agreements,” represents a change from macro to micro regulatory policies, and is based on the principle of “if it doesn’t work, don’t pay for it”. The mechanism establishes that the final compensation received by the industry for its products is not based on the number of units sold, as has traditionally been the case. But rather, on the number of patients a new therapy has been used to successfully treat.

Regulatory and policy frameworks have a clear impact on the price of medicines. Transparent mechanisms to evaluate and disseminate information on medicine prices at the country level are critical as a tool to measure the impact of policies as well as to diminish existing information asymmetries, both when effective competition and market exclusivity exists<sup>26</sup>. Recent initiatives launched in the Region establishing national and subregional medicine price databases address the need for pricing information to support public sector procurement and medicine pricing regulation, to measure the efficiency of the market in ensuring the availability of products at affordable prices, and to facilitate the evaluation of the impact of regulations that have been implemented.

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<sup>25</sup> The different criteria used by countries to set prices referenced in this document are based on a survey conducted by the Brazilian Sanitary Surveillance Agency (ANVISA) and PAHO, presented at the First Pan-American Seminar on the Economic Regulation of Pharmaceuticals, held in Brasilia on 17 March 2009.

<sup>26</sup> First Pan-American Seminar on the Economic Regulation of Pharmaceuticals. Brasilia, March 2009. PAHO.

Table 1: Economic Regulation of Pharmaceuticals in the Americas

| Country   | Pharmaceutical Price Regulation | Responsible Institutions   | Price criteria based on: |                     |                           |                     |                 |        |
|-----------|---------------------------------|--|--------------------------|---------------------|---------------------------|---------------------|-----------------|--------|
|           |                                 |  | Therapeutic efficacy     | Economic evaluation | Cost of similar treatment | International price | Production cost | Others |
| Brazil    | X                               | Inter-ministerial board, presided by the Ministry of Health, with ANVISA acting as the executive secretariat                                     | X                        | X                   | X                         | X                   |                 | X      |
| Colombia  | X                               | Ministry of Social Protection, Ministry of Trade, Industry, and Tourism, and a delegate representing the Office of the President of the Republic |                          |                     |                           | X                   | X               |        |
| Cuba      | X                               | Ministry of Finance and Ministry of Public Health  | X                        |                     | X                         | X                   | X               |        |
| Ecuador   | X                               | Ministry of Health, Ministry of Industry and the National Federation of Chemical and Biochemical Pharmaceutical Industries                       |                          |                     |                           |                     | X               |        |
| Mexico    | X                               | Secretariat of the Economy and Office of the Federal Prosecutor for Consumer Affairs   |                          |                     |                           | X                   |                 |        |
| Nicaragua | X                               | Ministry of Public Works, Industry and Trade   |                          | X                   |                           | X                   |                 | X      |
| Panama    | 2001 to 2004                    | Executive Branch and Consumer Protection Authority   |                          |                     |                           | X                   | X               | X      |

**Source:** Results of a survey carried out by ANVISA and PAHO and presented in the First Pan-American Seminar on the Economic Regulation of Pharmaceuticals. Brasilia, 17-19 March, 2009.

## 4.6 MANAGING PUBLIC SECTOR PROCUREMENT

The ability to effectively manage public sector procurement represents a powerful tool for improving access to medicines in general and to high-cost medicines in particular. It is important therefore to evaluate the experience of public sector in the Region with a view to determining best practices which may be adapted to the specific needs of a given country.

Throughout the 1990s, health service decentralization was promoted in Latin American countries, which has had the effect of diminishing the purchasing power of the health sector. Centralized procurement models were criticized for their inefficiencies and for their detachment from the health services (often purchasing items that were not needed at the level of the health services). It is now clear that centralized procurement of high-cost medicines would facilitate demand aggregation as well as negotiations for better prices for these products. Moreover, centralized procurement, combined with the decentralized delivery of products, facilitates the development and implementation of a robust management information system at the national level: when procurement is decentralized, it becomes difficult to consolidate information on what products are needed, what is being purchased and delivered, and the costs associated with the purchase.

Demand aggregation is a formidable tool which can be used at all levels within public health services, including the social security system. In 2002, Uruguay established its Centralized Procurement Unit for Medicines and Related Supplies (UCAMAE). UCAMAE purchases not only for the Ministry of Public Health but also for other Uruguayan government agencies, with a view to optimizing the centralized procurement of medicines, medical supplies, as well as surgical and related equipment. UCAMAE is an agency of the Ministry of Economy and Finance, but also serves the Ministries of Public Health, Labor, Social Security, and Defense. Member agencies place orders through the Unit, which carries out procurement activities on the basis of the quantities, quality specifications, and time frames requested. This system ensures transparency and demand forecast information for suppliers, while strengthening the government's negotiating power through the consolidation of demand.<sup>27</sup> The reorganization of Chile's Supply Center for the Ministry of Health (CENABAST) has helped strengthen its position as a mediator between the public sector and the market. Since 2004, CENABAST has been supplying pharmaceutical products and medical devices to public health establishments, acting on behalf of health institutions through agreements that set a fee for the services provided by CENABAST. Peru's Bureau of Medicines, Medical Supplies, and Medicines (DIGEMID) is tasked with purchasing medicines not only for the Ministry of Health but also for the Comprehensive Health System (SIS), and seeks to engage other insurance carriers in this process.

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<sup>27</sup> For more information regarding the Uruguayan model, see the summary provided in "The National Resource Fund of Uruguay," by Miguel Fernández Galeano in Annex II.

Considering the above, countries may contemplate a series of options to leverage its capacity in public sector procurement to improve access to high-cost and limited-source medicines:

- Centralized negotiation at the national level, combined with decentralized procurement;
- Consolidated demand in the public sector that includes the needs of the social security system;
- Systematic efforts to search for therapeutic alternatives to high-cost medicines and develop negotiation strategies by treatment regime;
- Pooled procurement among different countries supported by an international institution on behalf of the countries; an area in which the Region, with PAHO support, has had considerable successful experience; for example, through the use of the PAHO Strategic Fund or “Regional Revolving Fund for Strategic Public Health Supplies” (see **Box 7**).<sup>28</sup>

Strategies such as differential price fixing or “tiered pricing” continues to be a topic of debate among primary stakeholders involved in the production, procurement, and management of pharmaceutical products. This is especially true in the Americas given the specific social and economic conditions of the Region, where aggregated development indicators do not take into account the profound inequities and disparities affecting large segments of the population. Any discount considered for one country in the Region should be applied to all, even when economic and social conditions may vary, given that there is a certain degree of uniformity with regard to conditions relating to the limited resources available for health policy development and implementation.

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<sup>28</sup> Some of the experiences summarized in the PAHO Spanish-language report “Essential Medicines in the Region of the Americas: Achievements, Difficulties and Challenges,” published in 2007, and less well-known than the “Strategic Fund” (see **Box 7**) include the Malaria Control in Border Areas of the Andean Countries: A Community Approach” (PAMAFRO) in three Andean countries, which facilitated the purchase of malaria medicines at rates of between 36% and 90% below regular prices; or the Pooled Procurement Service /Organization of Eastern Caribbean States (PPS/OECS), a system with more than 20 years of experience in countries of the Eastern Caribbean for the purchase of products for the population with limited resources.

**Box 7: PAHO Strategic Fund**

The Strategic Fund is based on the principle of “Pan-Americanism,” through which countries of the Americas come together to address common problems in access to medicines and provide support to one another to ensure the supply of essential quality products for public health. The Fund offers the means to ensure a continuous flow of medicines and supplies at a reduced cost for priority public health programs, through a procurement process that links projected future demand, purchases, and supply.

The Fund’s objectives are to:

- Facilitate procurement of strategic supplies for public health at a reduced cost by taking advantage of the potential savings associated with economies of scale;
- Increase the continuous and timely availability of supplies;
- Encourage countries to improve planning capacity for the use of supplies;
- Promote implementation of appropriate quality assurance procedures; and
- Strengthen public health programs of the Member States.

PAHO recognizes the importance of promoting access to, and the continuous availability of, basic medical products that are essential for reducing mortality and morbidity in the Americas.

The Strategic Fund aims to provide added value to the countries in three main ways:

- Making technical support available to countries for procurement planning, distribution, and forecasting for pharmaceutical products;
- Ensuring the supply of quality products through the implementation of quality assurance procedures for the procurement of pharmaceutical products, including quality control; and
- Facilitating communication and coordination between suppliers and participating countries, with a view to improving the availability of and access to strategic public health supplies.

## 4.7 IMPLEMENTING THE RATIONAL USE OF MEDICINES

Building a culture for the rational use of medicines requires the commitment of all stakeholders. Consequently, the development and implementation of tasks such as awareness-raising, training, and institutional strengthening are critical at all levels. A national policy which not only promotes access to quality medicines but also presents strategies for promoting their rational use, will contribute to ensuring equity in access while discouraging inappropriate use. To ensure sustainable action in the promotion of the rational use of medicines, strategies consistent with the relevant WHO resolutions and in particular WHA60.16 (Progress in the Rational Use of Medicines) are recommended, including the creation of national commissions or groups responsible for implementation and monitoring.

As the foundation of the strategy, human resources and especially prescribers and pharmacists who have considerable influence on the way medicines are used, should receive continuous training and have access to unbiased information during their undergraduate and post-graduate studies, to strengthen professional practice from the public health perspective. The Region's health authorities rarely offer courses, training seminars or fellowships, or promote research in the rational use of medicines.

Regarding other tools already mentioned in Section 3.3—drug and therapeutics information bulletins, the establishment or strengthening of drug and therapeutics committees, the development and implementation of medicine formularies and standard treatment guidelines with criteria based on scientific evidence—are the starting point and basic building blocks of a rational use strategy. The preparation and implementation of treatment protocols and/or clinical guidelines for diseases requiring the use of high-cost and limited-source medicines is a priority. Ensuring equitable access for the entire population to a basket of cost-effective health care and surgical benefits under conditions of quality and sustainability will require the design of systems that use inclusion criteria based on scientific evidence and cost-effectiveness and that compares results between different treatments. For high-cost medicines, treatment protocols must be rigorously implemented in health care services.<sup>29</sup> See **Box 8**.

Information and knowledge management centers can provide valuable support in the development of strategies for continuous professional training as well as to promote the exchange, analysis, and provision of information for health services and the community.

The use of medicines must be monitored through an active pharmacovigilance system that, in particular, reports on the safety of products in circulation and use. Pharmacovigilance systems are essential components of the regulatory system and require strengthening based on the development of an operational strategy which, in turn, should be closely linked with the strategy for promotion of the rational use of medicines.

Another key element is the development of rational use incentives for both prescribers and patients. With respect to the former, strategies include compensation for efficient prescription practices with the elimination of potentially perverse incentives, such as contributions in cash or in kind from the pharmaceutical industry (e.g., gifts, training, and others) that may influence physicians to prescribe medicines other than those that are most cost-effective. For patients, co-payment mechanisms designed to discourage inefficient consumption may be effective if applied in an equitable manner; for example, through the establishment of payment ceilings based on the ability to pay and the needs of the individual (e.g., equitable co-payment, as applied in the Scandinavian countries of Europe).

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<sup>29</sup> See "The National Resource Fund of Uruguay," by Miguel Fernández Galeano in Annex II.

However, information technology capacity is required to implement these systems. Information on effectiveness, quality, and cost, combined with an appropriate system of incentives for physicians and users can assist in the task of demand forecasting, and result in efficient prescribing and user practices.

### **Box 8: Latin-American Experiences in the Development and Implementation of Clinical Guidelines**

In recent years, efforts in the Region have focused on preparing protocols and clinical guidelines to treat specific diseases using evidence-based medicine and cost-effectiveness criteria. Three experiences in this regard merit mention:

1. Chile's Universal Program of Explicit Guarantees in Health (AUGE) was developed to identify those diseases that carry most weight in terms of disease burden. AUGE identified and prioritized a limited group of 56 diseases, and developed and tested clinical guidelines for treatment and care. These guidelines presented diagnostic procedures and medicines, subsequently constituting the regulatory basis for AUGE in the management of these diseases through national care providers and insurers (FONASA and ISAPRES).
2. Brazil's Ministry of Health developed Protocols and Therapeutic Guidelines (PCDT) as regulatory instruments to protect patients and promote a policy of rational use. The PCDT depends on decisions of the Commission for the Incorporation of Health Technologies (CITEC) which is directly linked to the Secretariat of Science, Technology and Strategic Inputs (SCTIE).
3. In an effort to optimize the rational use of medicines and provide 100 percent coverage, the Costa Rican Social Security Fund has implemented protocols for treating diseases/ conditions. Diseases include multiple sclerosis, organ transplant, hemophilia, cancers (for example, chronic myeloid leukemia, and lymphomas), rheumatoid arthritis, multidrug-resistant tuberculosis, HIV/AIDS, and refractory epilepsy. The achievements in providing access to medicines were made possible with a medicine procurement budget accounting for between eight and ten percent of the total health care budget.
4. Also notable for its achievements has been the National Resource Fund of Uruguay, both in its efforts to standardize the practice of medicine and to implement universal care guarantees for diseases requiring highly-specialized medicines.

## 4.8 DEVELOPING TOOLS FOR INTERVENTION

The following section provides a summary list of a set of interventions which, if applied in a coordinated and coherent manner by national authorities, can improve access to high-cost and limited-source medicines in the Region of the Americas.

### SUMMARY OF STRATEGIES, MECHANISMS, AND INSTRUMENTS

#### 1. Developing integrated policies to promote access and innovation:

- 1.1 Identify priorities for innovation based on health needs;
- 1.2 Promote financing mechanisms for R&D and the transfer of technology;
- 1.3 Increase operating capacity in all areas of pharmaceutical production as well as in the supply of health products;
- 1.4 Mobilize political commitment and facilitate inter-ministerial coordination for the development and implementation of pharmaceutical, science and technology, and industrial/economic policies.

#### 2. Managing intellectual property to promote innovation and public health:

- 2.1 Ensure that flexibilities of the TRIPS Agreement are incorporated into legal and regulatory frameworks at the national level;
- 2.2 Prevent “evergreening” or the unjustified award of patents;
- 2.3 Improve the quality of patents awarded;
- 2.4 Improve patent system efficiency (e.g., amend the conditions and criteria for granting and applying for patents, such as presumed validity, transparency, and establish mechanisms to oppose the granting of patents, among others);
- 2.5 Evaluate the impact of changes in intellectual property rights on access to medicines through the use of different methodologically-tested models.

#### 3. Evaluating innovation and incorporating new health technologies:

- 3.1 Establish a regulatory procedure for evaluating health technologies that provides criteria and methods for conducting comparative studies;
- 3.2 Strengthen capacity at the national and regional levels to conduct economic impact studies;
- 3.3 Establish links between the outcomes of comparative economic impact evaluations with pricing regulations and medicine financing processes;

- 3.4 Ensure that the results of comparative health technology and economic impact assessments are used as main criteria for incorporating new technologies into health systems.

#### **4. Promoting the selective financing of medicines:**

- 4.1 Regulate the demand for medicines by identifying products to be covered through pooled financing systems and by adjusting co-payment methods;
- 4.2 Implement selection criteria to guide pharmaceutical coverage and financing;
- 4.3 With regard to co-payment systems, adjust co-payments in accordance with the individual's ability to pay and cost of treatment.

#### **5. Negotiating and regulating prices:**

- 5.1 Identify the government's capacity to negotiate prices for products under market exclusivity based on its purchasing power;
- 5.2 Evaluate options for the price regulation of high-cost and limited-source medicines based on price evaluation criteria; for instance, the value added of a medicine compared to that of an existing one and its reference price in other countries;
- 5.3 Develop transparency mechanisms (e.g. databases) to evaluate and disseminate medicine pricing information for products with market exclusivity as well as for multi-source products.

#### **6. Managing public sector procurement:**

- 6.1 Promote the centralized negotiation of prices at the national level with decentralized supply of high-cost and limited-source medicines;
- 6.2 Consolidate demand in the public sector by aggregating demand with the social security system and other public sector purchasers;
- 6.3 Systematically search for alternatives to high-cost medicines, and develop negotiation strategies by treatment regime;
- 6.4 Explore opportunities for public-sector procurement in coordination with other countries, for example through the PAHO Revolving Fund for Vaccine Procurement or the PAHO Regional Revolving Fund for Strategic Public Health Supplies.

#### **7. Implementing the rational use of medicines:**

- 7.1 Develop and rigorously ensure the use of medicine formularies and treatment guidelines for high-cost medicines;
- 7.2 Provide incentives for efficient prescription practices and eliminate potentially perverse incentives for prescribing medicines that are not cost-effective;
- 7.3 Strengthen training of prescribers and pharmacists in the use of medicines; and
- 7.4 Promote the availability of independent and reliable information to support the prescribing and dispensing of medicines.



## ANNEX I:

Origins of the  
First International  
Meeting on Access to  
High-Cost and Limited-  
Source Medicines

Brasilia, Brazil  
November, 2008



In 2003, ten Latin American countries—Argentina, Bolivia, Colombia, Chile, Ecuador, Mexico, Paraguay, Peru, Uruguay, and Venezuela—initiated a policy of joint price negotiation for medicines, beginning with antiretroviral medicines (ARVs) and diagnostics. This initiative was born out of concern over the lack of access to essential medicines in the Region due to the high cost of medicines and the existence of differential pricing policies that were not necessarily based on equity. Participating in these negotiations were the ministers and deputy ministers of health as well as other health-sector representatives, with the support of the Pan American Health Organization/Regional Office of the World Health Organization (PAHO/WHO); the Andean Health Organization, Regional Agency for Health/Hipólito Unánue Agreement (ORAS-CONHU), the General Secretariat of the Andean Community (SGCAN); and, the Joint United Nations Program on HIV/AIDS (UNAIDS).

According to the report on the negotiations, countries were satisfied with the results of the negotiation from a political, social, and economic perspective. Countries recognized the seriousness of the epidemic and the potential for addressing the problem through joint action, transcending borders and differences in the search for common solutions. Of the 37 items negotiated, 15 proposals were tendered at a price below the lowest reference price in the Region, resulting in a 30 to 93 percent decrease in the cost of the first-line triple combination therapy and a 9 to 92 percent decrease in the second-line triple therapy. A set of quality standards was defined for each product negotiated. Also achieved were reductions in the maximum and minimum price ranges for diagnostics, which varied by type: 62 to 81 percent for rapid tests; 13 to 33 percent for enzyme-linked immunosorbent assay (ELISA) tests; 5 to 70 percent for the CD4 test; and 25 to 82 percent for viral load tests.

In September 2004, one year after the first round of negotiations, the ten countries that participated in the June 2003 negotiations carried out an impact assessment on the first round of negotiations.<sup>30</sup> Worthy of mention in this regard is that access to HIV/AIDS medicines and diagnostics in the ten countries improved over the period studied (2003-2004). This improvement is attributable to a set of strategies which, in addition to price negotiations, included a variety of national, regional, local, and even international initiatives including development and implementation of projects financed by the Global Fund to Fight AIDS, Tuberculosis, and Malaria. Nevertheless, the evaluation reports of the first round of joint negotiations on ARVs revealed a number of difficulties with regard to linking joint regional negotiations with national procurement processes. The agreements achieved were not always compatible with regulations and policies governing trade, intellectual property, and public sector procurement in countries participating in the negotiations. Furthermore, some of the ARVs that were negotiated were not included in all the countries participating in the price negotiations.

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<sup>30</sup> Pan American Health Organization. Second joint negotiation of prices for antiretroviral medications in the countries of South America: Process and Results. [In Spanish only] Washington, D.C.: PAHO; October 2006. In: [http://www.paho.org/spanish/ad/fch/ai/II\\_Ronda\\_de\\_Negociacion\\_Procesos\\_Resultados.pdf](http://www.paho.org/spanish/ad/fch/ai/II_Ronda_de_Negociacion_Procesos_Resultados.pdf)

During the 45th Directing Council of PAHO in Washington, D.C. (September 2004), the 35 PAHO Member States addressed the problem of access to comprehensive care for people living with HIV/AIDS, and adopted Resolution CD45.R10 “Scaling up of Treatment within a Comprehensive Response to HIV/AIDS.” The Directing Council also adopted Resolution CD45.R7 on “Access to Medicines,” urging the Member States of PAHO to “continue to implement a broad range of cost-containment strategies for essential public health supplies to maximize efficiency and resource utilization, and to monitor and evaluate the impact of such strategies on price and access.” At the Fifth Meeting of South American Ministers of Health and Social Protection<sup>31</sup> held in Santiago, Chile (April 2005), the ministers underscored the countries’ need to have appropriate and timely access to medicines and medical supplies of good quality and at affordable prices. The ministers acknowledged the results obtained from the first round of joint negotiations for antiretroviral medicines and diagnostics held in Lima, and declared joint negotiations to be an effective tool for obtaining fair prices, improving access, and increasing coverage. Furthermore, the ministers approved a second round of such joint negotiations.

The second round of joint negotiations began in Buenos Aires on 5 August 2005. A total of 11 countries and 26 pharmaceutical companies were involved in the negotiations. Price reductions achieved ranged from 15 to 55 percent for the most commonly prescribed HIV/AIDS treatments in the Region. A basic therapy combination (AZT+3TC+NVP), which the pharmaceutical industry offered at a cost of US\$350 per year per patient in 2003 was reduced to US\$241 as a consequence of the negotiation. The countries also formed the “ARV Negotiation Monitoring Group” (GAN) to assist the countries to obtain these ARVs at the prices negotiated.

In 2007 and 2008, the countries studied changes in ARV medicine prices in the Region, assisted in this task by GAN and PAHO. In view of the extensive supply of generic ARVs in the Region, priority was given to developing strategies for reducing second and third generation ARVs—medicines subject to patent exclusivity in the Region that represent a high cost for countries and for which negotiations based on competition would not necessarily result in price reductions.

Based on the outcomes of this analysis, the countries, with the support of PAHO, recommended organizing a forum for regional dialogue to address the determinants of access to high-cost and limited-source medicines, with a view to developing regional and national strategies for improving access at both the regional and country levels. It was proposed that this forum be held as one of the first regional activities associated with the implementation of the Global Strategy on Public Health, Innovation and Intellectual Property, adopted during the Sixty-first session of the World Health Assembly (WHA61.21). In support of this measure, the 48th Directing Council

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<sup>31</sup> Declaration of the Fifth Meeting of South American Ministers of Health and Social Protection, Santiago, Chile, 1 April 2005.

of PAHO, meeting in October 2008, adopted Resolution CD48.R15 “Public Health, Innovation and Intellectual Property: A Regional Perspective.” Against this backdrop, the First International Meeting on Access to High-Cost and Limited-Source Medicines was held in Brasília, Brazil, on 4-6 November 2008.



## **ANNEX II:**

## Summary of Presentations



## 1. Access to High-Cost Medicines

**Odete Gialdi**

Department of Pharmaceutical Assistance (DAF)

Secretariat of Science, Technology, and Strategic Inputs (SCTIE), Brazil

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One of the main challenges facing Brazil's national health policy is to ensure that an individual's ability to pay does not limit his or her access to medicines. New technologies can be developed that involve lower associated production costs which, generally speaking, bring down prices. However, difficulties arise if upon incorporation of such new technologies, existing technologies are not retired from the system. This, jointly with health care marketing and interventions of the judicial system, creates a situation in which supply determines demand for new health care technologies. In turn, this tends to lead to the adoption of health technologies without first conducting the necessary evaluations with regard to efficacy and effectiveness.

The Unified Health Care System (SUS) accounts for nearly 30 percent of this amount, with generic medicines representing 14 percent of invoicing and 16 percent of total sales volume.<sup>32</sup> Considering the current health situation and in particular, access to medicines in Brazil, including current needs, rising costs, and limited resources, it becomes necessary to strive for maximum efficiency in the use of material, human, and financial resources.

The current challenges facing the SUS in this regard include:

- Ensuring coverage for medicines and health technologies through existing systems and promoting comprehensive care;
- Developing interventions or healthcare guidelines for specific segments of the population, and including access to medicines as a part of these efforts;
- Promoting access to effective and safe medicines including rational use;
- Limiting the expansion of medicine lists without first resolving how new medicines are to be delivered;
- Evaluating health technologies in accordance with the principles of public health, and based on scientific evidence and cost-effectiveness criteria;

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<sup>32</sup> Data from Intercontinental Marketing Services (IMS) Health shows that in 2008 the Brazilian Pharmaceutical market was estimated to reach US\$ 14.9 billion, jumping 23 percent from 2007.

- Developing Brazil’s Clinical Protocols and Therapeutic Guidelines (PCDT) as a means of enhancing regulatory controls, protecting users, and ensuring the rational use of medicines;

Based on these challenges, activities to promote access to medicines include:

- Refining the concept of “high cost” including criteria such as: rarity of disease; low prevalence; high prevalence with treatment provided at the first level of care; high-cost treatment or medicine;
- Organizing financing within health care services, for products used in basic care, strategic programs, exceptional use, hospital and mixed procedure use;
- Targeting priority population segments and diseases;
- Developing strategic programs with a specific format (e.g., HIV/AIDS or oncology).

The current financing of medicines in Brazil is broken down as follows:

- Exceptional high-cost medicines increased from R\$516 million in 2003 to R\$2.3 billion in 2008, representing a 347% increase. A total of 730,000 patients use the 220 available medicines, covering 76 diseases;
- Increase in the supply and financing for basic medicines: from R\$1.00 per inhabitant per year in 2003 to R\$4.1 in 2008, representing growth of 410%;
- Between 2003 and 2008, financing by the Ministry of Health increased 166% (from R\$2.2 billion to R\$5.9 billion).

Regulatory activities by the Brazilian government include:

- Development of Brazil’s Clinical Protocols and Therapeutic Guidelines (PCDT) to guide the development of therapeutic criteria and practices;
- Evaluation of health technologies translating into a technical, scientific and management effort to support decision-making;
- Establishment of the Commission for the Incorporation of New Technologies (CITEC), an agency of the Secretariat of Science, Technology, and Strategic Inputs (SCTIE);
- Economic regulation through:
  - Policy governing the maximum sales price for government purchases; and
  - Taxation.

## 2. Evaluating and Regulating the Prices of New Medicines: The Brazilian Experience

### **Alexandre Lemgruber**

Director, Office of Economic Evaluation of New Technologies  
Brazilian Sanitary Surveillance Agency (ANVISA)

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In Brazil, medicines became subject to price regulation in December 2000 with the creation of the Pharmaceuticals Market Regulatory Chamber (CAMED). In 2003, CAMED was succeeded by the Pharmaceuticals Market Regulatory Council (CMED), comprised of five ministries and chaired by the Ministry of Health. CMED is responsible for formulating medicine price regulation policies, which are subsequently implemented by the Brazilian Sanitary Surveillance Agency (ANVISA). In addition, ANVISA acts as the CMED Executive Secretariat. Within its CMED regulatory role, ANVISA is responsible for carrying out economic impact evaluations on new medicines, setting the prices of pharmaceuticals sold on the market, and overseeing the pharmaceutical market.

The criteria used to set the prices of new medicines have changed considerably since 2000. In the early days of regulation, the price of patented medicines was not subject to regulatory control. At that time, the fact that a medicine was patented was enough to consider it “innovative”: the prices of patented medicines were limited to the average price charged in five countries: Australia, Canada, Italy, Portugal, and Spain.

Following the approval of Decision No. 2 of CMED in 2004, important regulatory changes were introduced, including the implementation of the Methodological Guidelines for Appraisals on Health Technology to guide decision-making on the prices of new medicines, establishing an evidence-based pricing policy. Since that time, the regulation of prices for new pharmaceutical products has been based on the assessment of the therapeutic value of new products. Accordingly, new medicines are evaluated to determine whether or not they provide proven therapeutic advantage over existing medicines for the same therapeutic indication. If the results of this assessment indicate that a medicine provides a proven advantage, it is classified as a “category I” medicine, and a maximum price ceiling for that medicine is set, based on the lowest price charged for that product in the following countries: Australia, Canada, France, Greece, Italy, New Zealand, Portugal, Spain, the United States, and the product’s country of origin. Where no therapeutic advantage is found in terms of comparator medicines, the product is classified under “category II,” and the price will be set based on a pharmacoeconomic cost minimization analysis. In this case, the cost of treatment using the new product cannot be higher than the cost of treatment using the existing comparator product; hence, the price of the new product is determined based on this criterion. Moreover, the

price cannot be higher than the lowest price set by the above-mentioned countries. According to ANVISA's experience in these assessments, over 80 percent of the products analyzed have been classified as category II pharmaceuticals or those that did not provide any proven therapeutic advantage over existing products.

The main steps of the analytic process are: 1) manufacturers send the relevant product literature to ANVISA; 2) the literature is reviewed; 3) the most suitable comparator medicine is selected; 4) a comparative analysis is conducted, which considers the results and costs of the two therapeutic products; 5) a price ceiling is set; and 6) marketing authorization is granted, based on the established price ceiling. The deadline for this assessment process is 90 days.

The 2004 model of price regulation for new pharmaceutical products has contributed to significant improvements and innovation in the regulatory system, including:

- The requirement that new pharmaceuticals must be compared with existing products, and that pharmacoeconomic tools are to be used to set prices as a condition for granting marketing authorization of these products;
- The concept that an “innovative medicine” must provide effective treatment benefits, instead of simply being a product with a different chemical structure or a new delivery mechanism; and
- The ability to prevent “me too” or imitation medicines (more than 80 percent of cases) from being more expensive than products already on the market.

Without doubt, the use of pharmacoeconomic criteria in setting medicine prices is a major step forward; however, this must be combined with other strategies designed to increase the population's access to medicines. Based on studies carried out by ANVISA, in December 2006 the CMED approved a mandatory minimum discount on government medicine purchases, the so-called “Price Adjustment Coefficient” (CAP). The CAP is calculated on the basis of the average rate between Brazil's per-capita gross domestic product (GDP) and those of Australia, Canada, France, Greece, Italy, New Zealand, Portugal, Spain, and the United States. In 2008, the CAP was 24.92 percent. This coefficient is applied to medicine purchases from any federal, state, or municipal government institution for a specific list of medicines set by CMED. Accordingly, the CAP has resulted in very significant annual savings—in the order of hundreds of millions of *reais*.

In recent years, more and more attention has been focused on economic regulation. ANVISA has been involved in a number of activities that support this position, including: a) formation of a pharmaceutical economics group with the pertinent regulatory agencies; b) participating in a workshop on health technologies assessment and economic regulation, within the framework of the Third Latin American and Caribbean Congress on Health Economics (Havana); c) participation

in the Organization for Economic Cooperation and Development (OECD) High-Level Symposium on Pharmaceutical Pricing Policy; d) sharing the experiences of Brazil with other countries, such as Colombia, Cuba, and Uruguay; and e) development of technical cooperation projects in pharmaceutical economics and pricing policy with countries such as Cuba, Cape Verde, and Mozambique.

The countries of the Region of the Americas appear to be well positioned to explore cooperation options for regulating the prices of pharmaceuticals, such as: 1) sharing information on pharmaceutical prices in the countries of the Region; 2) sharing information on comparative evaluations for new products, including economic assessments; 3) searching for ways to integrate existing networks (e.g., the Network for the Economic Evaluation of Health in Latin America (NEVALAT) project); 4) joint development of standard methodologies; 5) developing training activities; and 6) carrying out joint studies.

### 3. The Cuban Experience in Pharmaceutical Innovation

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The Cuban government is firmly committed to the ongoing development of science. Some of its most significant milestones in this regard include the establishment of the Cuban Academy of Sciences in 1962, the formulation of the Scientific Technologies Policy in 1975, and the implementation of the National System for Science in Technological Innovation within the National Health System in 1998. A number of factors have contributed to advancements in scientific, technological, and innovation capacity with respect to the pharmaceutical industry, including Cuba's education policies, the national health care system, and the creation of an inter-related network of scientific institutions.

Education policies have helped to strengthen qualified human resources and are a necessary and essential prerequisite for future technological training and technology management activities in the health sector. A key feature of these education policies is their ability to provide ongoing training to graduate alumni.

Cuba's national health care system makes it possible to improve access because it is operated by the State and basically free to users. The health system places a clear emphasis on preventive care,

in which primary care plays a key role, together with community participation. Moreover, the Cuban health care system possesses advanced technology, which it makes available through its international cooperation projects.

Cuba's network of interconnected scientific institutions help boost the country's scientific capacity and facilitates development in biosciences, as well as in the country's pharmaceutical industry. Important in this regard is the priority granted by the country's science policy to funding programs for the development of biotech and pharmaceutical products, as well as funding for general research.

The system of science and technology innovation covers a whole spectrum of activities, everything from the generation and accumulation of knowledge to the production of goods and services; as well as research, technology development, interface activities and related scientific and technology services, technology transfer, marketing activities, and the use of modern management techniques. The health priorities within strategic and programmatic orientations in science and technology innovation in health for the 2008-2010 period include: the environmental determinants of health (e.g., water, hygiene, and vectors); lifestyle-related determinants (e.g., smoking, alcoholism, medicine abuse, diet and nutrition, and sedentary lifestyle); non-communicable diseases and other health problems; dental diseases; emerging and re-emerging communicable diseases; disabilities; special environments (e.g., the health of schoolchildren and workers); and specific population groups (e.g., children, women, and the elderly).

The priorities of the pharmaceutical industry include the manufacture of generic medicines from imported raw materials and the substitution of imports through means of local production: between 1992 and 2006, a total of 362 drugs were introduced, 296 of which replaced imported products.

Other pharmaceutical industry priorities include the ongoing improvement of production processes, the development of vaccines and other medicines used to treat the primary diseases affecting developing countries, and the formation of research and technology development networks (e.g., genetics, toxicology, clinical trials, and pharmaceutical epidemiology).

Moreover, priority is being given to the transfer of technology and sharing of results. To this end, Cuba has concluded—or is in the process of negotiating—bilateral and multilateral agreements for technology transfers (e.g., joint vaccine production with Brazil), as well as support for the creation of medicine manufacturing facilities.

The formidable capacity created by Cuba in its pharmaceutical industry, together with its production-related innovations in the sector, has resulted in the National Immunization Program, which protects all Cuban children from 13 childhood diseases free of charge.

## 4. Brazil's Policy of Science, Technology, and Innovation in Health

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Recently, Brazil has promoted several changes to its policy of science, technology and innovation. These changes include the creation of sectoral funds, the Innovation Act known as the “Good Law” (special tax exemptions), the enactment of regulations governing the National Fund for Scientific and Technological Development (FNDCT), and the PROFARMA I and II programs of the Brazilian Development Bank (BNDES).

These changes signal closer coordination with industry and the innovation process. One of the most important developments in this regard is observed in the countries that lead the world in health research (e.g., the United States, the United Kingdom, Canada, and France), which facilitate this approach on “vertical” bases, under the coordination of government agencies responsible for health sector policies. By contrast, in the developing world—and especially in the Region of the Americas—, the government agencies responsible for health sector policies are, for the most part, not engaged in this process.

Given this situation, Brazil needs to adopt a new health model based on verticality and provide the kind of leadership in the sector that will encourage the development of technology and innovation. The comparative advantages of a vertical model are obvious in terms of the ability to link research priorities with those of the health sector, in order to mobilize new and greater resources to promote research, development, and innovation. In the case of Brazil, the Brazilian Agricultural Research Corporation (EMBRAPA), PETROBAS, and the Ministry of Defense are all success stories of the vertical model.

Following these examples, the Ministry of Health is launching its own development model of science, technology, and innovation (CT&I), which will require new interpretations of some concepts and values:

- Health as a condition of citizenship and a relevant area of development;
- Source of income generation, investment, and employment, and source of innovation and strategic knowledge in the context of the “Third Technological Revolution”;
- Twenty percent of global expenditure for research and development (US\$ 135 billion).

The Situation of Science, Technology and Innovation in Brazil::

- The health sector employs 10 percent of Brazil's qualified workforce, with nine million direct and indirect jobs;
- Represents eight percent of GDP (R\$160 billion);
- Provides a platform for the development of new technological paradigms (e.g., fine chemistry, biochemistry, electronics, nanotechnology, materials, and others);
- Ensures linkage between health and economics; and
- Requires innovation to meet health needs as part of the National Health Policy (PNS).

Accordingly, to develop the medical-industrial complex, an overview of the pharmaceutical production sector is required:

- Around 850 pharmaceutical companies produced medicines for human use in 2007, generating nearly 95,000 jobs that year;
- Revenues of approximately US\$ 5.6 billion in 2003, as compared to US\$ 14.6 billion in 2007; and
- National companies were responsible for 25 percent of revenues in 2003, compared with 30 to 40 percent in 2007.
- Exports of US\$ 916 million in 2007, and imports of US\$ 4.77 billion, with a trade deficit of US\$ 3.8 billion.

Market estimates for 2008 forecast more than US\$ 20 billion in revenue, with Brazilian import and exports amounting to US\$ 8 billion and US\$ 2 billion, respectively.

The Ministry of Health has undergone restructuring to facilitate the development and modernization of the medical-industrial complex. The Secretariat for Science, Technology, and Strategic Inputs (SCTIE) was established between 2003 and 2006, and organized into three departments: the Department of Pharmaceutical Assistance or "DAF," wielding robust purchasing power; the Department of Science and Technology or "DECIT," which funds general science and basic research; and the Department of Health Economics or "DES." In 2007, DES underwent a reorganization and was renamed the Department of the Medical-Industrial Complex and Innovation (DECIIS), and in 2008, the Commission for the Incorporation of New Technologies (CITEC) was established.

In parallel with this internal reorganization, institutional progress was also observed in government policies, such as the Accelerated Growth Program (PAC), the Program to Support Scientific and Technological Development (PADCT), the Education Development Plan (PDE), and the "More Health" (*Mais Saúde*) and the Production Development Policy (PDP). In May 2008, efforts were

made to integrate the work of the PAC in Science and Technology (PACC&T), the “More Health” program, and the PDP, resulting in broad institutional and political commitment within the sector to develop the medical-industrial complex. The objective is to reduce the medical-industrial complex-related trade deficit from the current US\$ 5 billion to US\$ 4.4 billion by 2013, and to develop technology for the local production of 20 strategic products for the Unified Health Care System (SUS) by 2013. The challenges to address are: (i) to reduce the vulnerability of the National Health Policy; (ii) to increase investment in innovation; (iii) to increase and diversify exports; (iv) to increase the density of the medical-industrial complex production capacity and strengthen national businesses; (v) to strengthen, expand, and modernize management of the public laboratory network; and (vi) to encourage high-tech companies from abroad to establish production and R&D centers in Brazil.

The tools needed to overcome challenges include use of state purchasing power to stimulate local production, funding to increase production capacity, expanding access to R&D resources in strategic areas, and the creation of support networks for technological and industrial development. All of these activities require the collaboration of the Ministry of Health with other government agencies and the private sector. With a view to managing these objectives, the Executive Board of the Medical-Industrial Complex (CIS) was created in 2008 to promote specific measures and implement actions within the Brazilian regulatory framework regarding the development strategy of the federal government in health (comprising the “More Health” (*Mais Saúde*) and the Production Development Policy (PDP) program, and the 2007-2010 Action Plan of the Ministry of Science and Technology (MCT).

The CIS strategic areas are as follows: (i) ensure local production of blood derivatives (albumin and coagulation factors VIII and IX and globulins); (ii) develop vaccines for the National Immunization Program; (iii) produce health related equipment and supplies in accordance with the National Health Policy; (iv) develop diagnostics and equipment used for blood monitoring based on modern biotechnology; (v) produce medicines and active ingredients; and (vi) produce biotechnology products for the health field.

The CIS regulatory framework should also be updated with a view to including among its objectives ensuring the quality of products manufactured under contract, increasing productivity of the national pharmaceutical industry, promoting innovation, and increasing production capacity.

Regulatory measures will likewise need adjustments: in terms of the prequalification of companies; in the list of strategic products to ensure market guarantees and purchasing preferences with tax advantages; and the contracting of services, which take into account the need for health regulation and an industrial property policy.

Finally, it is important to mention those measures already taken by the Brazilian government:

- Establishment of the Management Committee for the Terms of Cooperation and Technical Assistance between the Brazilian Development Bank and the Ministry of Health, of which PROFARMA II (April, 2008) is a key aspect;
- Establishment of the National Committee for Biotechnology and the Forum on Biotechnology Competitiveness (February, 2007);
- Actions targeting the public production sector (e.g., medicines, vaccines, tests, and blood derivatives);
- Actions targeting the private production sector in pharmaco-chemistry, medicines, equipment, and testing; and
- Use of the purchasing power of the Ministry of Health as a technology policy instrument and a means for encouraging innovation and strengthening of the Unified Health System.

## 5. The National Resources Fund in Uruguay

**Miguel Fernandez Galeano**

Vice-Minister for Public Health

President of the National Resources Fund, Uruguay

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According to PAHO/WHO data, some 50 percent of the global population has limited or no access to medicines, up to 40 percent of the public expenditure is spent on medicines, 75 percent of antibiotics are inappropriately prescribed, and severe side effects associated with medicines use continue to be reported.

In the light of this situation, countries need to develop a pharmaceutical policy to ensure that government objectives and commitments are fulfilled in the medium and long term, and which take into account, inter alia, previously established goals and priorities. Government can support the formulation of strategies needed to achieve policy objectives and identify different actors responsible for implementing the different components of such policy, encouraging national debate in ethical and health related issues.

The key objective of a pharmaceutical policy is to ensure equitable availability and access to essential medicines that are of quality and efficacy, as well as the rational and cost effective use of these medicines by health care professionals and consumers.

To ensure rational medicine use within national policy, tools are required to coordinate interventions in the use of medicines: pharmacological/therapeutic training at the undergraduate level, continuous training for health professionals, access to independent and unbiased information on medicines, and consumer education on medicines use, amongst others are essential components of a strategy.

In this regard, Uruguay has established the National Resource Fund [*Fondo Nacional de Recursos*] whose mission is to ensure that the entire population has equitable access to a set of highly specialized and high-cost medical and surgical services, and in a manner that is sustainable for the health system. These services aim to provide coverage for highly-complex procedures and medicines, evaluate outcomes, and ensure the sustainability of the health system. The Fund's financing is provided through a variety of sources, including the National Health Fund (FONASA) and the Ministry of Economy and Finance.

Medical interventions to be covered by the Fund include procedures for implanting pacemakers, organ transplants, hemodialysis, as well as coverage for the newly developed, restricted-use and high-cost medicines. A management system has been designed and developed to manage the use of these medicines. These medicines must first meet certain criteria based on current scientific evidence, comparative cost-effectiveness studies, and the development of treatment guidelines for their use.

A list of high-cost medicines has been developed including oncology, hemato-oncology, immunosuppressants and other (e.g., multiple sclerosis) medicines. Not all requests receive authorization; however, between 75 and 96 percent of requests are ultimately authorized.

A centralized procurement unit (UCA) has been established to facilitate the centralized acquisition of medicines, medical supplies, as well as surgical and related materials. The UCA is attached to the Ministry of Economy and Finance, but it also provides procurement services to the Ministries of Public Health, Labor and Social Welfare, and National Defense. Participating government agencies may place procurement orders through the UCA, providing information on quantity required, quality specifications, and frequency of orders. Subsequently, their accounts are debited for the corresponding amounts. This system ensures transparency in procurement and improved demand estimates for suppliers, while enabling government to strengthen its negotiating power by concentrating demand.

These mechanisms are a reflection of a new commitment with society in health care, since the services are managed as public goods. This commitment emphasizes ethical and social values, the importance of the use of evidence-based medicine, and improved patient outcomes. Moreover, it lays the foundation for providing quality in care by applying principles that factor in opportunity costs while at the same time providing funds for that which is determined to be effective. It is also important to reconcile issues relating to medical ethics with ethical responsibility in the allocation of resources: it is not about saving but about spending wisely, and using cost-effectiveness as a criterion for evaluation.

## 6. Medicine Selection Criteria and Treatment Protocol Development

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The Costa Rican Social Security Fund (CCSS or *Caja*) is a three-party institution comprised of workers, employers, and the government. The *Caja* operates two systems: citizen health insurance and insurance for the elderly, disabled, and survivors of the deceased. With regard to the *Caja*'s funding, eight percent is financed from employee contributions, 14 percent from employers, and 0.5 percent by the government. The main principles of the CCSS are universal coverage, equity, solidarity, mandatory participation, and unity.

Costa Rica's essential medicines policy seeks to guarantee access to medicines as a human right. Costa Rica implemented the essential medicines policy for the public sector through Executive Decree No. 13878-SPPS, establishing the National Medicine Formulary, of 22 September 1982. Subsequently, this Executive Decree was replaced by Executive Decree No.19343-S of 23 November 1989.

The *Caja* has established a structure to promote and strengthen essential medicines policy, identifying two components which would simultaneously strengthen the rational use of its medicines: the scientific and technical component, under the *Caja*'s Medical Management Division, comprising medicine selection, prescription, and use; and the operational component, under the Logistics Management Division, responsible for medicine planning, budgeting, procurement, warehousing,

quality assurance, and distribution. These two components constantly share information with the overall objectives of ensuring the availability of medicines at the right time and in the right place, and with appropriate quantities required, thus guaranteeing the population's access to medicines.

The Medical Management Division lays responsibility for medicine selection with the Pharmacology Epidemiology Bureau and Central Pharmacotherapy Committee, made up of 13 physicians in specialized fields of medicine from the country's national hospital network, as well as two pharmacists whose primary objective is to ensure that all segments of the population have access to medicines and use them rationally. The main criteria used for medicine selection include the country's epidemiological profile, clinico-pharmacological criteria, and health system sustainability.

Specifically, the following pharmacological criteria are applied:

| <b>Criteria</b>         | <b>Value</b> |
|-------------------------|--------------|
| Efficacy                | 1-5          |
| Safety                  | 1-5          |
| Benefit/Cost            | 1-3          |
| Prescription compliance | 1-3          |
| Market availability     | 1-2          |
| Other indications       | 1-2          |

Medicines selected for use within the Caja are included in the Official Medicines List (LOM). A formulary system has been established which includes ongoing evaluation and selection of medicines, updating the formulary, and providing information for the LOM. This system has been designed as an "open system," allowing for the limited procurement of medicines not included in the LOM, often to be used by an individual patient.

The medicines included in the LOM are classified as:

- *Storable*. These include the medicines used to address the leading causes of morbidity and mortality among the population. These represent the medicines necessary to treat 97 to 98 percent of the diseases affecting the population. They are centrally procured by the Logistics Management Division.
- *Supplemental list*. These include the medicines primarily needed by the teaching hospitals of the system and require appropriate diagnostic infrastructure or technology for their use, as they cover the particular needs of specialized medical services within medical centers. Moreover, the centers directly purchase these medicines.
- *Medicines for exceptional cases*. These require clinical and pharmacological justification by the prescribing physician.

By supplementing the medicines included in the LOM with those for exceptional cases, the Caja's health insurance plan is able to provide treatment for 100 percent of the diseases and health problems affecting the systems beneficiaries.

As of 2008, the LOM included 376 active ingredients suitable for warehousing, 58 supplementary and 17 exceptional active ingredients, for a total of 451 active ingredients in 636 different pharmaceutical forms.

A five-year study (1998-2002) conducted by the United States Food and Drug Administration (FDA) revealed that the FDA had approved 415 medicines over the same period, of which only 58 (14%) represented actual therapeutic innovations. This underscores the importance of medicine selection. With regard to the Caja's health insurance system, the number of new medicines it includes each year fluctuates between nine and ten, which suggests that appropriate selection criteria are being applied, and only those medicines that are innovative (comparative therapeutic benefit and cost effective) are included.

Through this essential medicines policy, access to essential medicines has been guaranteed. This fact was pointed out by the Human Development Report 2003 of the United Nations Development Program (UNDP), which noted that Costa Rica and Cuba represent the only two countries in Latin America and the Caribbean offering their populations optimal access to essential medicines with coverage fluctuating between 95 and 100 percent.

A key component of the essential medicines policy is its focus on the use of generic medicines which has facilitated competition under equal conditions in medicine procurement processes through use of the International Nonproprietary Names for Pharmaceutical Substances (INN).

A study conducted by the Department of Pharmacotherapy noted that, based on the available budgetary resources for medicine purchases, and without the possibility of purchasing generic medicines, 81 percent of the country's population would lose their medicine coverage.

Currently, the essential medicines policy is facing significant challenges in terms of offering treatment for diseases such as:

- AIDS;
- amyotrophic lateral sclerosis (Lou Gehrig's disease);
- multiple sclerosis;
- cancers
- hemophilia; and
- organ transplants.

In an effort to optimize the rational use of medicines and provide 100 percent coverage to its members, the Caja has implemented treatment protocols for diseases and conditions, including multiple sclerosis, organ transplants, hemophilia, cancers, chronic myeloid leukemia, lymphomas, rheumatoid arthritis, multidrug-resistant tuberculosis, HIV/AIDS, refractory epilepsy, antibiotics, erythropoietin (EPO), and growth hormone.

The milestones achieved in ensuring access to medicines were made possible with a medicines procurement budget accounting for between 8 and 10 percent of the total health care budget.

The 2008 budget for health and medicines (in US\$) was:

|           | <b>Amount</b> | <b>Percentage</b> | <b>Amount per capita</b> |
|-----------|---------------|-------------------|--------------------------|
| Health    | 1.6 billion   | 100%              | \$372                    |
| Medicines | 150 million   | 9,4%              | \$33                     |

In terms of the budget for medicines (in US\$ millions):

|                         |     |     |
|-------------------------|-----|-----|
| Centralized purchases   | 134 | 89% |
| Decentralized purchases | 16  | 11% |

Given the evolution of the global situation since the 1970s when the essential medicines policy was initially established, and in contrast to today's reality where free trade agreements abound and different lines of treatment exist for various diseases, a set of strategies are needed to guarantee access to medicines, including:

- Establishing health care and pharmaceutical policies;
- Strengthening essential medicines policies;
- Establishing generic medicines policies;
- Identifying sources of financing;
- Establishing procurement process;
- Identifying opportunities for pooled procurement;
- Conducting research studies on the use of medicines;
- Patent protection;
- Parallel imports;
- Compulsory licensing; and
- Availing of non-disclosed information.

## 7. Is it Possible to Measure the Impact of Intellectual Property on Access to Medicines?

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With respect to intellectual property (IP) and access to medicines, there are two schools of thought: one believes that strengthening IP rights would contribute to the development of all countries that safeguard such rights; while the other takes the position that strengthening IP rights would hamper access to basic goods and that no evidence is available to suggest any benefit to be derived from IP protection. When it comes to medicines, advocates of the first school of thought are led by the developed countries and the transnational pharmaceutical industry which insists that the vigorous protection of intellectual property rights is necessary to ensure sustainable innovation, and that such innovation will benefit developing countries in the long term. In contrast, most developing countries and organizations advocating for improved access to medicines are opposed to strengthening IP rights claiming that doing so would increase price and limit access to essential medicines, with an adverse impact on health, especially for the most vulnerable segments of the population.

Against this backdrop, quantifying the impact that IP rights has on access to medicines and, ultimately, on the health care of the population has been an issue of concern and the subject of analysis by individual researchers, as well as national and international organizations. The paper will mention two studies led by the World Health Organization (WHO) and the Pan American Health Organization (PAHO), which have given rise to further studies on the impact of IP rights on price and their ramifications on access to medicines.

The first of these is the Intellectual Property Rights Impact Access (IPRI) study, which describes a “guide for estimating the impact of changes in IP rights on access to medicines.” The IPRIA is a model used primarily to evaluate the impact of IP rights on aggregated medicine markets, such as the “private market,” “public market,” or “overall medicines market”. The model has been applied and/or disseminated through formal workshops in countries such as Bolivia, Colombia, Costa Rica, Guatemala, Malaysia, Thailand, the United Kingdom, and Uruguay.

The model compares a basic scenario under a given condition, with alternative scenarios that simulate market trends under a different hypothetical set of factors associated with IP protection and market behavior. A basic scenario can simulate conditions under the TRIPS Agreement, while one or more alternative scenarios would simulate different market conditions. Moreover, alternative scenarios can include public policy provisions; for example, the implementation of

different IP protection measures. For each scenario (basic and alternatives), the model calculates the percentage of active ingredients—the active molecule in a particular pharmaceutical product—enjoying market exclusivity as a result of some of the types of IP rights evaluated. The degree of competition—comparator of medicines with the same active ingredient or medicines with different active ingredients but the same therapeutic indications—determines the price differentials between medicines; exclusive medicines set monopoly prices that are higher than the prices that would result when competitor medicines enter the market. The difference in the degree of market percentage between medicines with exclusivity compared with a scenario in which there is competition is what the model uses to determine the median price difference between scenarios. These price differences would, simultaneously, determine the impact in terms of consumption (access) and the expenditure (market value). Consequently, the model evaluates the impact for different time frames as follows:

- Degree of the medicine's exclusivity in the market;
- Impact on median market price;
- Impact on pharmaceutical expenditure; and
- Impact on medicine consumption.

The second study is known as the Intellectual Property Rights Impact Micromodels (IPRIM). In this case, the objective is to develop simulation models that would facilitate measurement of the prospective and retrospective impact of the changes in IP rights due to implementation of trade agreements or other policies in a specific market of competing medicines where medicines substitution is possible; for example, those with the same therapeutic indication, such as protease inhibitors for HIV/AIDS treatment, or proton pump inhibitors for the treatment of ulcers. This study makes it possible to individually characterize products by date of market entry, lifecycle, patent status, or any other IP protection characteristic—and by price and amount of units sold for each time frame. As in the case of the IPRIA, a variety of scenarios are developed and the difference between price and expenditure between alternative scenarios when compared with the basic scenario are used to assess the impact of IP rights. This study began in November 2006 as a joint project of PAHO/WHO, the World Bank, and the International Center for Trade and Sustainable Development (ICTSD).

In conclusion, measuring the impact of IP rights on access to medicines is possible, and to this end some methodologies have been developed, including the IPRIA and IPRIM models. These models are complementary: while the former measures the impact on an aggregated market; the latter is applied to disaggregated markets related to specific therapeutic groups.

Nevertheless, it is important to emphasize the need for quality data to ensure reliable results, and such data has not always been available in some of the studies carried out. The training and

monitoring of national teams that manage concepts, models, and evaluation of results is required, as well as a commitment from the government to provide reliable information on the pharmaceutical market and its development.







