CHAPTER 6

TOWARDS A SUSTAINABLE PLAN TO PROMOTE INNOVATION AND ACCESS

A GLOBAL CHALLENGE

The burden of infectious diseases that disproportionately affect developing countries continues to increase. Reducing the very high incidence of communicable diseases in developing countries is an overriding priority, but it is also important to consider how the growing burden of noncommunicable diseases in developing countries can be addressed. The health needs of the poor and vulnerable, in particular women and children, must receive the highest priority from the world community.

Our task is how to alleviate this enormous burden which is an affront to our sense of shared humanity. With the increasing power of science, and also a growing awareness of the fundamental inequities inherent in the disproportionate burden on developing countries, the world must find ways to tackle more effectively the health needs of poor people. This needs to take into account both the necessity of improving the access of all to new and existing products and the urgency of developing appropriate new products including vaccines, diagnostics and treatments. Among other factors, not least the organization and financing of health delivery systems, a prerequisite for access is that appropriate treatments should be available for diseases and conditions that disproportionately affect developing countries.

The Commission found that in industrialized countries there is an innovation cycle in biomedical R&D that is, to a large extent, self-sustaining. The incentive for R&D in the private sector is the existence of a large market for health-care products supported by both public and private demand, and underpinned by protection of intellectual property which allows companies to capture financial rewards from innovation. The market-driven R&D process in the private sector – in pharmaceutical and biotechnology companies – is supported by a substantial upstream research effort, funded principally by the public sector, in universities and public-sector research organizations.

This conjunction of positive conditions is generally not present in low-income countries. The innovation cycle is not self-sustaining. Upstream research capacity is generally weak or non-existent, except in a few mainly large technologically advanced countries. Many do not have sufficient resources to invest in public sector research, or a private sector with innovative capacity. Markets for products are usually small and health services underfunded. In those circumstances, the incentive effect of intellectual property rights lacks efficacy. Developing countries are therefore largely dependent on the products of innovation designed principally to meet the health-care needs of developed countries. In some cases these products meet their needs if funding is available (for instance, in the case of vaccines against universal childhood illnesses, or antibiotics) but in others, no treatments are available for prevalent diseases or are not adapted to the special conditions relating to delivery and compliance in developing countries. Also existing medicines, whether patented or not, are often too costly in the poorest settings for patients paying out of pocket or

for governments purchasing for public health programmes. Thus, current government policies and company strategies including incentive and funding mechanisms, both in developed and developing countries, have not generated sufficient biomedical innovation relevant to the needs of most developing countries. New, and even existing, treatments remain unavailable and unaffordable to those who need them.

As Bill Gates told WHO's World Health Assembly in 2005:

> Political systems in rich countries work well to fuel research and fund health care delivery, but only for their own citizens. The market works well in driving the private sector to conduct research and deliver interventions, but only for people who can pay.
>
> Unfortunately, the political and market conditions that drive high quality health
> care in the developed world are almost entirely absent in the rest of the world. We have to make these forces work better for the world's poorest people *(1).*

Too few R&D resources are directed to the health needs of developing countries. In the private sector, companies do not have the incentive to devote adequate resources to develop products specifically adapted to the needs of developing countries, because profitability is mainly to be found in rich country markets. The great majority of health research funded by the public sector takes place in developed countries, and its priorities principally reflect their own disease burden, resource position and social and economic circumstances.

An enormous cost to human and economic development arises from this. The report of the WHO Commission on Macroeconomics and Health calculated that extra expenditure on health interventions of all kinds (including R&D) in low income developing countries would, on conservative assumptions, produce direct benefits to human health (e.g. increased longevity) and to economic growth, on which improved prosperity and better health depends, of more than five times the amount of additional spending. For example, it estimated that implementation of its recommendations would reduce deaths in the developing world by 8 million per year by 2015. On that basis it called for a massive increase in funding of health services and investments in R&D. The cost of inaction, in lives lost and disabilities and lower economic growth, would be far greater than the relatively small cost of the actions it proposed *(2).*

A comprehensive attempt to estimate additional resource requirements for a particular disease is the recently published "Global Plan to Stop TB: 2006-2015", prepared by the Stop TB Partnership *(3).* Linked to the objective of meeting the MDGs, and the specific goal of halving TB prevalence and deaths compared with 1990 levels, the plan sets out the resources needed for actions, underpinned by sound epidemiological analysis and robust budget estimates. It represents a consensus view of what could be achieved by 2015, provided the necessary resources are made available both for the delivery of treatments to those in need, and investment in new diagnostics, dugs and vaccines.

Based on this analytical work, the Plan estimates total financing needs of US$ 56 billion in the period covered by the Plan, of which US$ 31 billion is not likely to be available based on projections of current funding levels. In the case of new

diagnostics, vaccines and drugs the total financing requirement in the period is estimated at nearly US$ 9 billion, of which only US$ 2.8 billion is projected to be met from existing funders, leaving a gap of US$ 6.2 billion (or 69% of the total). It therefore estimates that additional spending averaging US$ 3 billion each year is required in the next decade, of which US$ 0.6 billion should be for the development of new products to fight TB.

While comprehensive exercises are not available for other important disease areas, a recent assessment of current spending on malaria R&D estimated total investment in 2004 of US$ 323 million, of which 56% was provided by the public sector, 32% by not-for-profit institutions, and 12% by the for-profit sector. The biggest single investors were the United States Government and the Bill and Melinda Gates Foundation. Without doing detailed calculations of actual requirements, the report notes that malaria currently accounts for 3.1% of the global disease burden, but only 0.3% of health-related R&D investment. If malaria R&D were funded at the average rate for all medical conditions in relation to the global burden of disease, then it should receive over US$ 3.3 billion per annum *(4)*.

We also believe a significant increase in R&D on new health products, along with increased resources for delivery, is essential. And this effort has to be sustainable. Governments in both developed and developing countries should give a higher priority providing the continuing stream of innovations on which improved health care in developing countries depends, and to their delivery.

A GLOBAL RESPONSIBILITY

This tragic failure by all governments to address poverty and sickness in developing countries has become a worldwide subject of great concern. Since the beginning of this century, there has been a heightened global consciousness about this issue. This is not just because it represents an affront to commonly-held basic human values. It is also in recognition of our interdependence, and the potentially serious consequences of failure to deal with this, for all members of the world community.

The endorsement of the MDGs in 2000 emphasized the importance of investing in health improvements for economic development, as well as improving the health of poor people. In 2001, the Doha Declaration on the TRIPS agreement and public health stated that the TRIPS agreement should be interpreted in a manner supportive of the right to protect public health. During 2005 there were many other examples of this heightened consciousness. For instance, the G8 leaders in 2005 committed themselves and other developed countries to increase development assistance to Africa alone by US$ 25 billion per annum by 2010, and to all developing countries by US$ 50 billion per annum by the same date. There are also many specific instances of increased commitments by governments and foundations to the fight against diseases that disproportionately affect developing countries. New funding sources have arisen, in particular the Bill and Melinda Gates Foundation, and new players, including public–private partnerships, have emerged on the scene. On the part of pharmaceutical companies, heightened awareness has led to the setting up, inter alia, of dedicated R&D units devoted to diseases that particularly affect developing countries. Underpinned by the new opportunities arising from the rapid development

of science (e.g. genomics), a momentum has developed which it will be critical to sustain to promote innovation and access.

All these initiatives reflect a new awareness: relying on purely economic mechanisms cannot solve the problem. A worldwide mobilization of resources, both public and private, and political commitments at all levels, is necessary to address the issue.

Intellectual property rights have an important role to play in stimulating innovation in health-care products in countries where financial and technological capacities exist, and in relation to products for which there are profitable markets. However, the fact that a patent can be obtained may contribute little or nothing to innovation if the market is too small or scientific and technological capability inadequate. Where most consumers of health products are poor, as are the great majority in developing countries, the monopoly costs associated with patents can limit the affordability of patented health-care products required by poor people in the absence of other measures to reduce prices or increase funding. Because the balance of costs and benefits of patents will vary between countries, according to their level of development and scientific and technological infrastructure, the TRIPS agreement allows countries some flexibility in finding a balance more appropriate to their circumstances.

OUR PROPOSALS

Our Commission analysed the various effects of intellectual property rights on upstream research, the subsequent development of medical products in both developed and developing countries and the possibility of ensuring access to them in developing countries. We considered also the impact of other funding and incentive mechanisms and fostering innovation capacity in developing countries.

We present below our recommendations. These form an agenda which we think needs to be considered by developing and developed countries, as well as other governmental and non-governmental stakeholders.

CHAPTER 2 – DISCOVERY

The foundation of all innovation leading to the discovery of new health-care products is basic research in the life sciences and other scientific and technical disciplines which contribute, such as chemistry and informatics. In recent years the revolution in molecular biology and the development of wholly new branches of scientific investigation has offered the prospect that the process of biomedical innovation could be accelerated and made more effective. The process of drug discovery and development is not only a matter of science. It involves a complex interaction among a wide range of economic, social, and political actors. Governments play a critical role in providing the policy framework, including intellectual property rights, funding and tax and other incentives, but other actors in the public, private and non-profit sectors are essential components of this complex system.

In this chapter we reviewed the evidence concerning the science and the economic and policy choices faced by countries. In particular, we focused on scientific,

institutional and financial issues arising between basic research and the identification of lead compounds with possible therapeutic utility.

- What are the gaps in this process for diseases principally affecting developing countries?
- What policy measures might be appropriate to address those gaps?

The Commission concludes that it is in the interest of all countries to promote health research that addresses the health needs of developing countries and to set specific and measurable targets in this regard. To that end we made the following recommendations.

2.1 Governments of developed countries should reflect adequately this objective in their research policies. In particular, they should seek to define explicit strategies for R&D and devote a growing proportion of their total health R&D funding to the health needs of developing countries, with an emphasis on upstream and translational research.

2.2 Developing countries should establish, implement or strengthen a national programme for health research including best practices for execution and management of research, with appropriate political support, and long-term funding.

2.3 Government and funder attention should be paid to upstream research that enables and supports the acquisition of new knowledge and technologies that will facilitate the development of new products, including drugs, vaccines and diagnostic tests to tackle the health problems of developing countries. Attention should also be paid to the current inadequacy of the research tools available in these fields of research. These include techniques to understand new pathways to discovery, better ways to use bioinformatics, more suitable animal models and other disease-specific technologies.

2.4 When addressing the health needs of people in developing countries, it is important to seek innovative ways of combating Type I diseases, as well as Type II and Type III diseases. Governments and funders need to assign higher priority to combating the rapidly growing impact of Type I diseases in developing countries, and, through innovation, to finding affordable and technologically appropriate means for their diagnosis, prevention and treatment.[18]

2.5 Actions should be taken by WHO to find ways to make compound libraries more accessible to identify potential compounds to address diseases affecting developing countries.

2.6 WHO should bring together academics, small and large companies in pharmaceuticals and biotechnology, governments in the form of aid donors or medical research councils, foundations, public–private partnerships and patient

[18] The typology of diseases is explained in Chapter 1.

and civil society groups for a standing forum to enable more organized sharing of information and greater coordination between the various players.

2.7 Countries should seek through patenting and licensing policies to maximize the availability of innovations, including research tools and platform technologies, for the development of products of relevance to public health, particularly to conditions prevalent in developing countries. Public funding bodies should introduce policies for sensible patenting and licensing practices for technologies arising from their funding to promote downstream innovation in health-care products.

2.8 Patent pools of upstream technologies may be useful in some circumstances to promote innovation relevant to developing countries. WHO and WIPO should consider playing a bigger role in promoting such arrangements, particularly to address diseases that disproportionately affect developing countries.

2.9 Developing countries need to consider in their own legislation what form of research exemption might be appropriate in their own circumstances to foster health-related research and innovation.

2.10 Countries should provide in their legislation powers to use compulsory licensing, in accordance with the TRIPS agreement, where this power might be useful as one of the means available to promote, *inter alia*, research that is directly relevant to the specific health problems of developing countries.

2.11 Developing countries should ensure that their universities and public research organizations maintain research priorities in line with their public health needs and public policy goals, in particular the need for innovative research of benefit to the health problems of their populations. This should not exclude support of health-related research which meets their industrial or export objectives and that could contribute to improved public health in other countries.

2.12 Public research institutions and universities in developed countries should seriously consider initiatives designed to ensure that access to R&D outputs relevant to the health concerns of developing countries and to products derived therefrom, are facilitated through appropriate licensing policies and practices.

CHAPTER 3 – DEVELOPMENT

Although one of the most challenging aspects of drug discovery is identifying candidate compounds, the most expensive part is the process of taking the candidate through all the required stages of pre-clinical and clinical research and the regulatory process.

This issue of improving the efficiency of the drug development and regulatory process is receiving high-level attention from the scientific community and regulatory agencies such as the United States National Institutes of Health, the Food and Drug

Administration and the EU regulatory authorities. In order to promote the development of new products for the developing world there is also an urgent need to strengthen the clinical trials and regulatory infrastructure in those countries.

This issue is important because even in developed countries, the rapidly rising costs of health care, including supplies of medicines, are a matter of intense public concern. In developing countries, and even in some developed countries, the cost of medicines, often not available through public health-care systems, can be a matter of life and death.

New players, such as private-public partnerships and developing countries with innovative capacity, have an important part to play in developing new products that can potentially be delivered at prices that are affordable in developing countries. Increased collaboration is also important, in particular between researchers in the developing and developed world, both in the public and private sectors.

But this will not be possible in the absence of enhanced and sustainable funding, particularly from governments, for R&D relevant to developing countries.

Scientific and technical considerations, on the one hand, and economic, policy and institutional issues on the other, are relevant to this issue. Looking at the range of activities from optimization of a lead compound through to regulatory review of the safety, efficacy and quality of a new product, there are a number of key issues that require careful consideration, and we recommended as follows.

3.1 Governments and the appropriate national authorities and funders should assign a higher priority to research on the development of new animal models, biomarkers, surrogate end-points and new models for assessing safety and efficacy, which would increase the efficiency of product development. They should also work with their counterparts in developing countries to formulate a mechanism to help identify research priorities in this area for Type II and Type III diseases particularly relevant to developing countries, and provide funding for this R&D.

3.2 To enhance the sustainability of public–private partnerships:

- **Current donors should sustain and increase their funding for R&D to tackle the health problems of developing countries.**
- **More donors, particularly governments, should contribute to increase funding and to help protect public–private partnerships and other R&D sponsors from changes in policy by any major donor.**
- **Funders should commit funds over longer time frames.**
- **Public–private partnerships need to continue to demonstrate that they are using their money wisely, that they have transparent and efficient mechanisms for accountability, that they coordinate and collaborate, and that they continue regularly to monitor and evaluate their activities.**

- **The pharmaceutical industry should continue to cooperate with public–private partnerships and increase contributions to their activities.**
- **Research institutions in developing countries should be increasingly involved in executing research and trials.**

3.3 WHO should initiate a process to devise mechanisms that ensure the sustainability and effectiveness of public–private partnerships by attracting new donors, both from governments and the private sector, and also to promote wider participation of research institutions from developing countries. However, governments cannot passively rely on what these partnerships could eventually deliver; there is a need for a stronger commitment on their part for an articulated and sustainable effort to address the research gaps identified in this report.

3.4 Further efforts should be made to strengthen the clinical trials and regulatory infrastructure in developing countries, in particular in sub-Saharan Africa, including the improvement of ethical review standards. WHO has a role to play, in collaboration with interested parties, in an exploration of new initiatives that might be undertaken to achieve this goal.

3.5 Governments should continue to develop forms of advance purchase schemes which may contribute to moving later stage vaccines, medicines and diagnostics as quickly as possible through development to delivery.

3.6 Recognizing the need for an international mechanism to increase global coordination and funding of medical R&D, the sponsors of the medical R&D treaty proposal should undertake further work to develop these ideas so that governments and policy-makers may make an informed decision.

3.7 Practical initiatives that would motivate more scientists to contribute to this field through "open source" methods should be supported.

CHAPTER 4 – DELIVERY

However successful efforts might be to develop new products to address the public health problems of developing countries, they will be of no value if they cannot be made available and accessible to those who need them. Antiretrovirals for the treatment of HIV/AIDS have featured prominently in public discussions. The problem of access to medicines is certainly not limited to antiretrovirals, but concerns the whole range of medicines, whether patented or not, even when available at the lowest cost in the poorest settings, for prevention and cure as well as diagnostic tools.

For instance, in the case of malaria there is a massive gap in access, with the most effective treatments (artemisinin-based combination therapies) in short supply, and the finance available for their purchase small in relation to need.

In this chapter we examined the factors affecting the introduction of new and existing products into developing countries, including health delivery systems, regulation,

pricing, intellectual property and policies to promote competition. The following recommendations were made:

4.1 Governments need to invest appropriately in the health delivery infrastructure, and in financing the purchase of medicines and vaccines through insurance or other means, if existing and new products are to be made available to those in need of them. Political commitment is a prerequisite for bringing about a sustained improvement in the delivery infrastructure and health outcomes. Health systems research to inform policy-making and improve delivery is also important. The integration of traditional medicine networks with formal health services should be encouraged.

4.2 Developing countries should create incentives designed to train and retain health-care workers in employment.

4.3 Developed countries should support developing countries' efforts to improve health delivery systems, inter alia, by increasing the supply of their own trained health-care workers.

4.4 Governments have an important responsibility to put in place mechanisms to regulate the quality, safety and efficacy of medicines and other products. As a starting point, adherence to good manufacturing practices and effective supply chain management can ensure product quality and will also curb the circulation of counterfeit products.

4.5 Policies for biomedical innovation must take account of the fact that health systems in many developing countries remain resource-constrained. Policies must emphasize affordable innovations adapted to the realities of health-care delivery in developing countries, and covering appropriate technologies for the diagnosis, prevention and treatment of both communicable and noncommunicable diseases. Mechanisms for promoting such adaptive research in a systematic way must be improved.

4.6 All companies should adopt transparent and consistent pricing policies, and should work towards reducing prices on a more consistent basis for low and lower middle income developing countries. Products, whether originator's or generic, should be priced equitably, not just in sub-Saharan Africa and least developed countries, but also in low and lower middle income countries where there are a vast number of poor patients.

4.7 For noncommunicable diseases, governments and companies should consider how treatments, which are widely available in developed countries, can be made more accessible for patients in developing countries.

4.8 Continuing consideration needs to be given to the prices of treatments for communicable diseases, particularly of second-line drugs for HIV/AIDS treatment.

4.9 Governments of low and middle income countries where there are both rich and poor patients should formulate their funding and price **regulation with a view to providing access to poor people.**

4.10 Governments need to prioritize health care in their national agendas and, given the leverage to determine prices that patents confer, should adopt measures to promote competition and ensure that pricing of medicines is consistent with their public health policies. Access to drugs cannot depend on the decisions of private companies but is also a government responsibility.

4.11 Corporate donation programmes can be of great value in a number of fields in collaboration with the actions of governments and nongovernmental organizations. However, addressing health needs in developing countries requires more structured and sustainable actions by governments and other parties that stimulate accessibility to products, while generating new treatments and products adapted to the needs of developing countries.

4.12 Governments should remove any tariffs and taxes on health-care products, where appropriate, in the context of policies to enhance access to medicines. They should also monitor carefully the supply and distribution chain to minimize costs that could adversely influence the prices of medicines.

4.13 The Doha Declaration clarifies the right of governments to use compulsory licensing as a means of resolving tensions that may arise between public health and intellectual property, and to determine the grounds for using it. Developing countries should provide in their legislation for the use of compulsory licensing provisions, consistent with the TRIPS agreement, as one means to facilitate access to cheaper medicines through import or local production.

4.14 Developed countries, and other countries, with manufacturing and export capacity should take the necessary legislative steps to allow compulsory licensing for export consistent with the TRIPS agreement.

4.15 The WTO decision agreed on 30 August 2003, for countries with inadequate manufacturing capacity, has not yet been used by any importing country. Its effectiveness needs to be kept under review and appropriate changes considered to achieve a workable solution, if necessary.

4.16 Companies should adopt patent and enforcement policies that facilitate greater access to medicines needed in developing countries. In low income developing countries, they should avoid filing patents, or enforcing them in ways that might inhibit access. Companies are also encouraged to grant voluntary licences in developing countries, where this will facilitate greater access to medicines, and to accompany this with technology transfer activities.

4.17 Developing country governments should make available full and reliable information on patents granted. WHO, in cooperation with WIPO and others, should continue to pursue the establishment of a database of information about

patents, in order to remove potential barriers to availability and access resulting from uncertainty about the patent status in a country of a given product.

4.18 Developed countries and the WTO should take action to ensure compliance with the provisions of Article 66.2 of the TRIPS agreement, and to operationalize the transfer of technology for pharmaceutical production in accordance with paragraph 7 of the Doha Declaration on the TRIPS Agreement and Public Health.

4.19 The restriction of parallel imports by developed countries is likely to be beneficial for affordability in developing countries. Developing countries should retain the possibilities to benefit from differential pricing, and the ability to seek and parallel import lower priced medicines.

4.20 Developing countries need to decide in the light of their own circumstances, what provisions, consistent with the TRIPS agreement, would benefit public health, weighing the positive effects against the negative effects. A public health justification should be required for data protection rules going beyond what is required by the TRIPS agreement. There is unlikely to be such a justification in markets with a limited ability to pay and little innovative capacity. Thus, developing countries should not impose restrictions for the use of or reliance on such data in ways that would exclude fair competition or impede the use of flexibilities built into TRIPS.

4.21 In bilateral trade negotiations, it is important that governments ensure that ministries of health be properly represented in the negotiation, and that the provisions in the texts respect the principles of the Doha Declaration. Partners should consider carefully any trade-offs they may make in negotiation.

4.22 Governments and concerned international organizations should promote new purchasing mechanisms to stimulate the supply of affordable new products and to enhance the number of suppliers in order to provide a more competitive environment.

4.23 Developing countries should adopt or effectively implement competition policies and apply the pro-competitive measures allowed under the TRIPS Agreement in order to prevent or remedy anti-competitive practices related to the use of medicinal patents.

4.24 Countries should provide in national legislation for measures to encourage generic entry on patent expiry, such as the "early working" exception, and more generally policies that support greater competition between generics, whether branded or not, as an effective way to enhance access by improving affordability. Restrictions should not be placed on the use of generic names.

4.25 Developing countries should adopt or effectively implement competition policies in order to prevent or remedy anti-competitive practices related to the use of medicinal patents, including the use of pro-competitive measures available under intellectual property law.

4.26 Bilateral trade agreements should not seek to incorporate TRIPS-plus protection in ways that may reduce access to medicines in developing countries.

4.27 Governments should take action to avoid barriers to legitimate competition by considering developing guidelines for patent examiners on how properly to implement patentability criteria and, if appropriate, consider changes to national patent legislation.

CHAPTER 5 – FOSTERING INNOVATION IN DEVELOPING COUNTRIES

In the longer term, the development of innovative capacity for health research in developing countries will be the most important determinant of their ability to address their own need for appropriate health-care technologies. The determinants of that capacity in developing countries are many. Each country has a unique set of political, economic and social institutions, which means there is no single recipe for advance. Nevertheless it is possible that lessons can be learnt from those countries which have made significant progress in this area.

The most scientifically and technologically advanced developing countries (sometimes known as innovative developing countries) are becoming significant contributors to biomedical R&D, in both the private and public sectors. They are becoming more integrated into global biomedical research networks, particularly as their advantages in terms of their ability to undertake high quality research at very competitive costs are recognized.

Apart from growing scientific and technological expertise, developing countries have a massive indigenous resource in the form of traditional medicine – both the knowledge accumulated over centuries about the medical properties of natural products, as well as unique systems for diagnosis and treatment, which have a different paradigm from "modern" medicine as it has developed in the western world. This resource is more widely used than modern medicines in most developing countries.

The possibilities exist for making better use of traditional medicine, by making traditional remedies more widely available, and by applying this knowledge to accelerate the development of new treatments.

In this chapter we addressed the building of capacity in developing countries in the fields of science and technology, regulation, clinical trials, the transfer of technology and traditional medicine, as well as intellectual property.

5.1 A prerequisite for developing innovative capacity is investment in the human resources and the knowledge base, especially the development of tertiary education. Governments must make this investment, and donors should support them.

5.2 The formation of effective networks, nationally and internationally, between institutions in developing countries and developed countries, both formal and informal, are an important element in building innovative capacity.

Developed and developing countries should seek to intensify collaborations which will help build capacity in developing countries.

5.3 WHO, WIPO and other concerned organizations should work together to strengthen education and training on the management of intellectual property in the biomedical field, fully taking into account the needs of recipient countries and their public health policies.

5.4 Developed countries, and pharmaceutical companies (including generic producers), should take measures to promote the transfer of technology and local production of pharmaceuticals in developing countries, wherever this makes economic sense and promotes the availability, accessibility, affordability and security of supply of needed products.

5.5 Developed countries should comply with their obligations under article 66.2 of the TRIPS Agreement and paragraph 7 of the Doha Declaration.

5.6 Developing countries need to assign a higher priority to improving the regulation of medical products. Developed countries, and their regulatory institutions, should provide greater financial and technical assistance to help attain the minimum set of regulatory standards needed to ensure that good quality products are available for use. This assistance should also support infrastructure developments within a country, to ensure that good manufacturing practice and supply chain management standards are implemented and sustained.

5.7 The process of the International Conference on Harmonisation currently lacks immediate relevance to the needs of many developing countries, but those countries should maintain their participation in the process. In the meantime, developing country governments and regulatory institutions should give support to regional initiatives, tailored to the current capacities of their member countries, which offer more scope for lifting standards over time, exploiting comparative advantages, avoiding duplication, sharing information and facilities, and promoting appropriate standardization without erecting barriers to competition.

5.8 WHO has an important role to play, in collaboration with interested parties, in helping to strengthen the clinical trials and regulatory infrastructure in developing countries, in particular in sub-Saharan Africa, including the improvement of ethical review standards.

5.9 Apart from the European & Developing Countries Clinical Trial Partnership, donors together with medical research councils, foundations and nongovernmental organizations, need to offer more help to developing countries in strengthening clinical trials and regulatory infrastructure.

5.10 Digital libraries of traditional medical knowledge should be incorporated into the minimum search documentation lists of patent offices to ensure that the data contained within them will be considered during the processing of patent applications. Holders of the traditional knowledge should play a crucial role in

deciding whether such knowledge is included in any databases and should also benefit from any commercial exploitation of the information.

5.11 All countries should consider how best to fulfil the objectives of the Convention on Biological Diversity. This could be, for instance, through the establishment of appropriate national regimes for prospecting for genetic resources and for their subsequent utilization and commercialisation; contractual agreements; the disclosure of information in the patent application of the geographical source of genetic resources from which the invention is derived and other means.

THE WAY TO SUPPORT A SUSTAINABLE GLOBAL EFFORT

As is apparent, this is a very large agenda. The issues are complex and views diverse. The numbers of partners involved is large. Further progress will require a collective effort. There is the need for a wider consultation to identify the most appropriate way forward for the health sector. It is important that the contributions of all stakeholders are taken into account so that their respective energies can be mobilized towards the achievement of a common goal: an enhanced and sustainable basis for R&D relevant to the health needs of developing countries.

For this purpose, the need is to develop a Global Plan of Action which would provide a medium term framework for action by these partners, including the setting of clear objectives and priorities and a realistic estimation of funding needs if these are to be achieved.

Funders, whether private or public, of course have the right to decide their own priorities as do research organizations, including public–private partnerships. The purpose of a Plan of Action would be to aid forward planning and collaborative action. In examples such as the Global Plan to Stop TB mentioned above, there is a value to all partners in setting out strategic goals and objectives for the medium term, and in rigorously examining the activities, resources and institutional mechanisms required if these objectives are to be achieved. Viewed across the field, there are few or no available mechanisms at present to advise on appropriate priorities for resource allocation between R&D on different diseases, the balance between resources needed for R&D and delivery for each disease or the means to monitor and evaluate the impact of resources devoted to treatment and delivery. Such a Plan would also provide an important basis for measuring progress towards the achievement of these goals.

A central problem remains that previous calls for governments to invest more in health research for developing countries have so far had only limited success. Yet there is a widespread recognition that more funding is a necessity, and that it needs to be provided on a sustainable basis to support what is necessarily a long-term R&D effort.

For example, public–private partnerships currently rely in particular on philanthropic support. We think governments should do more to support the initiatives taken by foundations, thereby increasing resources available and sustainability. We endorse strongly the need for more resources if this research effort is to be sustained, and the

development of new arrangements that may facilitate the flow of new funds for greater impact. We seek a new approach which involves governments on a sustainable basis in the financing of health-related research relevant to developing countries.

Elements of this approach are contained in our recommendations but we summarize here an agenda of key issues that are worthy of consideration.

- Identification of gaps in the current coverage of research for diseases that disproportionately affect developing countries.
- Actions that might contribute to increasing the overall R&D effort on diseases that predominantly affect the developing world, and improved priority setting. For example, recognizing the possible need for increased support for those that currently receive less attention than HIV/AIDS, TB and malaria.
- Providing a sustainable source of funding for public–private partnerships and other R&D institutions in the field.
- Seeking ways to channel greater funding to research organizations in developing countries in both the public and private sectors.
- Whether common interests of product developers and producers in various areas might be better addressed collectively in areas such as facilitating clinical trials and product delivery.
- Supporting product introduction in developing countries through improved regulation, at national, regional and international level.
- Monitoring the impact of TRIPS and the Doha Declaration on innovation and access for medicines and other health-care products.
- Measuring performance and progress towards objectives, and monitoring and evaluation of programmes

In deliberating the way ahead we have considered a number of current examples that might serve both to attract additional funding to R&D devoted to the health needs of developing countries, and to improve the effectiveness of that effort.

Box 6.1 Examples from the health sector: the Global Plan to Stop TB, and the WHO Special Programme for Research and Training in Tropical Diseases

Global Plan to Stop TB

The Stop TB Partnership is responsible for the Global Plan to Stop TB. Here there are good mechanisms for coordination between the parties involved, for advocating realistically for resources required, for seeking to identify priorities, and for evaluating impact.

For instance, the implementation of the Plan is supported by a Secretariat based in WHO. The functions of the Secretariat include:

- promoting accountability, flexibility and coordination in the management of resources
- resource mobilization
- building new partnerships
- building skills and capacity at national level
- catalysing change
- monitoring and evaluating the progress of the Plan, and recommending appropriate tactical changes as necessary to achieve Plan objectives.

One of us described this initiative as follows:

> I think the Global Plan is a good model – the goals are ambitious but realistic, the price tag high, but defensible and appropriate and the commitment of the TB community very strong. This plan will test the medical and technical muscle, the WHO and G8 influence and, most importantly, the international and national will and political commitment of all parties to address this epidemic. If we fail, it will not be the TB community alone that fails, it will mean that, as a society, we did not place this disease as a priority and we will have to live with that decision *(5)*.

WHO Special Programme for Research and Training in Tropical Diseases

Another long-standing example is the WHO Special Programme for Research and Training in Tropical Diseases (TDR), supported by UNICEF, UNDP, and the World Bank. Since its establishment in 1975, it has been for a long time the central focus for the development of products to tackle diseases affecting developing countries. TDR focuses on neglected infectious diseases that disproportionately affect poor and marginalized populations. Its disease portfolio includes: African trypanosomiasis, dengue, leishmaniasis, malaria, schistosomiasis, tuberculosis, Chagas disease, leprosy, lymphatic filariasis and onchocerciasis. With a budget of about $50 million annually, covering activities relating to ten or more diseases, it is now a relatively small player in resource terms compared to the greatly increased funding now flowing through public–private partnerships. However, given its central position in the field and its strong networks and contacts, it has the possibility of playing a more strategic role alongside its operational roles in research and training.

Box 6.2 An example from the agricultural sector: the Consultative Group on International Agricultural Research

In the apparently analogous field of agricultural research directed at the needs of developing countries, the central funding mechanism is the Consultative Group on International Agricultural Research (CGIAR), with a Secretariat based in the World Bank. This has been in existence for over 30 years. Currently the CGIAR is disbursing over US$ 400 million per annum to a network of 15 agricultural research institutes, of which OECD governments provide more than two thirds, and the World Bank itself contributes another US$ 50 million. The balance comes from developing country governments, international institutions (including the European Union) and foundations. Members include both developed and developing countries, as well as international organizations and foundations.

Apart from providing a single channel for donors to fund a multiplicity of research institutions in developing country agricultural research, the CGIAR also provides strategic inputs in priority setting, monitoring and evaluation, coordination and advocacy, and impact assessment.

The idea that a similar arrangement might be appropriate to health research is not new, and has been suggested by several reports and commentators over the past decade or so. For example, the Commission on Health Research for Development in 1990 viewed:

> …the CGIAR…mechanisms as highly relevant to the needs of the health field. The functions of maintaining a global overview across many specific health problems backed by independent technical assessments and the capacity to mobilize resources in support of larger research efforts are sorely missing. Provided there is ample developing country representation in the decision-making process, analogues to the CGIAR…could be extremely constructive for the health field… *(6)*.

The World Bank's 1993 World Development Report "Investing in Health" made a similar suggestion, as did the Commission on Macroeconomics and Health in 2001.

There may be some features of this example that could be adapted to the specific arrangements in the health sector, but there are a number of institutional and other features which differ in significant respects from the agricultural sector. These need to be taken into account.

It is not for us to say at this stage which of the various ideas we have mentioned, or others we have not, might represent an appropriate way forward. But we do all agree on the urgent need for action to generate more and sustainable funding for R&D to address the health needs of developing countries, and to engage governments in this endeavour more than has been the case to date.

In these circumstances we see an important role for WHO, as the lead international agency for public health, to take responsibility for pursuing this objective.

6.1 WHO should develop a Global Plan of Action to secure enhanced and sustainable funding for developing and making accessible products to address diseases that disproportionately affect developing countries.

6.2 WHO should continue to monitor, from a public health perspective, the impact of intellectual property rights, and other factors, on the development of new products as well as access to medicines and other health-care products in developing countries.

6.3 WHO, including its regional offices, should consider the recommendations of our report, in consultation with others, and recommend how these should be taken forward in each region and country.