



Interim Report of the Task Force 5 Working Group on Access to Essential Medicines

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Note to the reader

This Interim Report is a preliminary output of the Millennium Project Task Force 5 Working Group on Access to Essential Medicines. The recommendations presented herein are preliminary and circulated for public discussion. Comments are welcome and should be sent to the e-mail address indicated above. The Task Force will be revising the contents of this document in preparation of its Final Task Force report, due December 2004. The Final Task Force report will feed into the Millennium Project's Final Synthesis Report, due to the Secretary-General on June 30, 2005

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Additional information on the Millennium Project is available on its website at www.unmillenniumproject.org

Contents

Executive summary

1. Introduction

- 1.1. The problem
- 1.2. Human rights, ethics, and the question of access
 - 1.2.1. *The rights of the individual citizen and patient*
 - 1.2.2. *The rights of the inventor*
- 1.3. An economic approach to the question of access
- 1.4. A cultural approach to the question of access
- 1.5. Historical development
 - 1.5.1. *General*
 - 1.5.2. *The involvement of WHO*
 - 1.5.3. *The emergence of a broadly-based access movement*
 - 1.5.4. *The situation and perspective of the pharmaceutical industry*

2. Access and barriers to access: a framework for discussion

- 2.1. Outline of elements essential to ensuring access to medicines.
- 2.2. Barriers relating to availability
 - 2.2.1. *Failure to innovate*
 - 2.2.2. *Failure to produce*
 - 2.2.3. *Failure to import*
 - 2.2.4. *Regulatory and fiscal obstacles*
 - 2.2.5. *Problems with distribution*
 - 2.2.6. *Issues of quality*
 - 2.2.7. *The challenge of counterfeiting*
 - 2.2.8. *Issues of civil stability .*

- 2.3. Barriers relating to affordability
 - 2.3.1. *Resources for procurement*
 - 2.3.2. *Affordability for the individual*
 - 2.3.3. *Problems posed by issues of intellectual property rights*
- 2.4. Barriers relating to appropriateness
 - 2.4.1. *Problems at the macro level*
 - 2.4.2. *Inappropriate prescribing*
 - 2.4.3. *Inappropriate use in the home*

3. The feasibility of providing access

- 3.1. Global trends towards a solution
- 3.2. National trends towards a solution
- 3.3. Conclusions regarding feasibility
- 3.4. Preconditions towards improving access
 - 3.4.1. *Global preconditions*
 - 3.4.2. *National preconditions*
 - (i) National medicines policy
 - (ii) Economic situation
 - (iii) Priority setting and political will
 - (iv) Availability of expertise
 - (v) Interdepartmental links
 - (vi) Donor co-ordination
 - (vii) Community participation
 - (viii) Monitoring

4. Success stories, promising approaches and failures

- 4.1. Global approaches
 - 4.1.1. *Innovation*
 - 4.1.2. *Price reductions*
 - 4.1.3. *Interpreting the TRIPS Agreement*
 - 4.1.4. *Revolving Fund schemes, insurance and pre-payment*
 - 4.1.5. *Global Procurement Schemes*
 - 4.1.6. *International Pre-qualification*
- 4.2. Regional approaches
- 4.3. Examples of National approaches

- 4.3.1. *Bhutan*
- 4.3.2. *Brazil*
- 4.3.3. *Chad*
- 4.3.4. *Costa Rica*
- 4.3.5. *India*
- 4.3.6. *Kenya*
- 4.3.7. *Uganda*
- 4.3.8. *Multi-country experiences*
 - (i) Generic prescribing
 - (ii) National Production of Medicines
 - (iii) Capacity building
 - (iv) Access to information
 - (v) Benefiting from Traditional Medicinal knowledge

5. Recommendations

5.1. Introductory remarks

- 5.1.1. *The concept of essential medicines*
- 5.1.2. *The need for a multilateral approach*
- 5.1.3. *The need for intersectoral support*
- 5.1.4. *The need to set firm priorities*
- 5.1.5. *Co-ordination of effort*

5.2. The significance of human rights

5.3. The availability of drugs

- 5.3.1. Improving the rate and relevance of innovation
- 5.3.2. Developing more reliable supply systems
- 5.3.3. Promoting the safety of medications

5.4. The affordability of drugs

- 5.4.1. An approach to fairer financing
- 5.4.2. Countering high prices

5.5. The appropriateness of drug treatment

- 5.5.1. Better prescribing and dispensing
- 5.5.2. Better use of drugs in the home

- 5.6. Cross-cutting issues
 - 5.6.1. Use of human resources
 - 5.6.2. Gender
- 5.7. Institutional structures

6. Closing remarks

Tables:

1. Elements essential to ensuring access to medicines and principal sources of failure
2. Bodies with current or proposed involvement in promoting access to medicines in developing countries
3. Some conditions for the success of Pooled Regional Procurement Schemes for Medicines
4. Summary of principal recommendations

- Figures:**
1. Drug Funding and supply: cumulative effects of system failure at various levels
 2. Theoretical model of a National Drug Policy

Appendix I : Ten recommendations to improve use of medicines in developing countries

Appendix II: Statement of dissent: Response by the representatives of the research-based Pharmaceutical industry to the present report.

Selected References

Executive summary

The present report represents the findings and views of the Working Group at the mid-point in its activities. On a number of major matters, much work has yet to be undertaken.

It should be noted that the research-based sector of the pharmaceutical industry, as represented in the Group, expressed its disagreement on certain matters with the tenor and content of the report. A dissenting statement by the industry representatives is appended to this report.

The fact that a very large part of the world's population has inadequate access or none to essential and often life-saving medicines is of grave concern. It results in a vast loss of life and much suffering, more particularly among the poor and underprivileged. It is in blatant contradiction to the fundamental principles of human rights. And, even if one were to set humanitarian considerations aside, it results in serious damage to the economy and to the functioning of society.

The extent of the problem can be illustrated in various ways, both globally and in individual countries. It has been estimated that one third of the world's population lacks access to the most basic essential medicinal remedies, while in the poorest part of Africa and Asia this figure climbs to one half. Bearing in mind that medicines are society's primary instrument in curing and alleviating disease and that they are a prominent tool for its prevention, it is clear that the world cannot hope to attain its Medium term Development Goals in the area of health so long as this situation persists. A high proportion of deaths in the developing world are due to illnesses which are in principle curable with medicines which currently exist; this is the case, for example, with tuberculosis, pneumonia and malaria. Many other deaths result from diseases for which medicinal treatments could, with due effort, be developed using knowledge already available.

During the latter part of the twentieth century numerous efforts have been made to alleviate these problems. At the global level one might cite the Essential Drugs concept, spearheaded by the World Health Organization over a period of nearly more than thirty years; the concept has laid the basis for numerous national Essential Drugs programmes. Other global programmes, supplemented by bilateral aid, have provided funding for the supply of essential medicines, have overcome a series of pricing barriers, and have provided guidance in the management of national programmes, in the supply of essential information and in rational use. At the national level these initiatives have often been followed up and adapted to local needs and resources. Overall, however, one finds that there has been a patchwork of effort, composed of largely uncoordinated initiatives. At worst one encounters duplication, waste, or failure to maintain initially promising initiatives, while in some parts of the world programmes have been thwarted by military conflict, famine or natural disasters.

At first sight, the problems underlying inadequate access to medicines are bewildering in their complexity: one encounters faults of many types and at many levels, often occurring in parallel, and the present report seeks to examine many or most of them. When setting out to remedy the situation in any particular country one will have to adapt one's approach to the specific challenges which that country presents. Nevertheless, when examining the situation

in the world as a whole one can identify a small number of fundamental problems common to many countries. The Task Force studying these issues as part of the work of the Millennium Project has devoted particular attention to those basic issues and to means of resolving them. It is rewarding to be able to conclude that solutions can usually be identified and that - as experience shows - many of them have already been implemented successfully in particular situations. It is equally gratifying to come to the conclusion that - given the necessary determination, and the setting of the right priorities, both at the national and international level - they could be applied universally. *The problem of impaired drug access can be solved, and the world has the resources needed to solve it.*

Three main areas for action can be recognized.

Firstly, the medicines, which are needed by poor populations, must be available:

- The research and discovery process must and can be reoriented to place more emphasis on creating and identifying the medicines needed to treat major diseases of poor populations, such as HIV/AIDS, malaria and tuberculosis. The private sector can be given incentives to do it, but contributions can also be made in the public sector and in developing countries.
- By using public, private and non-profit channels in parallel, procurement and supply systems in developing countries can be made more effective and reliable
- Unsafe medicines and situations of special risk can and should be more rapidly identified and eliminated than is the case at present in much of the world; information-sharing can accelerate the process of containing risk. Where users are unnecessarily injured by medicines, redress must be provided

Secondly, the medicines so urgently needed must be affordable:

- A basic supply of medicines should be based on giving priority to a list of “essential drugs” secured from reliable suppliers
- Within a country, a flexible combination of state financing of drugs and pre-payment systems can ensure that financial barriers to drug access are progressively eliminated. Appropriate donations (and in exceptional cases loans), though they can only be a temporary means of ensuring drug supplies, are for countries at a low level of development likely to be needed for many years to come; the level of such financing will for many countries need to be raised substantially if progress is to be achieved. Imposition of user fees on poor populations should be avoided wherever possible; those already in force should be progressively phased out. Prices of medicines must be reduced to the minimum sustainable level, particularly by promoting greater competition, eliminating tax burdens and making full use of the exceptions and flexibilities built into the TRIPS agreement. An open exchange of pricing and cost information must be developed.

Thirdly, medicines must be more appropriately used:

- Prescribing must be based on “essential drugs” principles and these principles must be as fundamental part of basic and follow-up training for health workers at all levels, ,

backed by reliable and impartial information services in the field

- Prescribers should be protected from temptations to over-prescribe, such as may arise if they also dispense products for profit, or if they are subject to irresponsible advertising and promotion.
- Prescribing and usage of medicines should be carefully monitored and policies adjusted to take account of the findings
- To ensure well-informed use of medicines in the home, understandable information on their use must be made available through appropriate channels

These primary measures will need to be backed by others, specific to the needs of a particular country or population, while at all levels there will be a need for institutional development and a sustainable extension of the available human resources .

To achieve progress there will be a need for political will both in industrialized and developing countries, as well as a need for transparency on all fronts. Above all there will however be need for an increased level of long-term financial support from the world community, directed increasingly to true development towards a sustainable situation as regards access to medicines.

1. Introduction

1.1. The problem

Medicines¹ are by far the most significant tool that society possesses to prevent, alleviate and cure disease. Some medicines are very ancient; many others have been developed through scientific and industrial research during the course of the last 120 years. Most illnesses can today be either prevented or treated in some way with medicines and some diseases can in principle be cured or eliminated entirely from the community.

Despite this fact, a very large proportion of the world's population today still has either only limited access to appropriate medicinal treatment or no access at all. It has been estimated that one third of the world's population lacks access to the most basic essential medicinal remedies, while in the poorest part of Africa and Asia this figure climbs to one half.(WHO 2000a, 2000c; 't Hoen 2002) To view it from a different angle: 20% of the world's population uses 80% of the worldwide production of medicines, while somewhere in the world, every 3 second, a child dies of one of the diseases of poverty, many of which are infectious and curable.(Amsterdam 1999) The problem is in part the non-availability to entire populations of effective medicines which are accessible elsewhere, but it also involves the failure to create and develop medicines for major diseases affecting the developing world. While the lack of adequate treatments for the treatment of HIV/AIDS, malaria and tuberculosis has received particular emphasis, the problem extends to a wide range of disorders, especially those associated with social disruption, poverty and tropical diseases. This situation - which is at its worst among the poor and the populations of rural areas - has serious repercussions for human welfare but also for the growth of the economy (CMH 2001), the general development of society and the risk of global epidemics.

The problem of access merits urgent study because, however serious, it is in essence amenable to resolution. (Quick 2003) Its various causes are known, and some of them can in principle be eliminated with attainable adjustments in national policies, economic, scientific and commercial priorities, and individual behaviour with respect to medicines. Most or all will however also demand strengthening of health services, and some will only be tackled successfully if much broader problems (notably poverty) are significantly alleviated. Various of the approaches to be considered have been defined by the Secretary-General of the United Nations (Annan 2001) in setting the framework for the implementation of the Millennium Declaration; these approaches and others are considered in the present report.

Although lack of financial resources (or support) is the most frequently quoted cause of inadequate access to medicines, and usually the most prominent, it is not the only one. The world as a whole undoubtedly has the financial means to provide all its citizens with basic

¹Terminological Note: For the present purpose the terms "medicines" and "pharmaceuticals" will be regarded as equivalent, referring both to therapeutic agents and to vaccines. The term "drugs" is ambiguous since it is often applied to substances causing addiction and prone to misuse, many of which have little or no significance in medical treatment; it will be avoided in the present report except in direct quotation. The Task Force has noted that certain other products are closely analogous to medicines and deserve similar approaches, notably the intra-uterine contraceptive device (IUCD, IUD); strictly speaking, however, they fall outside the scope of work of the Task Force and will not be further discussed in this report.

medicinal treatment,¹ but those means are not equitably distributed; even in countries which are reasonably financed, other priorities may be set. Finally, within the medicines sector itself, resources which are available may be poorly used or frankly misused; the fact that medicines are items having a small volume but high unit value and that they are universally in demand renders the sector unduly susceptible to legal or illegal personal enrichment, to theft and to corruption.

The Task Force has from the outset adopted a broad definition of the concept of access to medicines. In the narrow view it could be argued that an individual has “access” to a medicine if it is likely to be in stock at his neighbourhood drugstore. However, the treatment which the medicine can provide can only reasonably be regarded as accessible if the product is effective and of consistently good quality, if there is no financial obstacle to his receiving it, and if the knowledge and guidance needed to use it properly are available.

1.2. Human rights, ethics and the question of access

1.2.1. *The rights of the individual citizen and patient*

The promotion and protection of human rights is one of the principal purposes of the United Nations. It has many times been recognized in one way or another that, as an element in the fundamental right of people to health, there is a specific right of access to those means which exist to maintain and restore health, and these clearly include essential medicines. While one might be content to argue in general terms that access to medicines is morally and ethically proper, it is at least as important to note that these concepts of social decency have within the last two generations been rendered more concrete by their embodiment into law.

The earliest modern global statement relevant to human rights and health is to be found in the Constitution of the World Health Organization, adopted in 1946. This includes the following relevant passages:

- a. "The States parties to this Constitution declare, in conformity with the Charter of the United Nations, that the following principles are basic to the happiness, harmonious relations and security of all peoples.
- b. Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.
- c. The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition.....”

Thereafter the right to health was recognized in a series of other global instruments.

The Universal Declaration of Human Rights (1948) affirms that “everyone has a right to a standard of living adequate for the health of himself and his family, including.....medical care...” (UDHR 1948). The International Covenant on Economic, Social and Cultural Rights (1966, ratified by 147 states) and other international and regional treaties recognize “the right of everyone to the highest attainable standard of physical and mental health” (ICESCR

¹Writing in January 2001, Attaran and Sachs concluded that, in order to contain AIDS, grant aid would need to be increased within the succeeding three years to a minimum of US\$7.5 billion or more; they pointed out that this sum could easily be afforded by the OECD donor economies whose aggregate national income had recently surpassed \$21 *trillion* annually. (Attaran 2001)

1966). The right to health care facilities, goods and services mentioned in the Covenant includes a right to appropriate treatment of prevalent diseases, preferably at community level. The Covenant provides for progressive realization of the right to health and acknowledges the limits of available resources. States parties have however an *immediate* obligation to guarantee that the right to health will be exercised without discrimination of any kind, and to take deliberate and concrete steps towards its full realization, with emphasis on vulnerable and marginalized groups such as children, women or elderly people

By 2001, 193 countries had recognized in their law or constitution the right to health. The Economic and Social Council has stressed that the relevant section of Covenant means that medical goods, including medicines, should be available, accessible, affordable and of good quality (ESC 2000). A right to the provision of essential drugs as defined by WHO as was thereafter expressed by the Committee on Economic, Social and Cultural Rights on its General Comment No. 14 issued in March 2000.

The WHO Action Programme on Essential Drugs (now part of the Essential Drugs and Medicines Programme) has frequently referred to the adequate availability of pharmaceuticals as a component of the right to health, (WHO 2002f) and authoritative writers have made the same point (Pécoul 1999). A right to the provision of essential drugs as defined by WHO as was recently expressed by the Committee on Economic, Social and Cultural Rights on its General Comment No. 14 issued in March 2000

A Consultation on the Rights of Patients, held in Europe but with broader participation, has concluded that:

“Everyone has the right to receive such health care as is appropriate to his or her health needs....Services should be continuously available and accessible to all equitably, without discrimination and according to the financial, human and material resources which can be made available in a given society.” (Amsterdam 1994).

Finally it may be noted that, in the light of these international legal instruments and declarations the World Health Organization itself has adopted a rights basis for its activities in the field of essential medicines. The Organization has also identified, summarized and analyzed 15 national court cases in 6 developing countries where individuals or groups have won litigation cases against their government for the realization of their right to health through access to essential medicines. Preliminary conclusions would indicate that although reference is made to international Human Right treaties, the actual judicial rulings are usually based on national constitutions, and on notions of non-discrimination, while the association between the right to health and other fundamental human rights such as the right to life and physical integrity is often quoted as a definitive argument. [□]

Against this legal background the present situation can be summarized as follows:

1. Human rights concern the relationship between the state and the individual; they lead to state obligations and individual entitlements
2. All human rights are interdependent and interrelated. Health is a fundamental human right indispensable for the exercise of other human rights
3. Freedom from discrimination is a basic element in human rights

[□] Hogerzeil HV, Vidal Casanovas J (WHO): Access to Essential Medicines as part of the fulfilment of the right to health. Paper made available to the Task Force.

4. The existence of the right to health (like all human rights) imposes three levels of obligations:
- a. The right to respect; there must be no unwarranted interference and all individuals must have equal access to preventive, curative, palliative care
 - b. Right to protect – an obligation to ensure equal access to facilities provided by third parties
 - c. Right to fulfil – an obligation to facilitate, provide and promote processes ensuring the preservation of the right, be these administrative, budgetary, judiciary or promotional.

1.2.2. *The rights of the inventor*

While the considerations under 1.2.1. above delineate the rights of the individual subject and patient (i.e. the potential or current user of medicines) it can also be pointed out that international human rights instruments also confer rights on the inventor. Proponents of this view point in particular to:

Article 27 of UDHR: the right to "share in scientific advancement and its benefits"

Article 15 of ICESCR: the right of everyone to the "protection of the moral and material interest resulting from any scientific...production of which he is author".

While the first of these two articles could equally well or better be viewed as conferring an additional right on the citizen and patient, there seems to be no doubt that the second indeed confers a right which is parallel to (and reflected in) patent law and thus relevant to the rights of the inventor under the TRIPS Agreement. As such it merits consideration in the further study of the TRIPS Agreement and the significance of the flexibilities and exceptions for which that Agreement provides (sections 2.3.3. and 4.1.3. of this report). This issue will be further examined as the work of the Task Force continues.

1.3. An economic approach to the question of access

The investments needed to ensure access to medicines for the world's entire population are sometimes portrayed as presenting an insuperable hurdle, and questions as to the apportionment of the costs become the subject of debate and disagreement.

In fact, since effective medicines alleviate the burden of disease and reduce mortality, worldwide availability of such medicines and full access to them would provide extensive economic returns, to say nothing of their relieving much suffering. The World Bank's pioneering report "Investing in Health" (World Bank 1994) delineated the economic effects of improving the health of populations, and some of the most striking examples which it provided related to medicines and vaccines.¹ In the year 1990, alone the loss of Disability-Adjusted Life Years (DALYs) in Sub-Saharan Africa totalled 7.4 million years for tuberculosis and 16.1 million years for malaria, both diseases in principle being curable by medication. A subsequent study of tuberculosis in Eastern African countries showed that the

¹The programme to eradicate smallpox, primarily based on vaccination, cost more than \$300 million dollars over the whole of its twelve-year life but saved hundreds of millions of dollars a year in direct measurable costs. (World Bank 1994)

cost per life-year saved was between \$1 and \$3. Gains in life-years translate directly into gains in worker productivity, improved utilization of natural resources, reduced costs of medical care and other economic benefits for the nation, some of which are directly measurable. Loss of working time through illness is compounded by loss of working time in accessing medicines, where these can only be obtained with difficulty or at a distance. In the worst situations, the costs of medicines and of medical treatment can be one of the very significant causes of poverty. [□]

When assessing the merits of a particular project to improve the situation in this field, one often finds that the costs involved can be set directly against the anticipated or proven returns in terms of the sums saved on health care and disability and that in purely economic terms the return on investment is substantial (Rankin 2003).

Although many factors can impede access to medicines, absolute lack of funding within a country is one of them. A 1992 study showed that the annual expenditure per capita on medicines at that time ranged from US\$412 in Japan to \$2 or less in Bangladesh and parts of Sub-Saharan Africa. At the middle of the range, per capita expenditure was \$ 97 in the United Kingdom and \$ 89 in Norway. (Ballance 1992). At the end of the century these discrepancies had still not been reduced (Bannenberg 2000; Scrip 2000; WHO 2000b, WHO 2000d).

Finally, it is an incontrovertible fact that, once a medicine has been taken into mass production, the costs of manufacturing it are generally very low, perhaps less than 3% of the overall expenditure.² When one encounters a situation in which the wholesale or retail price of a medicine represents a serious obstacle to its use, one has to realize that this price is primarily determined by factors other than the expenses involved in making it; this at least suggests that this aspect of the problem can be solved.

1.4. A cultural approach to the question of access

The present examination by the Task Force and Working Group of the question of access to medicines is primarily a global one, though it will be supplemented by a series of country case studies in low-income countries, to be conducted in the course of 2004. As a global study it is inevitably subject to limitations, since in any given national culture access to medicines is determined only in part by global factors. Within a country (and within subgroups, regions and classes in that country) local influences do much to facilitate or obstruct access to drugs and these factors have to be taken into account in defining the causes of problems and in seeking appropriate solutions. A preliminary survey drawn up for the Task Force delineated some of these social and cultural influences. They include class-mediated relationships, patient and physician compliance, traditions of authority, dominance

[□] It has been estimated that about a third of the rural poverty in China was caused by catastrophic medical spending; the majority of medical expenses in China relate to medicines (Liu *et al*, evidence provided to the Working Group, 2003).

²The figures for manufacturing costs are not published, but the fact is common knowledge among those who have worked in the industry; see also Guilloux 2000 and Carter 2003. Certain pharmaceuticals are said to have a prohibitively high inherent cost, but that is not proven. The example has been cited of natural insulin, which even at the best generic prices is still out of reach for the poorest. Even here, however, it is not clear that, if synthetic human insulin were widely used, the cost would remain at this level. For a breakdown of the costs of pharmaceuticals produced by major research-based suppliers see Laing, 2001.

and resistance, a variable degree of illness stigmatization, differences between individuals according to gender, ethnicity, and generational shifts, as well as culturally-mediated perceptions of illness, health, and health care interventions. Underlying these intricate social constructions are the economic determinants that define, and in many cases severely limit, the therapeutic options realistically available within a particular geographic or social setting. The history of a community also plays a major role in determining how access might best be promoted: Increasing the availability of essential medicines in cultural and social settings in which biomedical treatments have historically been either absent or only nominally available carries with it the responsibility to provide appropriate training and educational resources to both health care providers (including pharmacists and pharmacy technicians) and the public. The commercial advertising and promotion of medicines, though a powerful tool to influence their use in any country, differs both in its approach and in its effects from one culture to another. It calls for especial vigilance in communities which have not previously been exposed to commercial pressures in this field and have therefore had no opportunity to build up a critical approach to them.

A further complication is likely to be presented by traditional medicinal practices, often insufficiently recognized and readily misunderstood. In areas with strong histories of traditional healing practices and other alternatives to biomedicine, there is less a system of “hierarchy of resort” than one in which people will utilize (often simultaneously) all of the health resources available to them. Both patients and healers often have a clear understanding of the appropriateness of biomedical vs. traditional therapies for specific illness symptoms. The critical issue becomes the extent and quality of access to biomedical health services and supplies. Assumptions that, for example, indigenous people will consistently first seek traditional modalities and that these patterns emerge from local (and immutable) “systems of belief,” rather than from economic and geographic exigencies, must be viewed with caution.

Finally, in seeking opportunities to influence the situation favourably, one will need to understand the manner in which public opinion and behaviour are most readily influenced. It will be necessary to understand where authority and respect lie and how support can be mobilized for a good – or less good - cause.

1.5 Historical development

1.5.1. *General*

The problem of inadequate access to medicaments in the less-developed parts of the world is not a new one; what is relatively new is the realization that it exists and that it can and must be alleviated. During the long colonial era entire populations were without any access to western medicines, except insofar as missionary services provided them. Traditional medicine was practised, but often morbidity rates were high and life expectation low. What has changed since then is the universal acknowledgement that all human life is valuable, and that every individual on earth deserves an equal right to live it to the full, benefiting from the world’s fund of knowledge to attain that promise. That realization is formally reflected in the international agreements in human rights considered under 1.2.1. above.

Despite this change in formal attitudes from 1948 onwards, the world community has been slow to take appropriate action to ensure global access to medicines. Bilateral aid

to improve drug supplies in developing countries has made some inroads in the problem, as have some global programmes (including the provision of low-cost drugs through UNICEF/UNIPAC, technical assistance from WHO). There have also been encouraging successes in closely related areas, such as the large-scale provision of contraceptives. It has indeed been estimated that the number of people with access to essential drugs doubled over a 20-year period (WHO 2002a). The advances made have however been overshadowed and even outpaced by new challenges, notably that from HIV/AIDS; in 2002 it was calculated that 40 million individuals were infected, and that only 4 million had access to treatment, while only 230,000 of the latter lived in developing countries (MSF 2002a).

It is true that pressure to solve the problem of access to medicines has greatly increased since the turn of the century and that there has been a substantial and continuing response (see 1.4.3. below). Unhappily, the initiatives actually taken have often fallen far short of those announced and promised, generally because funding has not been forthcoming. Surveying the global scene with respect to the major epidemics in July 2002, Médecins sans Frontières had to conclude that:

“One of the most significant barriers to scaling up treatment programmes is the failure of both donor governments and national governments in developing countries to mobilise promised resources for the Global Fund to Fight AIDS, TB and Malaria and other financing mechanisms. Donors have abandoned their responsibility and repeatedly broken promises made over the last two years by pledging just 8% of the estimated funding necessary to scale-up the global response to HIV/AIDS. The time is long overdue for donors and other governments to deliver on their promises” (MSF 2002)

With some creditable exceptions, that situation still persists.

1.5.2. *The involvement of WHO* (Quick 2003)

The World Health Organization, created in 1946, limited its involvement in the area of medicines during its first quarter-century to purely technical issues, particularly standards of manufacturing and quality control. In the mid 1970's the then Director-General, Dr Halfdan Mahler, introduced a broad change of policy in the Organization as a whole, directing it towards improvement in basic health services and coverage; the concepts of “Health for All” and reliance on primary health care (PHC) were introduced. To some extent this change in policy was a reaction to demands advanced by the growing membership of newly independent developing countries in the Organization. (Lunde 1984) In 1975 WHO introduced the concept of “essential drugs” as one of the basic components of primary care, later defining such agents as *“those considered to be of utmost importance and hence basic, indispensable, and necessary for the health needs of the population. They should be available at all times, in the proper dosage forms, to all segments of society.”* (TRS 1977). Thereafter the Organization went on to consider which “drugs” were safe, cost effective and affordable, especially to meet the most pressing needs of the third world. This approach led to the publication of the first Model List of 224 “essential drugs” in 1977, largely inspired by similar lists drawn up earlier as a basis for national policies

in countries ranging from Papua New Guinea to Cuba and Mozambique. The WHO List was emphatically intended only as a model for member states, but in fact many national lists developed since that time have adhered to it closely. Increasing involvement in the need for pharmaceuticals policies within developing countries by other U.N. organizations (notably UNIDO, UNAIDS, UNCTAD and UNICEF) encouraged WHO to create its own “Action Programme on Essential Drugs” in February 1981. This programme has in much expanded form been continued up to the present day as the primary component of what is now the WHO Programme on Essential Drugs and Medicines. The Model List has undergone repeated revision but has only gradually expanded; the principal difference today from early editions is that a number of recently developed medicines which still enjoy patent protection have been included where they represent important innovations, notably in the treatment of HIV/AIDS. The List is now complemented by the existence of a Model Formulary providing basic prescribing information on all the medicines listed (WHO 2003b).[□] WHO has become closely involved in measures to promote rational use of medicines. (WHO 2002c) and has development standards in many fields, such as tools for developing national medicine policies (WHO 2002d), means of measuring medicine utilization and needs (WHO 1988, WHO 2000f, WHO/EURO 1993) and informative aids to critical procurement (MSH/WHO 2000). Training courses for national staff are also provided in relevant areas. In September 2003 WHO announced the “3 by 5” initiative to expand antiretroviral treatment for HIV/AIDS.² In these and other matters relating to pharmaceuticals, WHO currently works closely with a series of other global public organizations including UNICEF, UNCTAD, UNFPA, UNAIDS and the World Bank, while an interagency coordination group for pharmaceutical issues has operated for several years.(IAPCG 2000)

1.5.3. *The emergence of a broadly-based access movement*

No single initiative alone can be credited with the emergence of the broad worldwide movement to improve access to medicinal care. The creation of new independent states where there had been colonies, the work of WHO and UNICEF, the experiences of bilateral donors and the work of idealistic organizations and of investigative authors and reporters from the world’s media all contributed to it. There was also something of a social reaction to the emergence of a free market society, a global economy and multinational corporations, with a call for action to reduce what was clearly a gross and apparently growing degree of inequity between the populations of North and

[□] Within the Task Force it has been argued that the development of the Model List of Essential Drugs may to some extent have been influenced and possibly distorted by commercial or political pressures to include certain agents and omit others. The Task Force did not find it possible to examine this issue, but it must be noted that the content of the list has not always been uncontroversial.

²The “3 by 5” goal represents a commitment by WHO to provide life-saving ARV treatment to *three million* people in developing countries by the end of 2005. It is not a separate programme or fund, but an objective which it hoped to attain through a series of mutually complementary measures. (WHO 2003) It must be borne in mind that the total number of individuals infected is currently estimated at *42 million*, (ibid) though not all require intensive medicinal treatment.

South. Popular pressure on governments and debates in the various fora in the framework of the United Nations insisted on change and on concrete steps to achieve such change. In parallel with all these developments, and in part fuelled by them, a series of institutions emerged which were intended to tackle the problem. Some of these involved the World Bank or development banks or the specialized agencies of the United Nations (WHO, UNAIDS), while others were independent initiatives with funding from philanthropic and other sources. The various missions, both Christian and Islamic, have also continued their long-term involvement in medicines supply.

The bodies most prominently active in the field of access to medicines are listed briefly in Table 2. Apart from national governments they include:¹

a. *UNICEF*: Maintenance of a global warehousing and supply system to deliver generic medicines to developing countries at favourable prices. Direct negotiations with manufactures and suppliers to secure patented or generic medicines at highly favourable prices to developing countries.

b. *Bilateral donors*: Danida (Denmark), DfiD (United Kingdom), SIDA (Sweden), DGIS (The Netherlands) and USAID (USA) have been important donors, involved both in providing emergency supplies of medicines in crisis situations and in developing facilities and long-term policies to ensure a stable supply of medicines

c. *Specialized bodies* working globally in particular therapeutic fields to improve pharmaceutical access. These include:

- The *Medicines for Malaria Venture*. Incubated within the TDR programme² at WHO, this venture is based on public/private collaboration. It selects, guides, funds and develops research done by others and works in partnership with research institutions, ministries of health, disease control programmes, industry, academia and non-governmental institutions.

- The *Global Drug Fund (to fight AIDS, tuberculosis and malaria)*. This UN-based fund, with elements of public/private partnership, seeks to mobilize additional resources to combat these three diseases. A major part of its funding is likely to be devoted to in-country activities and promoting access rather than to pharmaceutical development programmes.

- The *Global Alliance for TB Drug Development*, a non-profit international organization, intended to accelerate discovery and ensure that there are better and more affordable agents to fight tuberculosis. Funding is from governments and major philanthropists. While prioritizing support to institutions in TB endemic countries, the Alliance can work with commercial firms to identify promising and eligible substances and move them along the development pipeline.

¹Only those activities of these organizations which relate directly to access to medicines are noted here; various of these bodies also have a much wider health role.

²WHO Special Programme for Research and Training in Tropical Diseases.

- *GAVI (The Global Alliance for Vaccines and Immunization)*, a public/private partnership involving international organizations, governments, the vaccine industry, research institutions and major philanthropists. Alongside promotion and funding of national vaccination programmes, the Alliance aims to stimulate the vaccine industry to develop and supply vaccines vital to low-income countries, but will not provide financial support to this end.

- *IAVI (The International AIDS Vaccine Initiative)*. This is a global non-profit organisation working to speed the search for a vaccine to prevent HIV/AIDS. IAVI receives major financial support from a number of major philanthropic foundations, the World Bank and nine national governments.

- *MSF (Médecins sans Frontières)* a very prominent medical emergency operation, working in 80 countries, which is heavily involved in national access programmes and AIDS projects, and has sponsored major global initiatives in the area of medicines (see also below).

- *The Access to Medicines Campaign*, spearheaded by Médecins sans Frontières but also involving Health Action International, The Consumer Project on Technology, Oxfam, The Treatment Access Campaign and other bodies. The Campaign is both a significant lobbying organization and engaged in projects to improve access in many countries. (MSF 2003c)

- *The Drugs for Neglected Diseases Initiative (DNDI)*, again sparked by MSF but with partners, advisers and members which include WHO/TDR, government institutions and private companies. The Initiative aims to develop medicines in selected fields. Current projects seek to develop further existing compounds with potential usefulness in tropical diseases. In the longer run, creation of entirely new medicines is envisaged through work capitalizing on existing, fragmented R&D capacity in the developing world. Funding is sought from national and international agencies, foundations and private donors.

- *SEAM (Strategies for Enhancing Access to Medicines)* is a programme with five-year funding from the Bill and Melinda Gates Foundation to develop innovative private sector / public sector initiatives aimed at improving access to and use of essential medicines. Activities include country-level initiatives, production of manuals, training materials and management software, and the development of a business model for a franchise system to distribute essential medicines through private retail outlets.

- *Various private foundations* assisting the development of policies but also engaging on behalf of countries in price negotiations with manufacturers or suppliers. The Rockefeller Foundation has played an important part in this work. The Clinton Foundation is engaged primarily in assisting countries to develop HIV/AIDS programmes and in obtaining funding from various

countries for the necessary medicinal supplies. The Bill and Melinda Gates Foundation is not directly involved but very heavily supports various of the initiatives listed here.

- In the area of HIV/AIDS it should be noted that alongside UNAIDS as a separate agency there is also the new WHO “3 by5” initiative announced in September 2003 (see section 1.5.2. above), which again involves the large-scale provision of medication. It will be managed by WHO but will involve collaboration with other interested bodies and will solicit funding from other sources.

- Last but by no means least, *non-profit international wholesaling* has become prominent. The *International Dispensary Association* (IDA) in The Netherlands, established more than thirty years ago as a purely idealistic venture, has become a very large global supplier of medicines to the public health sector in developing countries. The supplies are obtained from low-cost sources, undergo rigorous quality testing, and are then supplied to developing countries either directly or through development programmes. A number of other similar non-profit intermediaries exist, particularly some (such as MISSIONPHARM in Denmark) working primarily for missionary health organizations.

The number of initiatives concerned with access to medicines has continued to increase during the period of work of the Task Force and this process seems likely to continue. In November 2003, during the compilation of this report, the Canadian government announced its own parliamentary initiative to provide low-cost generic medicines to poor populations in the developing world, particularly in areas suffering from pandemic infection. Shortly thereafter the South African Government announced its intention to provide appropriate medicines to all patients with HIV/AIDS.

1.5.4. *The situation and perspective of the pharmaceutical industry*

In line with its mandate, referring to cooperation with the pharmaceutical industry, the Task Force has examined the role which the pharmaceutical industry and trade can reasonably be expected to play in developing access to essential medicines. (Millennium Declaration, 2000). In doing so it is been necessary to recognize that the industry is very far from being a homogenous entity. It has various distinct components and it is necessary to consider each of them separately.

- The *research-based pharmaceutical industry*, largely composed of multinational corporations based in western countries, is the most widely recognized of these components and has been the most active in public debate and lobbying. Its importance in the western economy and its role in the introduction of new medicines have accorded it a strong role in public and political debate. Through its national and international bodies, the research based industry has expressed its commitment to serving the public interest through a chain of activities ranging from pharmaceutical innovation to the production and supply of high-quality medicines and the dissemination of prescribing information and advice. On the other hand, the industry

has its critics; insofar as developing countries are concerned the criticism relates among other things to:

- the western-orientated spectrum of innovation (see section 2.2.1 below)
- the high prices generally demanded by the innovative industry for its products (section 2.3.3)
- the high proportion of its earnings which the industry devotes to promotion and administration rather than research¹
- various means used by some innovative manufacturers to extend the protection of their intellectual property beyond the normal period of patent validity or otherwise impede the introduction of low-cost generic equivalents.²
- the generally very meagre access to these branded products in developing countries outside the upper-class urban environment (see section 2.2.5).

At the global level, the relationship between public sector organizations and the research-based part of industry has developed progressively though irregularly. When WHO created its essential drugs initiative in the late 'seventies the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) "lobbied national governments and international organizations to express its disapproval of the essential drugs concept" (Mamdani 1992). The Federation believed that the initiative represented an attempt to curtail its freedom of action in the production and marketing of its products, and declared that it was "completely unacceptable to the pharmaceutical industry". (Scrip, 1977). Only over the course of some 15 years did the industrial view become more positive. Hopes of a steadily developing partnership were however unhappily again deranged in 2000-2001 when major research-based firms took legal action against the South African government because of its attempt to make low-cost generic medicines available to the poor³ (Banta 2001). On the positive side of the equation one can note a certain number of initiatives by single firms or groups of companies to meet the developing world at least halfway on issues of price; one may also note the financial support provided by various corporations to global ventures to tackle the burden of disease (Table 2)

The notion of a fruitful partnership between international public ventures in this field and the multinational industry can be a healthy development provided it does not involve compromising the public interest, which need not be the case. The research-based industry is a powerful and highly successful entity, with a creditable innovative record, which inevitably and properly places its own interests and those of its shareholders first. "Partnership" at its best can mean *firstly* that this part of the pharmaceutical industry can assist the public sector in identifying ways in which progress towards the essential goal of access to medicines can benefit from private and

¹The National Institute for Health Care Management has raised the issue of "Finding the Right Balance Between Access and Innovation" in this field (NIHCM 2000)

²These methods include claims to proprietary rights in scientific data (see section 2.2.above) and technical enhancement of the original products so as to extend the patent period. (See NIHCM 2000; also MSF 2003a). Proposals for Free Trade Areas, in the Americas and elsewhere, currently embody provisions severely limiting the right of countries to issue compulsory licences on pharmaceuticals (MSF 2003b)

³After widespread protest the action was withdrawn in April 2001.

competitive initiatives, and *secondly* that industry itself can find approaches to the market which serve the broad public interest in a manner which is compatible with the maintenance and expansion of its business. It is clear that in recent years various major research-based pharmaceutical companies have either developed or accepted new approaches to such matters as sharply differentiated pricing by virtue of which they can serve both rich and poor communities.

The second component of the pharmaceutical industry *comprises firms specialized in the manufacture of generic products*, i.e. medicines on which the original patent have expired and which can therefore be made and sold by any firm.¹,[□] Since the prices of these products are as a rule considerably lower than those of the original specialities on which they are based, the relationship between the research-based industry and the generic firms has often been an uneasy and often hostile one. The fact that generic medicines have sometimes been manufactured to poor quality standards has inspired attempts to persuade the professions and the public that these are cheaply made and untrustworthy products, which in fact is today rarely the case where major generic suppliers are concerned. Based in part in western countries and in part in Asia and Latin America, the "generic" industry is today a major player, and in much of the world its products are more widespread than those of the research-based industry.

A third component of the pharmaceutical industry comprises *manufacturing firms in countries at a low level of development*, operating either independently or under state control to serve purely national needs. In essence these are simply generic firms but they merit separate consideration because they are generally smaller and often operate with some form of state subsidy (e.g. acceptance of somewhat higher prices than would be tolerated from a foreign supplier). Public manufacturing facilities were here often

¹It should be noted that some research-based firms in fact have "generic" departments or have created or acquired generic manufacturing subsidiaries.

□The definition of a generic drug employed here by the Task Force is in line with that in general use and used in Laurence DR and Carpenter JR (1998): A Dictionary of Pharmacology and Allied Topics (Elsevier, Amsterdam). For the research based sector of the pharmaceutical industry, Ms Susan Crowley, Member of the Task Force, has submitted the following note: "Throughout the text, the term "generic drugs" is used. Had there been closer consultation with innovative companies in the drafting, the confusion round this term might have been lifted. When the term "generic" drug is being referred to, it should be noted that they are, in most case, untested and unapproved copies of innovator drugs. Under AAI, some 80,000 AIDS patients are being treated with innovator ARVs that are competitive with copy ARVs. Amb. Tobias pointed this out in a Senate hearing on November 12. The term "generic" is further diluted when stating: "where new brands or generic equivalents of established medicines are concerned, agencies should limit their requirements as proof of bioequivalence". In many of the AIDS-infected countries, patients present with multiple co-morbidities, chief among these are diarrheal diseases. In such cases, bioavailability, the rate at which an ARM is absorbed in the gut, is of great importance to patient outcome. The report states regarding generics that attempts have been inspired to persuade the public that these are ...untrustworthy products which is in fact today rarely the case". This is a true statement in Europe and the US where generics are manufactured to FDA or EMEA standards. It is untrue in most every other part of the world. For instance, it was not until July 2003 that the first locally produced, similar (Copy) ARV was submitted for certification under Brazil's 1996 Generic Law. "Generics" duly approved by competent agencies should be differentiated from "copies" or "Similares" in the text." (end of statement)

created for political or strategic reasons. Manufacturing in these countries is often severely hampered by the fact that virtually all starting materials and equipment have to be imported and that their turnover is small; as a result they can have difficulty in competing in terms of cost and quality with generic manufacturers abroad. The future significance of national manufacturing in countries at a low level of development will need to be carefully considered. Arguments for maintaining at least some of these facilities include:

- the ability to produce simple bulk products where international transport costs can be prohibitive (e. g. intravenous fluids)
- the ability to produce indigenous (traditional) medicines
- the value of a production plant as an educational and research centre, e.g. to facilitate pharmacy training.

In very general terms, the Task Force has the impression that true partnership with these various segments of industry is necessary and is likely to be productive. Together with the innovating industry a number of the issues on which the industry has been criticized need to be debated and resolved. In partnership with the generic industry the community could work towards the creation and imposition of an industry-wide accreditation scheme for quality standards, supplementing the prequalification project already operating within WHO.

Table 1
Elements essential to ensuring Access to Medicines
and principal sources of failure

Element	Principal causes of failure
<i>AVAILABILITY</i>	
Relevant innovation	Innovation directed mainly to profitable markets, not to developing countries. Studies of effects in women and children in LDC conditions often missing
Production	Medicines for small patient groups unremunerative to manufacture
Importation	Medicine unaffordable for poor nations at world market prices Medicine needs overlooked/ignored by public or private sector importers
Entry	Regulatory obstacles - medicine not approved nationally Prohibitive import duties; delays at customs (expiry)
Nationwide distribution	<i>Private sector:</i> Little distribution outside cities <i>Public sector:</i> Inefficiency, corruption, theft, poor storage (expiry) Lack of transport. Inefficient ordering routines
Adequate quality	Failure to ensure quality of supplies at the procurement stage Lack of a national laboratory or of sampling routines Circulation of counterfeit medicines
Stable situation	Civil conflict
<i>B. AFFORDABILITY</i>	
Procurement	Lack of foreign exchange; inappropriately allocated state budget Prohibitive world prices Lack of negotiating power
Price prohibitive for user	Monopoly prices for patented medicines Inability of health system to subsidize end price Excessive retail/wholesale margins Women/mothers lack adequate family funding
<i>C. APPROPRIATENESS</i>	
Appropriate procurement	<i>Public sector:</i> Inadequate guidance from the field on needs Inexpert procurement staff <i>Private sector:</i> Overemphasis on profitable items
Appropriate donations	Donations guided by donor self-interest or lack of understanding of the field
Appropriate distribution	Lack of data on varying needs of regions, epidemic incidence etc.
Prescribing standards	Lack of education or guidance for prescriber Misunderstandings regarding generic quality Expensive prescribing where this benefits prescriber Misleading advertising to professionals; commercial inducements.

Incorrect use in the home	Lack of information from prescriber/dispenser Foreign language packaging Fear, misunderstandings regarding medicines and their use Illiteracy; general lack of education, especially women Gender power relationships within the home Misleading advertising to the public.
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2. Access and barriers to access: a framework for discussion

2.1. Outline of elements essential to ensuring access to medicines.

There are various ways of defining the elements essential to ensuring access to medicines. WHO has recognised four of them:

- (i) affordable prices
- (ii) sustainable finance
- (iii) rational selection and use
- (iv) reliable systems of medicine supply and health care (WHO 2000c, WHO 2000e)

Put another way, one could say simply that medicinal treatment can only fairly be regarded as accessible to a given population or individual if it is *available, affordable and appropriate* (Yuanli Liu, 2002). Each of these three elements for access requires some further definition. For purposes of discussion a more complete analysis of these three elements and their subcomponents is provided in the accompanying Table 1.¹ Where access to medicines is unsatisfactory one finds as a rule that more than one of these elements or components are missing or are deficient. This is well illustrated in Figure 1, showing how the cumulative effect of failures in the system at various levels may be the wastage of a very high proportion of the available resources. The various types of problem which can arise, as defined below, are not theoretical: each can be illustrated by numerous examples from the field, though their relative importance varies from country to country.

Before considering any of the individual barriers to access it is fair to make briefly the point that, in many of these matters, the two fundamental obstacles are a lack of *finance* and a lack of *appropriate human resources*.

As regards *finance*, the problem lies in part at the national level, but also in the inadequacy of international support. While echoing fully the general recommendation of the Commission on Macroeconomics and Health (CMH 2001) and others (Trouillier 2002) regarding the need for a drastic increase in the level of aid provided in the health field to developing countries, the Task Force has noted the difficulty which currently exists in obtaining a clear overview of the current level of assistance with respect to medicines because of a lack of coordination and transparency (see also 5.1.4. below).[□] In the

¹It must be noted that the separation of these components and subcomponents is somewhat artificial since they can interact.

[□] The sheer number of international organizations of various types committed to pressing the case for improved access to medicines is evident from Table 2. Some appear capable of achieving a great deal because of the manpower and financial resources which they have already acquired. Others appear to be developing strategies but with no assured funding to implement them. In some cases these bodies have acquired much less in the way of philanthropic funding than had been anticipated. There is also some reason to fear that these bodies are in a sense competing with one another and with established donor agencies for funding, and that acceleration on the one front could therefore be accompanied by retardation on the other. The emergent "AIDS Medicines and Diagnostics Facility" within WHO (Everard 2003), if it develops as anticipated, could perhaps provide a model for such coordination, as could the existing inter-agency coordination group for pharmaceutical issues. (IAPCG 2000)

medicines sector, as in others, there is however a clear need for a substantial increase in donor funding and investment, with a substantial part of international support being devoted to improvement of the infrastructure and to capacity building rather than to short-term relief or emergency supplies. In parallel with this and at the national level there is a need for states to quantify their needs for medicines and the extent of the shortfall in meeting those needs from national resources, so that well-documented requests for support can be laid before the world community. Finally, as noted in Section 1.5.1. above, promises made with respect to international aid need to be kept.

The development of *human resources* is as vital as the provision of goods. At all levels ranging from procurement to rational use one is heavily dependent upon staff who are properly trained and who are sufficiently motivated and rewarded to ensure that they are retained and perform conscientiously. Corruption, inefficiency and managerial weakness in the public sector will only be effectively be relieved when the government service is sufficiently well financed. Here as in other fields priorities have to be set if limited resources are to be used to the best advantage, and unorthodox solutions may need to be applied.¹

Finally, the Task Force would point to the difficulties which currently exist in measuring access to drugs in a consistent manner. Experimental approaches are currently being developed and the Task Force will return to the matter in its Final Report in 2004. The essential problem is to find measures which truly reflect the extent to which barriers today, in daily practice, impede access to needed drugs, and to do so in a manner which renders possible comparisons between one country or situation and another.

2.2. Barriers relating to availability

2.2.1. *Failure to Innovate*

A medicinal substance which is required must *exist*. A fundamental problem is that the medicinal treatments required for many purposes do not exist and that, in the case of diseases prevalent in developing countries, therapeutic innovation has largely been lacking. (MSF 2001) This in turn reflects the fact that industrial research has been preponderantly directed towards treatments for diseases of the western world, including the diseases associated with affluence. (Trouillier 2002) Even where the

¹In East Timor shortly after independence the number of physicians available to serve a population of 800,000 was negligible. Practical nurses with an elementary training were handling both diagnosis and treatment. A specially adapted handbook was therefore devised to assist them in performing this task as well as possible without the need for frequent referral. (Dukes, field report 2001).

In many developing countries, poorly paid health workers are found to be earning money by levying charges on the medicines which they issue to patients; rather than attempting to prohibit this practice it sometimes proves better to regularize it so that modest fixed charges (insufficient to themselves comprise a barrier to access) can be made in order to provide the health worker with a living wage.

basic discovery has been made in an academic institution it may fail to be developed if the pharmaceutical industry cannot identify a large and resourceful market for it. It has been estimated by Byström *et al* that between 1975 and 1997, only 13 of 1223 new chemical entities found to have useful pharmacological properties were for the treatment of diseases predominantly prevalent in poor countries (Byström 2001); very similar estimates have been made by others. (e.g. Yamey 2002, Trouillier 2002) It is beyond doubt that this is a market phenomenon: it is a great deal more profitable for a pharmaceutical company to seek to develop and sell new medicines to treat, for example, obesity or the disorders of old age in the North than agents to treat kala azar or Chagas' disease in the South. Examining the failure to develop drugs for neglected diseases, Trouillier *et al* have spoken of "a deficient market and a public health policy failure." (Trouillier 2002).

The need for new medicines relates only in part to conditions which are at present untreatable. A much more extensive need in terms of numbers of potential users is for new medicines to supplement or replace those to which microorganisms have become resistant, as is notably the case in malaria¹ and tuberculosis. A complementary approach to the resistance problem is to delay its extension by developing and employing novel combinations of drugs, but these combinations too require proper investigation before they can be accepted and used, and again there is little commercial incentive to study them.

2.2.2. *Failure to produce*

Even medicines which have been developed may not be in production if this is considered unremunerative.² Some medicines developed virtually to the point of application are then abandoned, while others are discontinued because of disappointing sales (see section 2.2.4 below)

2.2.3. *Failure to procure or import*

In the public sector, procurement of medicines may be either insufficient because of lack of resources(see 2.3.1. below) or frankly inappropriate. The latter can result from lack of information from the field on current needs, either nationally or within the districts. Drug Utilization Studies providing sufficient data to guide procurement are everywhere needed and in approximate form they are relatively simple to carry out using readily available data (WHO/EURO 1993). Technical support in this field can be provided by the various regional Drug Utilization Research Groups sponsored by WHO.

¹The mainstays of malaria treatment in the past have been chloroquine and sulfadoxine-pyrimethamine, both of which are available at negligible cost. The former is however no longer effective against *Plasmodium falciparum* in most tropical areas, and resistance to the latter is now very widespread. There are certain alternative drugs but their current cost puts them financially out of reach of entire populations. See White 1999 and Attaran 2003.

²An overview compiled by MSF in 1999 provided a series of examples. In the case of African trypanosomiasis, which leads to some 40,000 deaths annually, the supply of all four applicable medicines had either ceased (eflorinthine Hcl) or become insecure (suramin Na, melarsoprol, pentamidine isethionate) because of lack of commercial interest in production. (Pécoul 1999).

In the private sector, one finds that some medicines are inaccessible for a given country because there is no commercial channel able or willing to *import* them; again the motive is that these are medicines which would be used predominantly by poor rural populations who do not represent a viable market. Procurement by a state agency will be an alternative but only if funding is available and correct choices are made.

2.2.4. Regulatory and fiscal obstacles

(i) *Regulatory requirements* Technical regulatory systems in the field of medicines are and remain essential as a means of ensuring that medicines entering the market attain the necessary standards of efficacy, quality and safety and that the information provided with them is sufficient and reliable. In certain areas of the world (most notably the European Union) collaboration between agencies has been established and has progressed towards regional regulation. In theory, regulation should not constitute a barrier against access to *bona fide* medicines but in some circumstances it can do so; bureaucratic delays can occur or excessive demands may be imposed. In particular, when a new brand (or generic equivalent) of an existing medicine seeks to enter the market an agency may on occasion demand extensive research and/or documentation from the manufacturer despite the fact that it is a known product, for which it should be sufficient to demonstrate that it is essentially equivalent to that already on sale. So long as the original product has been available for a number of years, public evidence of its efficacy and safety will as a rule be available in the journals, and the question of misuse of proprietary data will therefore not be relevant. A restrictive approach may however be actively encouraged or demanded by the original manufacturer, advancing a claim of “data exclusivity”. Such claims are based on the view that the scientific basis for the approval of the original product is the property of the originator and that others should not be allowed to benefit from it.¹ If accepted, this policy would impede the entry of low-cost generic products to the market or obliging their manufacturers to repeat the original studies in animals and man (EGA 2003). In fact the relevant regulations of most countries do allow for the simplified approval of new brands or sources of an existing medicinal product provided the published literature acknowledges the latter’s efficacy and safety, and provided that the new version is essentially equivalent to that marketed earlier.

What “essentially equivalent” means is a subject of debate and will be further considered by the Task Force and Working Group. Some agencies have regarded “pharmaceutical equivalence” as a sufficient criterion (e.g. similar disintegration rate of tablets in gastric juice) but at least in those instances where the therapeutic margin is narrow it seems necessary that bioequivalence be demonstrated. This latter view, in a more extreme form, has been formulated for the Working Group on behalf of the research-based industry as follows:

“Bioequivalence is an important aspect of drug quality worldwide because how the human body absorbs a pharmaceutical product (“bioavailability”), and how that product then affects the body, is vital for determining the drug’s effectiveness. Even two products which may look the same *in-vitro* may, in practice, have significantly different effects when taken. Thus, effective treatment of a disease or condition will depend greatly on the bio-availability of a drug and therefore, if a copy is used instead of the original product, the copy product must meet standards of bioequivalence compared with the original.

¹This view is in direct conflict with the opinion that knowledge of this type constitutes a “global public good” in which no exclusive rights can exist. See Kaul 2000.

For these reasons, it is important for regulatory officials to insist upon valid and rigorous tests of bioequivalence when considering the registration of a copy of an existing product. Experience has shown that in-vitro tests are not sufficient in determining the efficacy of a new product. For this reason, leading developing countries such as Argentina and Brazil are promoting the registration of bioequivalent generic copies and moving away from the *similares*, which are copy products which had demonstrated only in-vitro similarity. Indeed, in these countries (and many other developing countries), *similares* may not be called “generics”, as this term is reserved for bioequivalent copies. Bioequivalence is also required in industrialized country markets, of course.

Our industry is firmly committed to one standard of quality for our products worldwide – we do not believe that people living in developing countries are second-class citizens deserving only of second-class products. Indeed, our companies are committed to helping improve access to products, which meet objective, internationally recognized standards of safety, quality and efficacy, including bioequivalence. The public health of people around the world, including in developing countries, deserves nothing less.” □

A related obstacle may be the claim that a generic manufacturer has no right, during the life of a patent, to make active technical preparations for manufacture following patent expiry. This type of claim can in principle be countered by making use of the so-called Bolar provision of the TRIPS Agreement which permits such preparatory work to be performed, thereby avoiding further delay in the introduction of a generic equivalent.

(ii) *Import duties or taxes*, imposed by another government department may lay an excessive burden on medical supplies. Delays at customs can also mean that medicines lie unused for long periods in port facilities, sometimes actually expiring during this time because of unfavourable storage conditions.

2.2.5. *Problems with distribution*

Medicines entering a country may be reasonably accessible only in urban centres because of lack of a countrywide distribution system, which is able to handle them. Private distribution systems (through wholesalers and pharmacies) operate in many developing countries only in urban areas. Public systems, set up in order to provide national coverage, often experience chronic or incidental problems: management and ordering routines may be poor, transport networks may be irregular or incomplete, (especially in areas with poor communications) and losses may occur due to poor storage (expiry, damage by damp or heat), theft or corrupt practices at one level or another. In all these various areas, lack of qualified and dependable staff is a major problem.

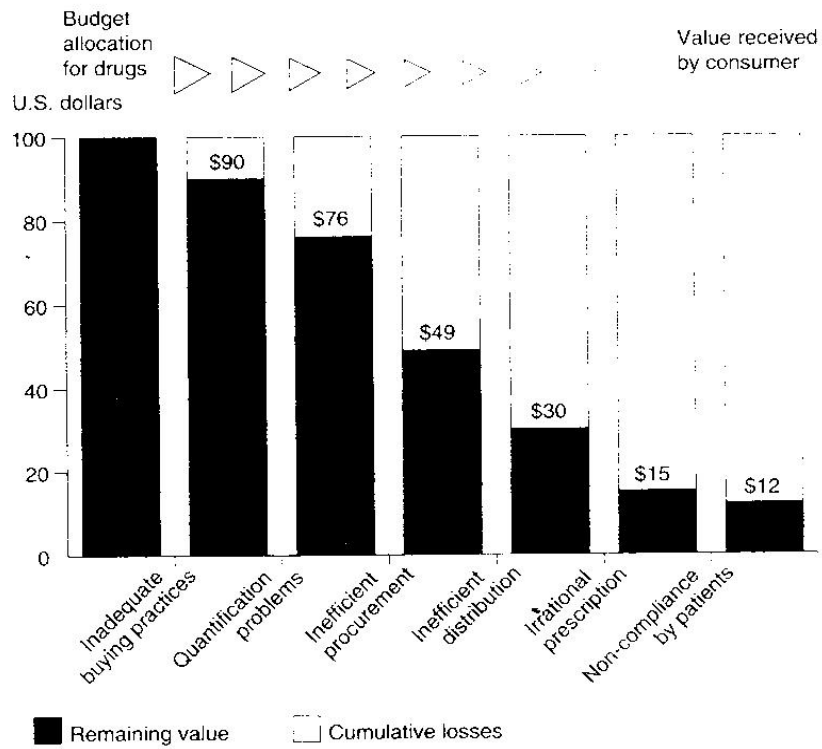
A realistic interpretation of the duties of a national government in this field is that it must ensure that there are effective means of supplying and distributing medicines to the entire population. There is no valid dogma to the effect that medicinal products can better be supplied through the public than through the private sector or *vice versa*. In many countries the two co-exist; sometimes the one has grown up because of defects in the other. The entire balance between private and public operation must be subject to ongoing review, and the system of control adjusted as necessary to counter shortcomings identified in the system. Where a public supply system is proving unsatisfactory, the possibility of transferring operations to the private sector, or

□ Susan Crowley, Merck Inc. (Member of the Working Group)

subcontracting certain tasks (e.g. procurement, transport, administration) to the latter may need to be considered.

FIGURE 1

**Drug funding and supply: cumulative effects of system failure at various levels
(World Bank, 1994)**



2.2.6. *Issues of quality*

It is evident that if a medicinal product is of poor quality it cannot realistically be regarded as accessible. Quality assurance is to a large extent possible at the stages of registration and procurement, and many countries do maintain their own quality control laboratories of varying size and competence, particularly in order to check suspect samples from the field. A problem from the global point of view is that the experiences of agencies in this matter are not generally published, and it is difficult to determine how watertight the methods in use are (Kaplan 2002, Kaplan 2003). The same applies to some excellent studies of the matter known to have been conducted by bilateral aid agencies. Certainly however there is abundant evidence that widespread quality problems persist even where life-saving medicines are concerned (e.g. anti-malarials in Africa). (WHO 2003c).

There can also be some difference of view on the quality standards to be applied. Standards for older drugs are usually to be found in national pharmacopoeias, and during the last twenty years the concept of Standards of Good Manufacturing Practice (supported by WHO) has come into use. There are however higher standards, such as those propagated primarily through the International Conference on Harmonization (ICH) in which the research-based industry collaborates with the regulatory agencies of some major industrialized countries. The latter standards are justified in certain specific situations¹, but they are complex and costly and have been criticized as unnecessarily strict.

One may also encounter situations at the present day where a generally reputable supplier, while working towards GMP standards, has not yet attained them. Of the many thousands of medicinal manufacturing plants which currently exist throughout the world only a minority are as yet producing medicines to GMP standards and many more must be induced to do so. This will only be achieved if procurement agencies are firm in insisting on these standards as a condition of purchase. Where these standards have not yet been attained, the decision will have to be taken from case to case whether a particular product or supplier offering lesser standards can as a temporary measure be regarded as tolerable. Much will depend here on the nature of the medicine concerned; no flexibility can be allowed for medicines with a narrow therapeutic margin (i.e. where the effective dose is only slightly less than the toxic dose) but some flexibility may be tolerated for certain simple remedies with a broad safety margin.

2.2.7. *The challenge of sub-standard and counterfeit drugs*

“Sub-standard drugs”, is a term applied to those medicinal products which prove to be a seriously inadequate standard of quality because of negligence or dishonesty on the part of the manufacturer. While sound procurement practice can counter this problem to an important extent, constant vigilance is needed once a medicine has been

¹There are a small number of medicines the toxic dose of which is only slightly higher than the dose normally used in treatment (e.g. digitalis used in heart disorders). For these substances and their pharmaceutical forms exceptionally high standards have to be maintained. See also section 2.2.6. above.

procured or admitted to the market since standards may otherwise in some cases fall appreciably.¹

Even more serious is the phenomenon of spurious and counterfeit medicines; these are as a rule superficial copies of well-known items but having little or no content of the active component. Often originating at unknown sources they represent a major danger to public health, as well as depriving the public of access to genuine treatment.

2.2.8. *Issues of civil stability*

In a stable civil situation the supply of medicines can evolve progressively as funding, infrastructure and experience permit. Medicine access has however very frequently been deranged by war and insurrection, while in some instances severe obstacles to progress have been raised by those intolerant of change.² In such situations, emergency aid in the form of donated or heavily subsidised medicinal supplies may for a considerable time be the only means of maintaining even a modicum of access.

2.3. Barriers relating to affordability

By far the most serious and challenging obstacle to access to drugs in poor populations and countries is that posed by their price. Whether the price of a medicine be reasonable or unreasonable from the point of view of a manufacturer or supplier, if the patient or health system cannot afford it then it will not be bought and used.

Evidence of the role of price in obstructing access to drugs is abundant and beyond dispute, though much of it has, strictly speaking, until now been anecdotal. Fortunately much work has now been undertaken to obtain exact data on the prices which are actually being charged and paid for medicines in a given environment; (WHO/HAI, 2003); the same type of investigation can also provide valuable data on the level of availability and the reliability of supplies of medicines over time. Such exact data are essential in devising and implementing policies. However important astute procurement may be in countering excessive price levels, it has not of itself prevented situations arising in which the prices of important medicines put them entirely out of reach of most potential users. In the year 2000, for example, the costs of using didanosine for HIV/AIDS in the Ivory Coast amounted to US\$ 3.48 per patient day, yet the GNP per head of population was only \$1.94 per day and the health services were only able to make a contribution to the cost equivalent to some \$0.03 daily.³ (Mossialos, 2001).

¹During an epidemic of meningitis involving 41,000 cases in Niger in 1995, the country was promised a donation of 88,000 vaccine doses from Nigeria, with Pasteur Mérieux and SKB as manufacturers. In fact the vaccines were found to have been replaced on the way with spurious copies containing no active ingredient but with labelling meticulously copied from the original. (Pinel 1997).

²The creation of a low-cost Essential Drugs Programme in Yemen was viewed by some parties as a threat to the income enjoyed by private sellers of medicines. The programme was disrupted in 2001 when threats to the life of the expatriate coordinator necessitated his withdrawal. (Weeda G., personal information; also press cuttings, 1998)

³Curiously, the argument has sometimes been advanced that high prices are not an impediment to medicinal access in the developing world. The striking effects on consumption

The issue of affordability can best be considered at two levels, though they are obviously interlinked.

2.3.1. *Resources for procurement*

A medicine must be affordable for the *nation*. Foreign exchange is often too limited to allow for adequate purchases in this field, or the government may allocate too small a portion of its foreign exchange reserves to the health sector generally. However the world market prices of many medicines, especially those supplied only by research-based companies, are attuned to the purchasing power of wealthy nations, and may be out of reach of even moderately poor countries. This issue is considered in detail in later sections of this report since it raises issues of pricing on the one hand and financing on the other.

2.3.2. *Affordability for the individual*

Whatever the prices at which medicines are procured, they are still likely to be out of reach of many consumers in poor countries. The state of internal government finance in many developing countries is too parlous to permit subsidizing pharmaceuticals when they are supplied to the population at large or providing them entirely free of charge to patients with no significant family income. The cost of using medicines in these countries thus devolves very heavily on the individual, and if he or she cannot meet the costs the products will not be purchased at all or will be bought in small quantities inadequate to serve their purpose, and perhaps doing more harm than good, e.g. by inducing bacterial resistance. (WHO 1998)

In this connection, *gender issues* can be very relevant. It has truly been said that “the mother is the most important health worker for her children” (Schultz 1989). This means, among other things, that it is the wives and mothers who as a rule buy medicines for their entire family, and within a family the mother may not be allocated a sufficient part of the limited family funds to cover these prices or dispensing fees charged. These issues are being considered further by the Working Group in consultation with Task Force 3 (Primary Education and Gender Equality) and will be considered more extensively in the final report.

In seeking to solve the issue of affordability of drugs for the individual, three complementary approaches need to be examined in parallel:

- the attainment of sustainable prices which are no higher than is reasonably justifiable
- the development of some degree of state financing of medicine supplies, particularly for the very poor and indigent
- the creation of some form of public contribution to the costs of medication insofar as this can alleviate the burden on the patient in times of illness; some

when prices are drastically reduced (for example in the Brazilian AIDS initiative) seem to have discredited that view, quite apart from other evidence, and it will not be further considered in this report.

Examples of gross discrepancies between global prices of medicines and the ability of poor individuals to pay are numerous; see for example Mossialos 2001.

form of insurance, pre-payment or user fee may be appropriate but only where this does not itself create a new barrier to access.

The extent to which each of these approaches contributes to access will vary with the situation studied.

2.3.3. *Problems posed by issues of intellectual property rights¹*

Particularly in the case of newer pharmaceuticals, the high prices charged by the originating company and referred to under 2.3.1. above can present an insuperable problem both for the country and the individual patient. The originating company holds a patent on the product and there is therefore no alternative and cheaper form of supply so long as the patent remains valid. The existence of patents in this and other fields of scientific discovery is in itself defensible. It has been recognised for centuries - and is today virtually unquestioned - that, if enterprise and innovation are to be encouraged, the innovator must be in a position to exploit his discovery so as to reap his due reward and finance future innovative work. To this end, the issuing of a patent on the discovery, e.g. for a period of 20 years, provides him with protection from competitors seeking to use his discovery to their own financial advantage. In general, the patent system works well in that the inventor will have every reason to make his discovery widely available to the community through production and licensing; it will therefore benefit both himself and society generally.

There are however some situations in which checks and balances on the patent system are needed. In a world where wealth is so unevenly distributed it will often prove tempting to an innovator to maximalise and accelerate his financial return by selling his product at a high unit price. Whilst at this price only the world's wealthier populations will be able to afford, these populations (which include affluent urban groups in developing countries) are the most readily reached through established channels for distribution, publicity and banking (Mossialos 2001). This situation, in which poor populations may not have access to an innovation for many years, is of no great social consequence if the new product is for example in the leisure and luxury class, but it can have grave consequences where the innovation confers major benefits, as can be the case with certain new medicines.

In the past, the most severe consequences of this situation could in part be avoided because many countries at a lower level of development had no comprehensive national systems of patents. It was therefore possible for low-cost copies of the innovative medicine to be manufactured and traded by secondary firms both in and between such countries. This situation began to change with the initiatives taken when establishing the World Trade Organization to create a watertight worldwide network for patent protection of inventions of all types, notably through the "TRIPS" Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS 1994; Drahos 2002). The Agreement in fact embodies a number of provisions for exceptions to be made to its rules in matters affecting health or in national emergencies, and allows for compulsory licensing. However, the interpretation of

¹For documentation see in particular the British report on Intellectual Property Rights: CIPR 2002.

these provisions in the field of medicines has been a matter of dispute since the Agreement was concluded. The issue is further considered under section 4.1.3. below.

Whatever the ultimate approach to the patent issue and TRIPS, it seems certain that developing countries and poor populations will for a long time to come be primarily dependent for their medicinal supplies on generic items. While the Task Force appreciates that the costs of maintaining the operations of research-based innovative firms must ultimately be borne by the world community, it would seem no less than equitable that those expenses should be borne primarily by the nations with the broadest shoulders, i.e. western industrialized countries with a strong economy which are capable of paying relatively high prices for the medicines which they require.¹

The maintenance of a generic policy will involve measures both at the level of procurement, manufacturing and prescribing and will have to surmount the obstacles represented by the TRIPS Agreement, Regional Free Trade Agreements and claims of data exclusivity considered elsewhere in this report.

2.4. Barriers relating to appropriateness

The fact that medicines are sometimes inappropriately used is not a marginal phenomenon. As noted in Figure 1, when the World Bank reviewed the causes of waste in the medicines field in Africa, it suggested that for every thirty dollars of medicines reaching the periphery fifteen dollars were squandered as a result of poor prescribing, and a further three dollars as a result of non-compliance by the patient. (World Bank 1994).

Inappropriate use leads not only to waste; it can also result in injury. In infectious disorders, such as malaria, it can also result in a massive increase in resistance to treatment. In one study in Tanzania, 75% of health workers were found to be dispensing sub-therapeutic doses to stretch inadequate state funding, (Mnyika 1991) a practice which is notoriously prone to induce resistance.

Inappropriate use of pharmaceuticals can result from failure at the macro or micro level.

2.4.1. Problems at the macro level

Inappropriate choices may be made in the course of *public procurement* (e.g. because of inadequacy of data on current needs, or lack of expertise or sufficient funding), in giving and receiving *donations in kind* or in operating a public *distribution chain* (because of failure to recognize differences in regional and local requirements).

The issue of drug donations in kind made by pharmaceutical companies is a particularly controversial one. It has been argued that the process is inefficient and costly. In the present connection it is particularly relevant that the nature and timing of donations may be determined more by the interests of the donor (e.g. tax rebates

¹The fact that these wealthy nations are themselves to an increasing extent challenging the prices of medicines and seeking lower cost solutions for their domestic markets must be noted, but falls outside the scope of the present report.

obtained by donating drugs approaching their expiry date) than by the needs of the recipient (Guilloux 2000). There are repeated examples of donated supplies having been discarded because they are unusable (WHO 1999, MSF 2000).

Policies with respect to the *private sector* may similarly fail to ensure that this sector makes optimal use of the available foreign exchange by purchasing medicines that provide reasonable value for money and meet genuine health requirements.

2.4.2 *Inappropriate prescribing*

Even where a pharmaceutical reaches the periphery, appropriate treatment with it may be out of reach because of lack of knowledge or independence on the part of the prescriber (“inappropriate prescribing”). Inappropriateness may for example involve over- or underdosage, the use of several drugs where one would be sufficient, or the use of an entirely unsuitable agent (Pavin 2003). It can also involve the prescribing of an expensive speciality despite the fact that a virtually identical “generic” product is available free of charge or at fraction of the price. Both industrial persuasion on the one hand and poor experience with some generic products on the other often lead both prescribers and patients to believe that the expensive version of the medicine is bound to be more efficacious than that which is available at low cost or free of charge.¹

It is tempting at first sight to attribute much irrational prescribing to the fact that in much of the developing world prescribers commonly do not have a full medical training. While it is beyond doubt that basic training is commonly inadequate, this is not a sufficient explanation of the fact that remedies are poorly selected and applied. Bearing in mind that at the primary care level the number of “essential drugs” likely to be available and in regular use is quite small, it is not an impossible task to provide prescribers who have a basic education in nursing or as medical assistants with sufficient guidance to diagnose the most common conditions likely to be encountered and to prescribe with a reasonable degree of competence. Fully qualified prescribers, on the other hand, may prove to prescribe irrationally, especially where their prescribing is linked to an income from dispensing, which creates a temptation to overprescribe as a means of increasing earnings (Trap 2002).

Some excellent work has been done on examining the quality of prescribing in a particular country so that corrective action can be taken where necessary (Laing 2001, Pavin 2003). A simple method is a so-called “ABC” analysis of the medicines procured nationally, which is likely to point to certain gross faults in prescribing (MSH 1997), e.g. large scale turnover of an injectable antibiotic which is equally effective when given orally or the use of which is only rarely justified at all (Yemen 1986, Pavin 2003). One commonly finds that in a given country some data on prescribing are available from Ph. D. theses or work conducted by bilateral aid agencies. Supplementary evidence of faults in prescribing may be found in comparisons between orders received from comparable districts or institutions (which may point to over-consumption) Studies carried out in comparable countries can

¹See examples from the Philippines, Pakistan and Nigeria cited by Velásquez (1998)

suggest the type of fault likely to be encountered. More sophisticated methods for the study of prescribing include the establishment of a prescribing and patient care survey, using WHO's well-proven health care facility medicine use indicators (Hogerzeil 1993) and country progress indicators (WHO 2000f). Where sufficient resources are available, one may establish a series of periodic medicine-use surveys, e.g. as carried out biennially in Zimbabwe (Trap 1995) or monthly self-monitoring at health centres or district level, as developed successfully in an area of Indonesia. (Sunartono 1995).

In all these respects, however, it is necessary to consider carefully how much investment in research is justified before proceeding to action, particularly since some of the faults in the existing situation may be entirely obvious or may have been documented in previous studies. A particularly evident problem is the pressure which can be exerted by advertising, generally amounting to intensive persuasion to prescribe newer and more expensive remedies even in situations where these offer no advantages over older products available much more cheaply.

Realistic and cost-effective approaches for developing more rational prescribing have been documented (e.g. by Laing 2001b) although not all these have been tested under strictly controlled conditions. Measures to correct prescribing faults must involve both short and long-term efforts; some recognized approaches are summarized in the Appendix to this report and a considerable fund of experience is available through the International Network for Rational Use of Drugs (INRUD) which works in a range of developing countries as well as organizing training courses (INRUD 2002). Short-term approaches include the development of national Standard Treatment Guidelines (which can well be based on the numerous established handbooks of this type which exist), Formularies and Bulletins. There are many excellent publications of this type which can be adapted to national needs; where Medicines Bulletins are concerned, the International Society of Drug Bulletins is a valuable source of advice, support and draft texts.

Longer-term approaches to rational use must be based on the modification of basic medical teaching relating to medicines and prescribing; using well-tested university models and follow-up courses. A widely used curriculum model is that originally tested at the University of Groningen in The Netherlands and later adapted by WHO for international use (De Vries 1994). In hospitals and other institutions, Therapeutic Committees, with full participation of medical and pharmaceutical staff, appear to be capable of setting and maintaining good standards, both in order to improve patient care and economise on resources. The reorientation of the pharmaceutical profession can in some countries provide a promising new resource working towards the better use of medicines (see section 4.3.8.).

The Task Force would reiterate here a point touched on above to the effect that when seeking to influence prescriber behaviour it is essential to use means which will not be resented by those concerned; physicians in particular are most likely to be responsive to efforts to improve their standards of practice if these emanate, at least in part, from within their own profession instead of being imposed upon them. The creation of

Therapeutics Committees, noted above, is an important step in this direction. A national Medical Association and a Nursing Association should at least participate in the development of these approaches and should be encouraged progressively to assume responsibility for them.

In addition, the point must be made that when medical training is extended and upgraded efforts must be made to develop the professional's social skills as well as his technical abilities; in particular there is a need to develop skills in communication with patients, including the provision of facts and advice relating to medicines. Finally, the issue of advertising and promotion for medicines will need to be tackled, generally in line with international ethical standards but also taking into account the particular susceptibility to commercial persuasion which a population may have when it is exposed to these influences for the first time

2.4.3. Inappropriate use in the home

A medicine is not always used as instructed by the prescriber or indicated on the package (see Figure 1). The verbal instructions may not have been clear or they may have been misunderstood. The text on the package may be in a foreign language or the patient may be illiterate. Common misunderstandings ("two doses are better than one") may call for correction. *Gender issues*, already considered in part under 2.3.2, can also play a role in determining the extent to which medicines are used appropriately in the family. It is often the woman who brings home the medicines and often administers them. Women must thus have sufficient knowledge to select those medicines which are available without prescription, and to ensure that the medicines entering the home are used appropriately. Female education unfortunately in many countries leaves much to be desired.

As in the case of health professionals, it is necessary to envisage both short-term and long-term approaches to the population in order to promote the rational use of medicines

Short-term approaches can be constructed around the fact that irrational use commonly reflects generalized misunderstandings regarding the nature and use of medicines. Both poster campaigns in clinics and brief messages transmitted by radio and TV have proved effective in correcting some of these misconceptions. They can also encourage the user of medicines to actively seek the advice and information which he or she needs to understand the proper use of a medicament, especially where no written information is accessible or the user is illiterate.

In the longer-term the main solution must lie in improved standards of education, particularly where there is a need to correct a lag in progress in educating girls and women. The proper use of medicines should be a component of popular health education.

These efforts must be complemented by others, especially those concerned with the information provided to the purchaser of pharmaceuticals at the point of sale. Both

pharmacists and other medicine sellers need to become accustomed to providing information and advice to all customers purchasing medicines, whether on free sale or prescription. Finally, as noted in the Appendix, there needs to be an ongoing effort to involve the public and its representatives in developing better standards of medicine use and improved accessibility of information and advice to the individual patient.

3. The feasibility of providing access

3.1. Global trends towards a solution

The emergence of a broad movement to promote access to medicines in poor populations (section 1.4.3. above) is highly encouraging. New bodies have emerged to advance the cause. Activities within WHO or the bodies with which it is associated have continued to increase. Various multinational pharmaceutical companies have taken steps either to provide selected products at preferential prices to developing countries or even to supply selected medicines free of charge for specified purposes.¹ Not all these trends are significant, finance is still seriously insufficient and the overall situation is so complex as to be confusing but the current atmosphere is clearly conducive to further progress.

Impartial *guides to the sourcing and prices of medicines*² have proved of great value to procurement bodies at all levels and *should be maintained and developed*. Their compilation is labour-intensive, and additional financial support may be needed to ensure their continued viability and quality.

3.2. National trends towards a solution

Most developing countries have within the last decade taken measures to improve access to medicines, thought with varying degrees of success. The experience gained however strongly indicates that on all fronts progress is possible, and where both the initiatives and the results have been monitored, lessons emerge which can be applied elsewhere. A number of selected experiences are presented in Section 4 below.

3.3. Conclusions regarding feasibility

However serious the access problem, it has to be borne in mind that, on the evidence adduced by WHO (WHO 2000a) there has been a very substantial improvement in the accessibility of medicines over a period of twenty years,³ again suggesting, as do some national experiences, that many of the many problems in this field can with due effort be overcome. This optimistic view must however be tempered in some respects. Firstly, the world has apparently made most progress in countries and

¹Many different offers have been made by various pharmaceutical companies, each with particular conditions attached. MSF (Médecins sans Frontières) has taken the initiative of issuing periodic overviews of the special discount arrangements currently in force and the applicable conditions (see for example MSF 2002b)

²The three leading guides at this time comprise:

- The MSH/WHO *International Drug Price Indicator Guide*
- The UNICEF/MSF/WHO list of *Sources and prices of selected medicines and diagnostics for people living with HIV/AIDS*
- The periodic MSF overview of *current special offers by drug manufacturers* (discounts, donations etc.). (MSF 2002b)

³In 1977, 2.1 billion people had access to essential medicines; by 1997 the figure had risen to 3.8 billion. (WHO 2000e)

regions where the obstacles are least. Secondly, as noted already in Section 1.5.1. above, new problems have arisen since the original estimates were made - notably the HIV/AIDS epidemic - and they have rendered the overall goal more difficult to attain. A MSF team, reviewing the situation in 1999 published its paper under the title "Access to Essential Drugs in Poor Countries: a Lost Battle?" (Pécoul 1999). They concluded that:

"Access to essential drugs is a basic human right often denied to people in poor countries. However, it would serve no purpose to demand new public health or human rights in a manner that would suggest that such rights will soon become a reality. The current situation points to the opposite. For a great proportion of the world, health conditions are worsening, and without fundamental change in the pharmaceutical market, perspectives for improvement are not encouraging."

Since 1999 there have been some signs of change in the pharmaceutical market but there is no indication of a radical alteration in the overall situation. Some factors will aggravate the situation just as others alleviate it. Vigorous efforts to contain the problem should however at least enable it to be kept in check, thus opening the prospect of change for the better as the century progresses.

In assessing progress during the next two decades, it will be important to apply valid indicators for access, such as those developed by WHO (WHO 2000f). While one will need apply the more specific indicators in that list to evaluate most of the processes involved in access (see 2.1. above) the most valuable overall indicator of the degree of access must indicate the *proportion of the population with access to affordable essential medicines on a sustainable basis*. Since within a given country, the extent of access is likely to vary by district (and particularly between urban and rural areas) as well as by class, ethnicity, caste or gender the calculation should where possible also be applied to various areas and subgroups so as to detail the overall picture.

Various methods for the ongoing monitoring of access have been proposed. The Task Force is currently considering the most reliable means of calculating this overall access figure in a consistent manner so that more valid comparisons can be made between countries than has generally been possible to date.

3.4. Preconditions towards improving access

3.4.1. *Global preconditions*

While it can well be argued that access to medicines should be high on the agenda of the world community, it competes in fact with many other priorities, some of the most significant being the issue of international conflicts and the problem of terrorism. Only in a very exceptional situation, notably the world HIV/AIDS epidemic, does the issue of medicines come sufficiently to the fore to gain a fair measure of social and political support. At the same time, as pointed out in Section 2.2.8 above when discussing the internal situation of countries, situations of armed conflict seriously

derange the supply of medicines in particular countries and regions as facilities and stores are destroyed and donors and aid organizations withdraw. A major precondition for continuing and expanding global efforts to develop access to medicines is therefore the attainment of a greater measure of *international peace and security*.

A second prominent precondition is the *state of the global economy*. Despite the evidence considered above under 1.3. that one consequence of improved access can be a significant stimulus to economic development, paying for itself many times over, investment in health is still not sufficiently accepted at the global level as a significant tool to promote economic welfare and growth when resources are limited and other priorities present themselves. On the contrary, when the economy stagnates or contracts it is common to see health budgets reduced. It is not clear whether economic recession has been responsible for the failure to meet international commitments to provide assistance (Section 1.5.1), but it is likely to have played a role.

3.4.2. National preconditions

National health policies and systems are not always fully attuned to ensuring that medicines are indeed available, affordable or appropriate. A number of basic structural problems are often encountered which underlie the barriers to access catalogued in Section 2 of this report and render them impregnable. It is a precondition to successful access programme that all these fundamental defects be tackled. Some defects commonly encountered in the literature and in national or consultant reports are outlined below.

(i) *National medicines policy*

A balanced medicines policy is a necessary component of an overall health policy. Without it, one is likely to apply patchwork solutions to the problems which exist, with little prospect of long term improvement. The policy will need to be comprehensive and well planned; while being based on well-proven general principles it will have to be adapted to national needs; and its implementation will need to be monitored (WHO 2002e). One theoretical model of a national medicines policy is presented in Figure 2, showing the various components of such a policy and the manner in which they interact. This is a complex model yet one must be wary of adopting too simple an approach to the matter and thereby neglecting vital aspects. In many countries, for example, issues such as the prioritizing of marginalized or underprivileged groups will a distinct component of policy which is not even mentioned in this graphic example.

(ii) *Economic situation*

A weak national economy will not be rendered strong overnight, but if there is a realistic plan for economic development the country will have a much

greater ability to attract both donor funding and loans in a field such as health care and drug supply than if there is only the prospect of stagnation.¹

(iii) Priority setting and political will

The priority accorded to health issues and the associated supply of medicines will generally need to be raised. A Ministry of Health is not uncommonly among the weakest of government departments, the least capable of attracting a sufficient proportion of the state funds which are available. As at the global level, the link between medicines, health and economic growth (Section 1.3. above) has not always been appreciated or accepted as a component of practical policy.

(iv) Availability of expertise

Medicines policy is a specialised field, and while much of the expertise needed exists in the world at large it may not at first be available nationally. To create that expertise nationally, donor and loan aid needs to have a major ongoing training component which is fully institutionalized, otherwise a long-term situation of dependence may result; short-term training courses are helpful but not an adequate substitute. As noted elsewhere, the issue of expertise in drug procurement is especially critical. However in other areas such as rational drug use, quality control, the creation of a strong and independent medicines inspectorate, the study of drug utilization and the reorientation of the pharmacy profession the development of expertise can play an important role in bringing about improvement.

(v) Interdepartmental links

One consequence of the relative weakness of Ministries of Health (see above) is likely to be their inability to influence the policies of other departments, especially those dealing with import duties and taxation, where these adversely affect the flow of medicines. Similarly a Health Minister may be unable to influence basic medical or pharmaceutical training in university faculties or secure free radio time to disseminate messages to the public on the proper use of medicines.

(vi) Donor co-ordination

In the medicines field it is commonly the case that horizontal and vertical programmes exist alongside each other, sometimes resulting in duplication in one area and gaps in another. A number of governments have also preferred to negotiate with donors individually on medicines issues, apparently hoping in this way to obtain a larger volume of support. Donors and development banks may succeed in establishing mutual links but coordination only appears to be optimal where there is a broad and open development programme

¹The rapid inflow of donor funds for health and medicines into Uganda after the fall of the Amin regime and the restoration of a democratic regime with which donors could work constructively provides a classic example. (DMFA 1995)

involving the government and managed by it with the donors and banks as participants.

(vii) *Community participation*

Experience suggests that mobilization of public opinion, whether in organized form or not, is a major influence in determining government priorities in matters which directly affect the well-being of the individual. Formal consumer movements were slow to emerge in developing countries, as were fora for consultation between governments and the public on policy issues. The AIDS pandemic has done a great deal to mobilize the public will for change and create a determination to influence pressure on governments. In many countries it is also possible to identify natural opinion leaders who enjoy both authority and respect in the community, and some of these can play a valuable role in progressively influencing the public to attain and demand an improvement in the situation.

(viii) Monitoring

Ongoing feedback from the system at all levels will enable failures and impediments to access to be identified and corrected and progress measured. An independent inspectorate - capable not only of identifying problems but also of helping to correct them - is an important tool to this end. The inspectors should ideally be senior figures with their own personal experience in the area which they monitor, enjoying sufficient respect for their criticisms to be taken seriously and their proposals for change to be respected and adopted.

Table 2
Bodies with current or proposed involvement in promoting access to medicines in developing countries

BODY	MAIN AREAS OF INVOLVEMENT
National Governments (100+)	Policy/Regulation; ; Procurement; Financing; Rational Use; Industry policy
WHO (general activities within EDM)	Policy development; training; materials
World Bank, MAPS; Regional Banks	Financing of medicines supplies; capacity building, coordination
UNICEF/UNIPAC	Procurement; price guides
Other UN Agencies	UNIDO, UNCTAD (industry and trade); UNAIDS (AIDS support)
Regional Procurement Schemes (7-9)	Pooled procurement of medicines and vaccines for several countries
Médécins sans Frontières (MSF)	Policy development; information; innovation (DND); procurement
MSF Campaign for Access to Ess. Medicines	Multilateral lobby
Bilateral Donors (DK, UK, NL , US etc)	Policy development; financing of supplies
Non-profit intermediaries (IDA etc.)	Procurement with inbuilt quality control
Global Funds (TB, Malaria, AIDS)	Mobilizing funds, Aid to national procurement; Global procurement
Global Aids Alliance	Advocacy, Action Network
WHO Prequalification Scheme	Prequalification of suppliers, products etc. to assist national procurement
WHO/TDR (Tropical Diseases)	Promotion of research and management for tropical diseases.
WHO/MMV	Research into Medicines for Malaria
WHO AIDS Facility (AMF)	Market intelligence; buyers' group; global procurement if needed
WHO Green Light Committee (TB)	Guidance to nat. programmes for MDR-TB. Global price negotiations
Foundations (Rockefeller/ Gates/Carter etc)	Financing funds/initiatives; financing of supplies; price negotiations
Strategies for enhancing access to medicines	(SEAM); Multilateral policy support; policy research
Intern. AIDS vaccine initiative (IAVI)	Raising and distribution of funds for AIDS vaccine research
Global Alliance for TB Drug Development	Promotion of industrial/institutional research in this field
Management Sciences for Health (MSH)	Non-profit consultancy; rational pharmaceutical management; management of SEAM
Generic pharmaceutical firms	Worldwide supply of low-cost medicines
Research-based pharmaceutical firms	Differential pricing; special price agreements; innovative research Contributions to country and international programmes, e.g.. a. <i>TDR</i> : >\$800 million from the private sector b. <i>Accelerating Access Initiative</i> : supported by Abbott, Boehringer-Ingelheim, Bristol-Myers Squibb, Glaxo Smithkline, Merck and Roche. c. <i>MECTIZAN Donation Programme</i> : Supported by the Merck Company Foundation (more than one billion courses of treatment administered) d. <i>African Comprehensive AIDS Program</i> : Partnership with Merck Company Foundation, Gates Foundation, Enhancing Care Initiative (Harvard Medical School) e. <i>Secure the Future</i> : funded by Bristol-Myers-Squibb f. <i>International Trachoma Initiative</i> : funded by Pfizer

4. Success stories, promising approaches and failures

With the overall picture of attempts to improve access to medicines one finds, alongside a few unqualified success stories, instances of partial or complete failure as well as a number of ventures which bear promise but the ultimate effects of which cannot yet be assessed. All are instructive.

Since, as would be expected, some of the most successful approaches, particularly within countries, are multifaceted they are best considered according to their location.

Note: Some of these accounts may be modified or expanded when the country studies are completed.

4.1. Global approaches

An extraordinary number of bodies are now involved - or are proposing to become involved - in improving access to medicines in developing countries. The list presented in Table 2 of this report gives an impression of the situation, but it is certainly not exhaustive. The interlinkages between these various bodies are not always clear.

4.1.1. Innovation

Some important global initiatives relate to attempts to attune innovation better to the needs of the developing world. Within the multinational research-based companies there is to date little sign of a significant re-orientation of research in order to correct this imbalance. It is indeed doubtful whether any such reorientation is to be expected so long as developing countries find themselves unable to pay prices which are more than a fraction of those customarily charged in the west.

That being so, various parties have examined the extent to which innovative medicinal research is being conducted, or could successfully be undertaken, outside the purely industrial environment. In that respect there are some reasons for optimism. The first of these is that *a fair proportion of the basic discoveries made in this field in fact originate in public laboratories*, the role of industry being to develop these further to the point of practical application. Classically, penicillin was discovered by chance at a London academic hospital and further developed for clinical use at Oxford. A number of antimalarial medicines have originated in research programmes carried out for the U.S. Military.¹ Taxol, a prominent anti-cancer compound sometimes regarded as a major achievement of industrial research, in fact saw the light of day at America's National Cancer Institute. (Edwards 2003)[□] There are other

¹The Walter Reed Army Institute of Research created chloroquine, mefloquine, halofantrine and tafenoquine.

[□] On behalf of the innovative industry, Ms Susan Crowley (Merck Inc.), member of the Task Force has submitted the following statement relating to Taxol: "The bench research for this drug did take place in the national lab, at a cost of some \$35 million. A research based firm (BMS) then took that candidate chemical entity, scaled it up in their laboratories, conducted the necessary clinical trials, worked it through the FDA for approval, built a production facility, trained staff to operate it, and obtained a GMP certificate to operate the plant for this one product. After some 7 years of risk and \$800 million of sunk investment, the first woman was able to receive a life-saving cancer therapy and the National Cancer Institute was reimbursed for its \$35 million in research costs." (end of Statement)

examples, in addition to which research-based companies often find it necessary to subcontract work to academic and other public institutions. What this means is that a greater emphasis in *basic academic research* on the treatment of neglected diseases of the third world could have important repercussions for medicinal research as a whole. In addition it is worth considering whether the fruits of this basic institutional and academic research, could not be used directly to the public benefit, e.g. by using royalties earned from industrial licensing to further develop investigational work in the public sector.

A second consideration is that *several major national and international organizations* have indeed either assumed responsibility for developing particular medicines or participate already in medicine development programmes to benefit poor populations. The World Health Organization carried through a successful programme to develop and obtain regulatory approval for a rectal form of the antimalarial artemesin, derived from Chinese herbal medicine; some part of the research requiring special technology were subcontracted to industrial companies.

A third relevant development is that it *today seems feasible to establish non-industrial research programmes* in this field. Alongside the work planned or ongoing through various global programmes (see 1.5.3. above and Table 2) there is the important example of the *Drugs for Neglected Diseases Initiative*. Spearheaded by Médecins sans Frontières, this is a collaborative research programme involving a worldwide group of public research institutions, with firm central planning and management. Its initial emphasis is likely to be on identifying and developing existing compounds with potential usefulness in neglected diseases, but more fundamental research may follow. One should note that a successful non-academic innovative project would in all probability entail sub-contracting certain activities (particularly in the later development phase) to the pharmaceutical industry, such as happened with artemesin; this would be logical in view of industry's long experience in certain fields such as specialised toxicological, metabolic and clinical studies. The patent situation arising in such multi-partner ventures will naturally demand special consideration.

4.1.2. *Price reductions*

There is no general trend for the manufacturers of specialties to reduce their worldwide prices; as a rule these prices only fall where there is strong generic competition in a significant market. Manufacturers however tend to advance the fact that they have for many years engaged in "differential pricing", i.e. charging prices which vary from country to country. Some manufacturers have also in recent years reduced prices of selected medicines significantly for low-income countries, and a few have provided particular medicines free of charge, but these are exceptional cases.

The essential question is whether multinational industry will be prepared to move from "differential pricing" to "equity pricing". A careful distinction has to be drawn between the two concepts, though the terms used are not consistent. "*Differential pricing*" relates to the traditional commercial principle of charging for each market the highest price which buyers will tolerate, as a means of maximalising income. In a country with a generally poor population a global firm may well find that it can obtain

the maximum return by selling at relatively high unit cost to affluent urban groups, the price remaining a barrier for the remainder of the population. “*Equity pricing*” on the other hand involves markedly adjusting prices strongly downwards for a low-income market to a level which the bulk of the population can afford.

To date, firms have only agreed to “equity” pricing in very specific situations and on strict conditions. The principal condition is that measures be taken to prevent “leakage” of medicines from a developing country where they have been sold at equity prices to more affluent countries where higher prices pertain, thus undermining the market in the latter country. From the commercial point of view this condition is reasonable, and experience with a number of equity pricing agreements seems to show that it can in general be enforced, given the collaboration of the regulatory authorities and medicines inspectorates in the countries concerned. Only a few cases of “leakage” have been reported.¹ This approach therefore seems promising, but to date the negotiation of equity pricing agreements (usually for one country at a time and one product at a time) has been both labour-intensive and time consuming.

4.1.3. *Interpreting the TRIPS Agreement*

As noted under Sections 1.4.4. and 2.3.3 above, the TRIPS Agreement has been criticized as representing a threat to the supply of low-cost medicines to poor populations. If interpreted literally and without applying the flexibilities and exceptions allowed for in the Agreement, it would render it impossible for countries to manufacture a low-cost version of any patented medicine for their own or other populations during the entire lifetime of the patent. However countries can take certain measures to overcome patent barriers to access to medicines that are fully compliant with the TRIPS Agreement. (Love 2000).

The exceptions provided for by TRIPS itself are found in Article 30, stating that:

“Members may provide limited exceptions to the exclusive right conferred by a patent, provided that such exceptions do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties”.

An example of such an exception is the Bolar clause that allows for fast introduction of a generic after the patent term by permitting technical preparation for registration of the drug before the patent has expired.

The most important tool for use by the governments of developing countries in dealing with obstacles presented by patents is however Article 31, which sets out the procedures for compulsory licensing and government use of a patent. A patent, as

¹ A particularly notorious example was reported from The Netherlands in October 2002, when some 6000 packages of HIV/AIDS medications were found to have been reimported after having been sold by GSK to francophone west-Africa at discounted prices. It was estimated that up to a third of the total supply of discounted antiretroviral medicines had been reimported into various European countries (e-drug-digest, 2002)

noted in section 2. 3.3, is a government grant that permits its holder to exclude third parties from the market for a product. A “compulsory license” is an authorization by the government to itself or to a third party to use that patent without the permission of the patent holder. Most or all countries – developed and developing – allow the government to make use of patented inventions for public purposes with less bureaucratic obstacles than apply to the private sector. A compulsory license authorizing the government to use the patent for its own purposes is also referred to as a “government use” authorization (in British terminology, “Crown use”). There remains an obligation to pay the patent holder “adequate remuneration in the circumstances of compulsory licensing or government use, taking into account the economic value of the authorization”.

Article 31 also requires the government concerned to seek in advance the agreement of the patent holder to the use of his invention on reasonable terms (i.e. to seek a ‘voluntary license), and rules that a compulsory licence can only be issued if such agreement cannot be obtained “within a reasonable period of time” (Clause (b)). However, this requirement may be waived by a Member in the case of “a national emergency or other circumstances of extreme urgency or in cases of non-commercial use.” Countries are free to determine what they consider a national emergency and do not need to follow any official procedures; it is not for example obligatory to declare formally that a state of emergency exists. □ Countries are also free to define what constitutes “public non-commercial use”. This can for example be defined as covering procurement or production of health care products for use in the public sector. In practice this means that a procurement authority in a country can start the purchase of generic versions of needed medicines without prior negotiations with the patent holder. The patent holder will be informed of the decision to make government use of the patent and the government will have to offer to patent holder adequate compensation, the level of which is however to be decided by the government itself. Article 31 f further rules that such use “shall be authorized predominantly for the supply of the domestic market of the Member authorizing such use”:-

The Fourth WTO Ministerial Conference, held in 2001 in Doha, Qatar, adopted a “Declaration on TRIPS and Public Health” which affirmed the right of national governments to take measures to protect public health and appeared to legitimize the broad use of these flexibilities ~~exceptions~~, including compulsory licensing, (Abbott 2002) where medicines were concerned. (WTO 2001) While because of opposition from some industrialized countries the Declaration was weaker than that originally proposed, and is not legally binding, it is nevertheless in the legal point of view an important document that will have to be taken into account by a WTO panel dealing with this issue in practice. The Doha Declaration has also created new rights, for example the right of countries at a low level of development (LDC’s) to exclude pharmaceutical products from patenting. This right again is legally binding and cannot

□ It should however be noted that the Governments both of Kenya and of Brazil, in announcing programmes to supply generic medicines for the treatment of HIV/AIDS, have referred to the epidemic as a “national emergency”; on September 22nd 2003 the Director of WHO, announcing the “3x5” programme, described HIV/AIDS as a “global health emergency.” (WHO 2005)

be challenged. It has been criticized by some representing the research-based component of industry (Gillespie-White 2001) but others have seen it as a major step to protect the interests of developing countries.(Correa 2002) and the generic component of industry has welcomed it though pointing to the problems which remain.

One residual problem is the fact that clause 31(f) only permits unlicensed use of the invention where this is “predominantly for the supply of the domestic market”. This can be regarded as prohibiting, for example, the export of significant quantities of a low-cost generic version of a patented medicine from Brazil to an African nation having no production facilities of its own. The matter has not been resolved in the Doha statement, though the Ministers instructed the Council for TRIPS “to find an expeditious solution to this problem” and report on it before the end of 2002. Since the adoption of the Doha Declaration on TRIPS and Public Health the thirty LDC members of the WTO have been able to benefit from a special regime with regard to pharmaceutical product patents. Paragraph 7 of the Doha Declaration provides a special extension of the TRIPS transitional period for pharmaceutical products. LDCs do not have to “to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement or to enforce rights provided for under these Sections until 1 January 2016”. This means that LDCs do not have to grant product patents for pharmaceuticals, provide protection of undisclosed test data[□] nor to enforce patents that have already been granted until at least 2016. In LDCs patents should never be a barrier to purchasing or producing generic versions of medicines. LDCs have the maximum flexibility to disregard patents and data protection rules and they are encouraged to do so to ensure the purchase of the lowest priced medicines.

Debate on the interpretation of the rules has however continued with strongly divergent views being presented. The discussion has now been further complicated in that certain new or pending bilateral and regional “free trade agreements” may, as noted elsewhere in this report, in fact prohibit countries from making use of the flexibilities and exceptions permitted under the TRIPS Agreement itself.

The latest developments are those resulting from a decision of the TRIPS Council of August 30th 2003, A key issue that remained unresolved in Doha is, as implied above, how to ensure that production for export to a country that has issued a compulsory license, but does not have manufacturing capacity, can take place within a country that itself provides pharmaceutical patents. Since Article 31(f) of TRIPS limits compulsory licensing to uses which are predominantly for the supply of the domestic market, countries agreed that further action was necessary to ensure that countries without production capacity can make use of compulsory licensing provisions to the same extent that countries with manufacturing capacity can use these provisions. The Doha Declaration acknowledges the problem in Paragraph 6 and on August 30 2003 the WTO adopted a decision on a waiver to the 31 f requirement.

[□] WTO Members are obliged to protect undisclosed test or other data, the origination of which involves a considerable effort and which are required to obtain marketing approval by the drug regulatory agency, against unfair commercial use. (WTO TRIPS art. 39.3)

In the final report of the Task Force the discussion of this matter will be updated and relevant recommendations reviewed. At the same time the Task Force will take into consideration the view noted in Section 1. 2. 2. above regarding the rights of the originator of a drug in the light of human rights principles.

4.1.4. *Revolving Fund schemes, insurance and prepayment*

The *Bamako Initiative*, launched in 1987¹, proposed a series of measures to alleviate the funding problem, the principle element in which was the creation within countries of community-based revolving funds for medicine purchase. It can fairly be regarded as a global step, in that it launched a concept developed by wide international agreement and which could be applied in any country. It was stated to represent a means of mobilizing those funds which can reasonably be said be available in a community for the purchase of medicines and to ensure that they are employed more efficiently to this end than is often the case. Bamako based schemes have been introduced at least experimentally in a range of countries, particularly in Africa. While it is often pointed out that the results of this initiative have been mixed or disappointing, it has been argued that this is not due to any shortcoming in the original concept (Osmond 2002). A revolving fund is a means of mobilizing a sufficient proportion of the spending money which circulates in the community. Provided other approaches ensure that the prices of medicines are not entirely exorbitant, a user fee approach of this type can make these products available to a substantial part of the population which, though poor, is not entirely indigent. Some promising experience with revolving funds seems to have been gained at the local level where the population of a small community gains some measure of control over its payments and purchases and is able to ensure an equitable distribution of costs. There is little in the way of positive experience with larger or national schemes and current thinking appears to be that user fee systems should at most be regarded as a temporary initiative until more satisfactory means of financing medicines can be introduced. The least successful interpretation of the Bamako initiative is to be seen where it leads to a large monolithic national system, within which there can be too much opportunity for inefficiency, loss of contact between the centre and the periphery, diversion of funds and frank corruption. It also remains a fact however that the introduction of any type of user fee for medicines can all too readily create an obstacle to access for a part of the population (Kim 2000; Leon 2001), and this has to be taken into account when introducing the Bamako principle into any country.

It is currently argued that in the long run a *health insurance scheme* or *pre-payment scheme* will provide a sounder alternative to a revolving fund. Experience seems to show that insurance schemes only operate successfully in communities with an efficient banking system and a considerable degree of economic sophistication and where the concept of making payments throughout life rather than only times of illness is understood and accepted. It would however seem entirely feasible to

¹Launched by UNICEF at the WHO/AFRO Regional Committee meeting in Bamako, Mali in 1987.

envisage at some future point in time a progressive transition from a revolving fund to an insurance or pre-payment system, while perhaps maintaining the principle of local community supervision of the flow of finance. All these approaches however, like user fee schemes, suffer from the grave defect that they fail to provide for the very poorest element in a generally poor population; one cannot create adequate funding where the money is quite simply lacking.

4.1.5. *Global Procurement Schemes*

Pooled procurement on behalf of a large number of countries can result in substantial price reductions because of volume discounts. Such a scheme can operate globally or (see 4.2. below) within a region. UNICEF has engaged in global procurement and provision of items for a long period, securing considerable price benefits; though the bulk of its work relates to vaccines it also supplies a wide range of medicines. In addition, both UNICEF and the Rockefeller Foundation have made special purchasing agreements on behalf of a range of developing countries for medicines in special fields (oral contraceptives, vaccines). More recently a range of specialized global funds and agencies have entered the field of global procurement, e.g. for HIV/AIDS remedies (see Table 2).

It is commonly calculated that pooled procurement schemes, operated either globally or regionally can secure discounts of some 35% or more on regular prices but in some fields the economies are much greater. UNICEF has claimed that, while it supplies some 40% of the vaccine market in unit terms, it covers only 5% of the market in financial terms, (Jarrett, 2003) which would indicate that its vaccines are procured at only a small fraction of the prevailing western market prices. In mid-2003, the pool representing the countries of the Andean region agreed with producers of antiretroviral medicines on drastically reduced prices; the price for one three-component product, which had been as high as \$5000 in one participating country fell to \$365 for all ten countries. □

4.1.6. *International Pre-qualification*

Some national procurement agencies have for many years limited their purchasing in principle to prequalified suppliers, i.e. firms or individual products which they have investigated in advance and find to be of sufficient standard. International pre-qualification of suppliers and suppliers is also feasible and is notably operating within WHO to serve a number of agencies purchasing drugs for HIV/AIDS, Tuberculosis and Malaria (QSM 2003). Key steps in the process include both the assessment of product dossiers for safety, quality and efficacy and the assessment of manufacturers for compliance.

4.2. Regional approaches

□ It has been argued that a large pooled procurement scheme might actually exert *excessive* downwards pressure on prices, thus rendering the market so unattractive that some suppliers withdraw (Jarrett 2003); this risk probably only arises in the case of a very large and powerful joint procurement agency with global outreach, but it should be borne in mind.

Regional approaches conducive to improved access have mainly been concerned with schemes for the *pooled regional procurement* of medicines on the world market by a group of countries, usually within a particular region. The basic principles are the same as those involved in global pooled procurement (see 4.1.5. above), i.e. medicines can be ordered on a larger scale, as a result of which important bulk discounts can be obtained.¹ In addition, access is substantially widened, since major suppliers which would not ordinarily tender for very small national markets are willing to tender to the larger regional procurement bodies.

It should be noted however that a regional scheme may demand much more of its participants than a global scheme. A global project is essentially operated on a “take it or leave it” basis, countries being at all times free to benefit from its services or not, and as a rule retaining their own individual procurement agencies. In a regional scheme the participating countries are likely to be small, agreeing that in matters of procurement they cannot act cost-efficiently on their own and need to pool their efforts. Essentially the pool takes over the task of providing all medicines for the member states, either across the board or within a defined therapeutic area. The pool must be capable of relying on forecasts of need, if necessary assisting member states to conduct these, so that ordering is adjusted to real requirements. Some schemes go further: The regional procurement body operating in the Eastern Caribbean area provides for example considerable support to its member countries in such matters as the encouragement of good prescribing by means of well-constructed formularies, hence promoting the most efficient use of resources. The same scheme also provides central financial guarantees to suppliers which will apply should any member state default on payment. Table 3 summarizes some of the conditions which have been found relevant for the success of a pooled procurement scheme for medicines.

4.3. Examples of National approaches

Note: The information from these countries will be expanded in the final report.

4.3.1. *Bhutan*

The Essential Drugs Programme in Bhutan dates from 1987 when the government adopted a National Drug Policy and supporting legislation. The programme was heavily supported by international consultants during its first six years of operation. Whereas drug access was earlier very limited, it is estimated that 90% of the population now enjoys access to high quality essential drugs. In 1995 retail prices

¹The nations of the Eastern Caribbean have jointly procured medicines in this manner for many years. There are also operative schemes for the Gulf States, the Arab Maghreb League and a group of Pacific islands. A West African procurement scheme is developing (OECS/PPPS), while the Pan-American Health Organization operates joint procurement for vaccines for a group of South American Countries and has more recently established a joint procurement arrangement for medicines as well. Two schemes are in development for the countries of southern and south-eastern Africa. (SEAM 2003) There has also been some pooling of procurement by Thailand and India (WHO discussion paper, unpublished), and a joint procurement agency operates in the Gulf states.

were on average 6% less than those pertaining in 1985, and the prices paid by the programme in the course of procurement are currently some 50% below world market prices. Monitoring is intensive, with facilities reporting twice yearly on their stocks and use of medicines; only 0.75% of the overall budget was wasted as a result of drug expiry. Standard Treatment Guidelines have strengthened rational prescribing and the programme has invested heavily in ongoing development of human resources and formalization of working procedures. (WHO/Bhutan 2002)

4.3.2. *Brazil*

Brazil has enjoyed dramatic success with a three-pronged venture. Basically the decision was taken in 1996 to provide HIV/AIDS medicines *free of charge* to those needing them. This in turn led to the need for the country to obtain these at low cost. Following a Presidential Decree declaring that compulsory licences on patented medicines could be issued in the event of a national emergency, the AIDS epidemic was declared to constitute such an emergency. *Manufacturing of generic AIDS remedies* was then initiated with considerable success; at the same time, Brazil entered into successful *negotiations with western speciality manufacturers*, to obtain patented products for this purpose at highly preferential prices. Striking is the fact that, alongside other elements of Brazil's ambitious programme to counter HIV/AIDS, the investments made in these activities have paid off in terms of savings, e.g. in the costs of hospitalization and in the purchase of patented medicines at world prices. The Ministry of Health has estimated that the universal free provision of HAART¹ prevented 234,000 AIDS-related hospital admissions during the period 1997-2000, resulting in a saving of US\$ 677 million for the country's health system.(MOH Brazil, 2001).

The Brazilian experience is one of the most convincing demonstrations of the fact that one can secure substantial benefits in terms of prices by taking a firm line on public health needs. Prices do fall where there is strong generic competition in a significant market, or where governments threaten to break patents on the basis of national emergencies.

4.3.3. *Chad*

The case of Chad illustrates both the challenges faced by a low-income country and the extent to which they may be faced successfully. A national drug policy was adopted in 1998, including strategies to improve public sector financing of medicine supply, the prices of medicinal products and the management of donations. The proportion of the population with access to essential medicines rose from 46% in 1999 to 60% in 2001, and annual public expenditure on medicines was trebled over a six-year period, though it still amounted to only \$ 0.12 per capita. On the other hand the average percentage of essential medicines available in health facilities fell from 80 to 70 over the same period, while the average duration of stock-outs increased from 41 to 59 days. Standard treatment guidelines were updated, but no improvements were recorded in the use of antibiotics or in the (excessive) use of injections.(Kawasaki 2002)

4.3.4. *Costa Rica*

Costa Rica provides an example of what can be achieved over a long period in a country at a medium level of development. The Costa Rica Social Security Fund was introduced as early as 1942 and currently handles over 80% of all health expenditure. 10% of the total is devoted to medicines. The Fund's Formulary has been operating for several decades; it currently comprises some 535 medicines and is revised annual. The medicines are on average available in 90% of hospitals and out-patient clinics. An effective quality control system, including a well-equipped laboratory, has existed for some thirty years.(Quick 1997)

4.3.5. *India*

The unusual situation of the pharmaceutical industry in India merits study.

¹HAART = Highly Active Retroviral Therapy

India has become a *major producer of low-cost generic medicines* in all fields, meeting a large proportion of its own needs but also exporting these products to many developing countries; it is estimated that several thousand manufacturing units exist. The development reflects a liberal approach to industry and trade, a progressive growth in the economy and access to advanced technology.

At their best, Indian medicines have been found to be of a standard at least equivalent to that of the equivalent specialities. A persistent problem is however the complex and inadequate system of official inspection of manufacturing plants, partly as a consequence of the division of responsibility between the Federal and State authorities. As a result, some manufacturing sources remain well below acceptable standards of quality assurance. (Dukes 2001) Many developing countries therefore find it necessary to apply strict batch quality control to products of Indian origin, or prefer to purchase such medicines through a non-profit intermediary capable of exercising its own quality control procedures.

4.3.6. *Kenya*

Kenya is one of several countries where the most successful medicine supply system (i.e. one providing drugs to the mission health sector) has been managed by an NGO rather than a government agency. (WHO 1997; Kawasaki 2002) The country's Mission for Essential Drugs and Supplies (MEDS) was set up in 1986 by the Catholic Secretariat and the Christian Health Association to supply medicines to church-managed health units. Financial support has been provided by various bilateral donor agencies, but by 2002 the system was found to be financially self-sustaining. Supplies are procured in bulk from local agents and local producers and the system maintains its own facilities for storage, distribution and quality control. Monitoring for efficiency is intensive, with operating expenses averaging only some 10% of total costs. There have been extensive training programmes for health facility staff, though these cover only part of the training need.

4.3.7. *Uganda*

Uganda presents a picture of a ten-year transition from emergency aid to stable operation. In 1985, towards the end of a period of non-democratic government, medicinal supplies had largely collapsed. The Danish Red Cross instituted at this time a large programme to supply ready-packaged "kits" to health units, each kit providing a range of drugs sufficient for average needs. With restoration of stable government, the project, now primarily financed by the Danish bilateral donor Danida, established a national Essential Drugs Management Programme became which over a five-year period sponsored and supported a broad national Drug Policy programme. Activities ranged from the establishment by law of a new National Drug Authority and a National Medical Stores to projects for training, the production of Standard Treatment Guidelines and establishment of local revolving funds. Problems experienced in the course of the first decade of development included however an instance of serious financial mismanagement in the Medical Stores and complications caused by rapid decentralization of government. (DMFA 1995; WHO 1997) . It may be noted however that the Joint Medical Stores, a similar but smaller operation for the missions, has continued for many years to operate smoothly and successfully,

4.3.8. *Multi-country experiences*

(i) *Generic prescribing.*

A series of developing countries have attempted to promote *generic prescribing*

rather than the use of branded products. Such campaigns are directed to prescribers and the public. As a rule, the introduction of simple prescribing guides for health workers (Standard Treatment Guidelines, Formularies), in which the recommended medicines are listed primarily or exclusively by generic name, has had a significant effect, especially where these generic products are readily available countrywide through a national supply system. However, in various countries (and in the urban and private sector in most countries) much resistance to this concept has been experienced, and there has been relatively little impact on urban private practice where branded products have remained dominant. Efforts in this field in Nigeria, Pakistan and the Philippines, as well as in some parts of Latin America have stranded on the deeply rooted professional and public perception that “lower-priced pharmaceutical equivalents...are necessarily of a quality inferior to the brand-name products sold by large, well-known firms.” (Velasquez 1998). This failure is striking in view of the relative success of generic prescribing schemes in a range of western countries such as Denmark, the USA, Germany and Great Britain, but in these countries very firm measures have been required to change prescribing habits. It seems obvious that the successful introduction of generic prescribing requires good public relations and persuasion if not compulsion, and not merely favourable prices. The literature on this topic is now very extensive and goes well beyond the scope of the present review.

(ii) *National Production of Medicines.*

A frequently disputed point is the extent to which a country at a low level of development and having no broad industrial tradition should itself seek (or continue) to engage in the production of medicines. Political, strategic and status considerations have sometimes in the past led to the establishment of such units, and the future of these is often open to question in an economic situation where most essential medicines can be acquired in generic form at very low cost on the world market, particularly from countries at a rather more advanced level of development but still having low cost levels¹ More than a decade ago, consultations within the World Bank led to the view that, with certain well-defined exceptions (see section 1.5.4. above), investment in medicine production in countries at a low level of development was unlikely to be justified. Quite apart from the difficulties in maintaining adequate staffing and ensuring sound quality standards, the products of this relatively small-scale production would be unlikely to compete on cost grounds with generic products produced on a large scale in countries such as India and China. Starting materials (including active components) and packaging materials would in almost every case have to be imported.

(iii) *Capacity building*

It has frequently been pointed out that most developing countries need to expand the numbers both of health system administrators, managers and health professionals and raise the standards of their training, both basic and recurrent, when their

¹This is currently the situation in Afghanistan where the Avicenna Institute was in the past re-equipped for large scale medicine production in order to ensure national self-sufficiency. Production has largely ceased and the future of the Institute as a manufacturing centre is under review. (Dukes, personal report. 2003)

economy allows them to do so. It is however equally clear that this process can take many years, and that it is not realistic to expect that complete national coverage by professionals trained to full academic standards will be attained in the foreseeable future. Experience to date in the medicinal field can be summarized under three main headings:

Management: Many development projects have found it possible to train competent managerial staff in areas such as finance, procurement, stock management and distribution, partly through diploma-level courses and on-the-job training when working for a period alongside expatriate experts. Key managers may benefit from training periods abroad, especially in other developing countries where analogous situations have been tackled successfully.

Prescribing: Given an adequate information flow (see (iv) below), and regular recycling, a great deal of clinical management of common disorders, including diagnosis and medication, can be competently handled by staff trained to diploma level (2-3 years); fully trained physicians can then handle cases referred to them from primary care.

Pharmacy: Field experience indicates that the situation of the profession of pharmacy remains unsatisfactory. While the pharmacy profession continues to argue for a considerable increase in the number of fully trained pharmacists in developing countries, the profession has hitherto made only a minor contribution to medicine access in such countries. A small number of pharmacists play a valuable role in drug regulatory agencies, inspectorates, hospitals and drug manufacturing units, but the remainder generally operate urban retail pharmacies which serve only the affluent part of the population. It has almost everywhere proved impossible to attract fully trained academic pharmacists into rural areas where earnings are substantially less. Bearing in mind that at the present day the most useful role of the retail pharmacist is likely to lie in the provision of information and advice to patients, (WHO 1990, WHO/EURO 1988) the primary need for the foreseeable future would seem to be for an expansion in the number of pharmacy assistants (dispensers, technicians) trained to diploma level to play this specific informational role throughout the country. In the meantime, the reorientation of academic pharmacy training for more specialized tasks (such as drug policy, inspection and manufacturing, which has proceeded favourably in various industrialized countries, appears to be taking root more widely in the world.

(iv) *Access to information*

Access to reliable non-commercial information in medicines and their appropriate use has proved essential to their rational employment in every country. It proves particularly necessary in countries where professional training is limited (see point (iii) above). In many places a great deal has been achieved by relatively simple and low-cost methods. One of these is the production of simple “*Therapeutic Guides*” or “*Standard Treatment Guidelines*” for prescribers, setting out the means of diagnosing and treating the disorders and symptoms most likely to be encountered, for example in a rural health centre. Such Guides, well edited and of pocket format, have (in combination with other measures) proved to have a considerable effect in

improving the quality of medicine use in the countries where they have been introduced.¹ An acceptable variant on this is the “*National Formulary*” in which similar information is provided but is presented in relation to medicines rather than to disorders. The availability of well-proven national models and of a recent “*Model Formulary*” from WHO (WHO 2003) mean that the production of new prescribing guides or national formularies is today neither difficult nor costly.

A complementary approach which proves similarly promising is the production and dissemination to health workers of national “*medicines bulletins*” at regular intervals. Such bulletins can serve to update the therapeutic guides and formularies where necessary, but their primary purpose is to alert professionals to current problems relating to disease and the use of medicines, and to deal with ways of avoiding errors and misunderstandings. The globally active “*International Society of Drug Bulletins*” has proved able to give valuable support in terms of draft texts and advice when new bulletins are established. Like the Prescribing Guides and Formularies, such Bulletins have shown themselves capable of promoting rational use of medicines to an extent which is entirely disproportionate to the very low expense involved in their production.

(v) *Benefiting from Traditional Medicinal knowledge (WHO 2002f)*

The role which traditional medicines play - and could play in the future - in complementing western medicine and relieving the burden on the health services has often been overlooked in discussions of access. It is a fact that many developing countries have a rich flora, that in each a tradition has been created of using these plants to prepare medicinal products, and that a large proportion of the population relies heavily on traditional practitioners using his knowledge to make and provide “*natural*” medicines. Traditional healers commonly enjoy a greater degree of popular trust than the official health services and often provide care to those unable to provide monetary payment - payment in kind is often welcome. There seems little doubt that many of the remedies employed in traditional medicine have at least symptomatic value and that some have curative effects.[□] In addition, the fact that traditional healers are trusted enhances their ability to provide support and relief in some situations which are best treated without recourse to medicines at all, thus further relieving the strain on the health services.

Despite this, there has been little in the way of global attempt to examine herbal medicines and identify new therapeutic opportunities. Major pharmaceutical companies have only sporadically examined the possibility of developing new scientific medicines on the basis of indigenous remedies. Exceptional is the programme of research into herbal medicines currently operating in China. The World Health Organization has however done much to promote a positive approach to the field through its traditional medicines programme, now closely associated

¹Good examples of successful handbooks of this type include those from Ghana, Zimbabwe and Uganda.

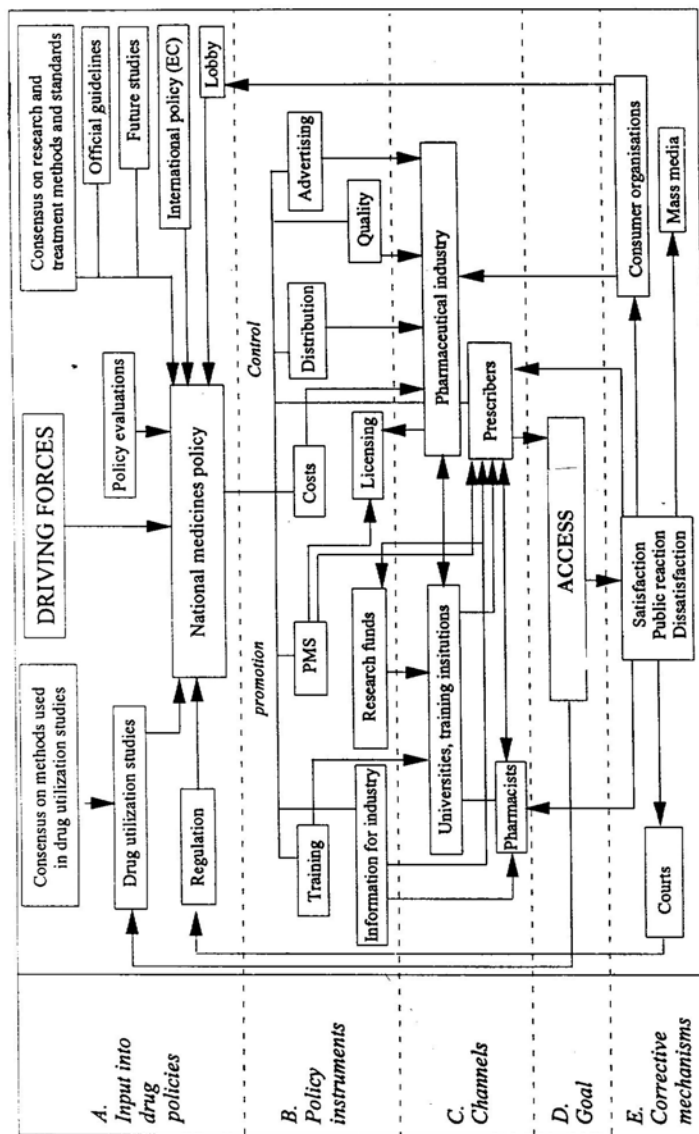
[□] There are many examples of “*western*” medicines with herbal origins; they include both long-known agents such as morphine, atropine and ephedrine, and others which have entered medicine in the current era (the Vinca alkaloids for malignant disease and artemesin for malaria).

with its main essential medicines activities; the Organization has now published its first Global Strategy for Traditional and Complementary Alternative Medicine.(WHO 2002)

The most successful attempts at the national level exploit the use of the traditional healing system as a complement to the office health services have been made in those countries where cross links have been encouraged between western-style and traditional practitioners, with the possibility of cross-referral.

Here as in other respects however one must beware of making unjustified assumptions as to costs and the prospect of savings; while for example herbal medicines prepared *ad hoc* from the local vegetation may be available at negligible cost, it is not unknown for a family to pay excessively large sums of money to a traditional healer to prescribe and provide them; public education in this respect is vital.

FIG 2: THEORETICAL MODEL OF A NATIONAL DRUG POLICY
(Oslo 2003)



5. Recommendations

The formal recommendations of the Task Force at this interim stage of its work are presented in the present section and are also summarized in Table 4 at the end of this report. It must be stressed however that on many matters on which no formal recommendation is made the Task Force has gained firm impressions of the existing situation and of the need for change, and those impressions have been presented in the earlier sections of the report.

It should be noted that recommendations at the national level are addressed primarily to those countries at a low level of development, and those in which drug access to the poor and underprivileged is a problem. Recommendations at the international level include both steps which need to be taken by the international community as a whole (including both public and private global organizations) and those measures which need to be taken in industrialized and producer countries in order to support access elsewhere.

5.1. General Principles

Whatever specific recommendations are recommended and adopted to improve access to medicines, several general principles must be borne in mind. They are of relevance both at the national and international level.

5.1.1. The concept of essential drugs

The “essential medicines” or “essential drugs” approach, tested over a period of more than thirty years, remains basic to any effort to develop adequate access medicinal supplies. They are not the only medicines which will be needed in the long run, but they meet the great bulk of the population’s requirements and the first goal in any programme to guarantee “access to medicines” must be to ensure that these fundamental products – a range of between 200 and 350 items, varying with the country, are consistently available and are properly used.

5.1.2. The need for a multilateral approach

Since the problem of access has many causes, no one of the measures which can be proposed to improve the provision of medicines can on its own be expected to succeed; it must be complemented by others. What this means is that *every country has need of an overall national medicines policy and strategy*. The aim such a policy has been succinctly defined as being to ensure that “Safe and effective drugs of good quality are available and affordable to the entire population and that they are rationally used.” (World Bank 1993) and the World Health Organization has issued both brief and extensive guidelines to introducing such policies at the national level. (WHO 2002 and 2003a). Simpler variants on the complex model provided in Figure 2 (Leufkens 1993, Oslo 2003) are possible and necessary; the most important step is to develop a model which meets national needs and to employ it as a basis for the development and management of the system as a whole.

5.1.3. The need for intersectoral support

As noted in 3.4.2., national medicines policy cannot succeed in isolation from broader health policies and government policies in general. A Ministry of Health is unlikely to succeed in this area - and therefore in ensuring the best greatest possible degree of access to drugs - unless it has clear and acceptable understandings reached with other government departments dealing with such matters as the apportionment of finance, the training curricula for health professionals, the salaries of public employees and practices regarding trade, taxation and customs duties, all of which are likely to impinge on the supply of medicines.

5.1.4. The need to set firm priorities.

There will for the foreseeable future be a need to set priorities so that the most

catastrophic aspects of a situation are dealt with first. In particular this will entail ensuring better access for the poor and underprivileged, in parallel with efforts on a much broader front to eliminate inequity in society. The decisions to be taken will sometimes be hard – for example where expenditure on medicinal supplies has to be deliberately limited in order to allow for commensurate expenditure on training¹ - but they will be ultimately serve the general good. Priority setting demands that resources available for procurement be used exclusively for “essential drugs” until such time as basic needs have been met and the available resources permit a broader approach. As noted under section 3.4.2., the AIDS pandemic has sparked a mobilization of public opinion and community pressure on governments. It is very necessary that this form of community involvement be developed (though in the form of ongoing bilateral consultation rather than unilateral pressure) in setting policies and priorities in the entire field of medicines.

5.1.5. Coordination of effort

As noted in Section 3 above there is both at the international and national levels need for a great deal more transparency and coordination of effort between the large number of organizations which have already become involved in one way or another in this field. The involvement of so many bodies can and does lead to duplication of effort and to wastage, and both are unacceptable. Some specific proposals are advanced in later paragraphs.

¹In one African state in 2003 a delegation from a foreign foundation proposed that it provide a massive sum of money from Western countries to be used for the purchase of AIDS medicines. Consultation led to the conclusion that the population would be better served if the proposed supply were somewhat reduced and a fair proportion of the total sum were used instead to provide training in the management, diagnosis and treatment of the disorder. Medicines would otherwise not be used to the best advantage. (Dukes 2003, personal report).

5.2. The significance of human rights

Despite the fact that there is well-defined human right of access to medicines, as considered in section 1.2. of his report, the right is commonly not reflected in the current situation, in which entire populations, and particularly the poor and underprivileged, commonly have little access to essential medicines or none. This situation calls for correction .

-At the national level, principles of human rights relating to access to medicines need to be translated into concrete rights for the individual, enforceable in law.

-At the international level, both public and private organizations need to acknowledge access to medicines as a human right and to act in accordance with this right.

5.3. The availability of drugs

5.3.1. *Improving the rate and relevance of innovation*

Although new medicines continue to be created and developed, very little of this effort is currently devoted to meeting the particular needs of poor populations in developing countries.

S *At the national level, governments should determine the correct priorities in medicinal innovation in accordance with the most basic and unfulfilled needs of their populations, and bring these priorities emphatically to the fore both in their domestic policies and in the global fora in which they participate. Even in countries with very limited resources some steps can and must be taken to formulate a national research policy and provide the funding and infrastructure needed to implement it, either independently or in collaboration with foreign, regional or global institutions. Alongside the development of new synthetic medicines, governments should promote research (and where appropriate development) into the merits and safety of medicines indigenous to their countries, particularly traditional herbal remedies*

S *At the international level, much can be done to define an expanded role for public investment in medicinal research to meet the most pressing needs of developing countries and poor populations. Within industrialized countries an environment should be developed which is conducive to the private sector making a greater contribution to innovation in public health, including the creation of medicines attuned to developing country needs. Bearing in mind that most innovative programmes in this field are based in industrialized countries, these countries can and should exert a stronger influence both on the content of the research and the manner in which it is conducted, particularly as regards the need to maintain recognised ethical standards in clinical research wherever it is carried out.*

5.3.2. Developing more reliable supply systems

Many national supply systems for medicines, whether public or private, are inefficient or poorly attuned to current needs. Procurement is not always in line with what is needed, funds are not optimally used and both centrally and in the periphery drugs are commonly out of stock.

- S *At the national level, all potentially efficient systems for the procurement and distribution of supply of medicines, whether public, private or maintained by non-governmental organizations, should be encouraged and assisted to develop; often the various types of system will be found to complement one another so that together they ensure a reliable and sustainable supply chain. Regulations on drug supply should be clear and comprehensive, and the judicial system should be provided with the human and material resources to enforce these regulations and eliminate abuses which can lead to wastage and loss..*
- S *At the international level, exchange of information and advice on successes and failures in the operation of national or pooled procurement systems will be valuable in establishing new agencies or reforming those which already exist. Bringing together data from many countries on current and anticipated needs and priorities will create a basis for producers to provide appropriate supplies. International standards for the operation of procurement agencies are needed and means of prequalifying procurement agencies which attain these standards should be developed.*

5.3.3. Promoting the safety of medicines

In the developing world, injury due to unsafe medicines - some of them inherently risky and others poorly produced - is still much more common than it need be.

- S *At the national level there is a need to ensure more effective regulatory control on the entry of medicines into the market than currently exists. A government should strengthen its Drug Regulatory Authority by providing political backing to its activities, ensuring that it is adequately financed and providing it with adequately reimbursed and well-trained staff. National systems for monitoring suspected adverse reactions to medicines need to be rendered more effective. They should be capable of defining not only the overall pattern of unwanted reactions in the population and in particularly susceptible groups but also cases of frank injury due to medicines. There needs to be progressive development of systems to provide redress for such injury, either in the form of compensation schemes or through the courts.*
- S *At the international level, countries which are active in the production and export of pharmaceuticals should make a much greater effort to raise the standards of quality so that GMP criteria are met. Between countries, whether importing or exporting, there needs to be an ongoing exchange of information on various matters of mutual importance relating to the safety of medicines .*

These must include data on benefit-risk assessment of particular agents or products, regulatory decisions involving safety issues (such as the withdrawal of disproportionately risky medicines). Recent initiatives to pre-qualify both individual products in high-priority areas and the plants producing these products need to be vigorously pursued and extended, and the emergent information should be exchanged internationally.

5.4. The affordability of medicines

5.4.1. *An approach to fairer financing*

At the present day, the drug supply system in poor countries is as a rule seriously under-financed at various levels. It would be unrealistic to imagine that all the countries concerned will succeed in correcting this situation on their own during the coming 15-20 years. Especially because of the major pandemics, a considerable degree of support from other parts of the world is likely to be needed for many years to come, alongside efforts to ensure that national self-reliance does develop progressively.

S *At the national level there must be a progressive increase in the public sector budget for essential medicines, particularly in order to ensure improved access for the entire population, including the poorest; this is likely to demand a shift in the allocation of government resources. User fees do not provide an adequate or long-term solution to the problem and they should be progressively phased out. Where individuals are in a position to make at least some contribution to the costs of medicinal care this should to a large extent be in the form of pre-payment and insurance schemes, including schemes sponsored or financed by employers. It is however realized that the infrastructure needed for such schemes and their general social acceptance will only be attained by guided development over a period of time. Payments made to providers at all levels - importers, wholesalers and retailers - should be commensurate with the degree of service which they provide. The acceptance of public or private donations of medicines should follow strictly the internationally accepted guidelines.*

S *At the international level there must be a very substantial increase in international financing of essential medicines, especially those intended for the poor and for the relief of the current pandemics. It is important to obtain a much clearer picture than exists at the moment of the total flow of funding through all of the many channels involved and the extent of the shortfall. Loans will on occasion be justified in order to provide acute relief, but in principle funding should be in the form of outright donations, preferably provided without ties. The world community can also provide valuable support in acquiring, analyzing and disseminating comparative financial data on drug supply and the flow of finance both between and without countries; this will form a valuable basis for policies designed to ensure sufficient, fair and equitable financing. Some part of the finance provided by the international community should be directed to the support of national health policies and systems in this area, and not exclusively to the supply of medicines.*

5.4.2. Countering high prices

Sometimes drugs are inevitably costly, but in a great many instances they are disproportionately expensive. The reasons for high prices are multiple, and the problem therefore has to be tackled vigorously at various levels.

S *Within any country, the promotion of competition is a potent tool to ensure that prices fall to a fair level. It must include competition between various therapeutic approaches but also between specialities and generic medicines and their individual producers. The prices charged for essential medicines at all levels - import, wholesale and retail - must be monitored so that excessive charges can be detected and eliminated. Inappropriate taxes and tariffs on essential medicines should be eliminated, and particular attention devoted to the excessive levels of some dispensing margins or to hitherto tolerated "informal" charges linked to the supply, prescribing or dispensing of drugs. Above all, developing countries with a drug access problem will need to adapt and apply their national legislation so as to take advantages of the flexibility provided for in the TRIPS Agreement including the possibility of bypassing or suspending pharmaceutical patents.*

S *At the international level there is need to identify and adopt strategies which will render it possible to continue the production and dissemination of low-cost generic drugs for poor populations after the year 2005; this is likely to involve providing new options, beyond those already incorporated in the TRIPS Agreement. The international community and its individual members must at the same time ensure that global understandings of this type, favouring drug access to poor populations, are not undermined by the conclusion of more restrictive regional or bilateral free trade agreements. The impact of all these international agreements and their application must be monitored in order to ensure that the aim of serving poor populations is achieved. Similarly, the impact effects of commercial trade agreements should be monitored and corrective action taken if these impede access to drugs for the underprivileged. Consultation between corporations, the global community and member states must also be directed to extending the practice of strongly differential ("equity") pricing of high priority pharmaceuticals in a manner benefiting poor populations.. Both within exporting states and in international consultation, policies must be such as to favour international competition in the pharmaceutical field, including unhampered competition between individual firms and between innovative companies on the one hand and generic producers on the other. Finally, much will be gained by the sharing of information between countries and agencies on producer prices, mark-ups, tariffs and taxes and other charges, so that successful approaches to the reduction of consumer prices in one country can be emulated in others.*

5.5 The appropriateness of medicinal treatment

Medicines cannot truly be said to be fully available to a population unless the treatment in which they are used is provided in such a way that the patient is most likely to benefit. In many situations, inappropriate prescribing or dispensing of medicines means that this aim is not achieved.

5.5.1. *Better prescribing and dispensing*

S *At the national level a co-ordinated policy should be devised and introduced to promote the rational use of drugs. There should be an essential drugs list, developed not only in accordance with established international practice but also so as to reflect the health needs and priorities of the particular population concerned; it should also be in line with evidence-based standard treatment guidelines for the most prevalent guidelines and used alongside them. The standard treatment guidelines should also provide the basis for teaching, recycling, practice and evaluation of health professionals where the use of medicines is concerned.*

With the list and the guidelines providing a standard, there should be ongoing monitoring of the manner in which medicines are in fact being used, to ensure the maintenance and progressive development of standards. Similarly, dispensers will need to be trained in accordance with these standards and their performance monitored. The tasks of prescribing and dispensing should wherever possible be separated; it is very undesirable for the prescriber to have a financial incentive to over-prescribe, as will be the case where he earned a profit on each medicine which he prescribes for a patient.

Finally, it is vital to provide reliable information on medicines and their use, both during the education of professionals and on an ongoing basis during their professional careers (e.g. through the publication of formularies, standard treatment guidelines and regular prescribing bulletins. The information provided by manufacturers and importers may supplement this, but measures should be taken to ensure that it adheres at least to the standards established internationally for the content of medicinal promotion.

At the international level, donors and global agencies engaged in the health field need to work together to promote the rational use of drugs./ The WHO ethical guidelines for the promotion of medicines should be updated and at the same time extended to deal with newer issues, including the trend to promote prescription drugs to the public at large and the publication of promotional material on the internet. WHO should also ensure the worldwide sharing and dissemination of authoritative texts on the best means of treating major and epidemic conditions, so that these can form the basis for national guidelines.

5.5.2. *Better use of drugs in the home* It is often the case that even medicines which have been appropriately prescribed and dispensed are still improperly used in the home, either because of ignorance as to their proper mode of use or misunderstandings regarding the nature and use of medicines in general.

-At the national level governments should seek to develop a broad

understanding among the public of health issues, including the proper use of medicines. This general information should be supplemented by drug-specific information, disseminated to households or patients in a culturally appropriate manner. This should not be a unilateral task for the authorities: one can well mobilize community movements to promote the proper and cautious use of medicines.

As is the case with commercial promotion to professional, pharmaceutical advertising directed to the general public should adhere to well-defined standards of objectivity.

5.6. Cross cutting issues

5.6.1. *Human resources* Though the current weakness of national systems concerned with the supply and use of drugs is in part a question of lack of finance, the lack of appropriate human resources is at least as critical. Basic schooling, further education and recycling of health workers all leave much to be desired in a great part of the world, and correction is needed at all levels. Some countries also suffer severely from emigration of health workers and inability to attract or retain competent workers from abroad.

At the national level, institutional training both in medical and pharmaceutical work needs to be expanded and upgraded, while the availability of more public finance is likely to increase the possibilities for attracting and retaining staff. Though the specific problems vary from one country to another, a widespread need is for the education of more pharmacy workers at all levels, while curricula need to be upgraded both in the medical and pharmaceutical fields. In most communities it is possible to identify resource persons who have influence and enjoy authority among the population, and much can be done to develop their role, support their activities and enlist their help both in designing and in implementing policies in the field of medicines..

At the international level greater financial support can be provided for the development of institutionalized training[□] in these various fields in low-income countries.

A network of international agreements is needed to develop collaboration between countries on the migration of health workers, both in order to encourage health workers to seek employment where they are most needed, and in order to remove purely bureaucratic obstacles to migration.

5.6.2. *Gender*

As noted at various points in this report, the fact that female emancipation has not proceeded sufficiently in some countries places the woman at a serious disadvantage in some aspects of health care, including access to medicines and their appropriate use. The adverse consequences also extend to her family which is in large measure dependent on her ability to secure access to health care for them, to ensure that they receive medicines when needed and to administer them appropriately.

□

At the national level a range of measures are called for to correct this situation and ensure that women and children have as ready an access to medicines as do men. Measures called for range from improved access to schooling generally for girls and women to the provision of reliable medicinal information to women in a form which they can assimilate even when their education is minimal – e.g. oral information for the illiterate. Both in medicines research and in social research relating to medicinal usage women need to be approached as a separate sub-group so that information specific to their situation and needs is generated. Informed policies will need to be based on such disaggregated data. Wherever possible, women should be actively involved in the design and implementation of medicines policy.

5.7. Institutional structures

As is evident from the various sections of this report, a range of institutions are involved in the conduct of a medicines policy: they include a Medicines Control Agency, an Inspectorate, Educational Bodies and Financial Institutions (dealing for example with health insurance).

At the national level there must be the necessary political will to create and maintain these institutions and to provide them with the necessary finance, staff and authority to work effectively.

Table 3
Some conditions for the success of Pooled Regional Procurement Schemes for Medicines

(derived from SEAM 2003)

<p>Homogeneity of Member States <i>(Size, range of needs, economic development, culture, political tradition, language)</i></p>
<p>Harmonized national requirements <i>(Drug regulation; taxes; import duties)</i></p>
<p>Financial stability <i>(Stable currencies; countries able to pay for pooled services and for supplies received)</i></p>
<p>Common approach to quality <i>(Agreed quality standards; agreed procedure for control of suppliers and batches)</i></p>
<p>Reasonable accurate prediction of needs</p>
<p>Competent and stable central staff</p>
<p>Reliable data on patent situation of medicines</p>

Loyalty of member states
(National procurement agencies must not compete with the pool)

Monitoring of performance at pool and national level

6. Closing remarks

When the Task Force examines the massive literature which has grown up over the last thirty years on the problems of access to medicines it is struck by the fact that almost every conceivable barrier to access has over the years been experienced, but also examined and tackled; very commonly realistic solutions have been devised. Sometimes those solutions have been successfully applied, especially where the approach has been a broad one.

Ideally the Task Force would have wished to propose a relatively simple approach to the challenge of improving access to medicines. Because however the obstacles to access are many and diverse, and because they differ in nature and degree from one country to another this is not possible. One is obliged to point to an entire armoury of solutions, some of which need to be applied at the global level, while others need to be selectively employed in particular countries or regions depending on the situation which exists. At the risk of overshadowing the other vital issues presented in this report, , the Task Force would however point to four general matters which merit special attention and action at this time:

- the first of these is the *complex and confusing structure of international aid in this field*; it is not unlikely that more could be achieved, and the situation better assessed, if it were simplified by a merger of effort
- the second is the fact that the *international community has to date produced more in the way of words than of deeds and dollars*
- the third problem is that *the existing flow of money in and around the pharmaceuticals field is poorly and unjustly apportioned*; undue enrichment on a massive scale is to be seen alongside deprivation and neglect; scientific resources are primarily directed to detecting new medicinal benefits for the privileged few; the funds devoted worldwide to administration and promotion massively exceed those which could be used to right wrongs
- the fourth issue is that of *human resources*. Whether one is dealing with procurement, prescribing or patient behaviour one repeatedly finds that the resources available for medicinal care are too limited and that even those which exist are not being used to the best advantage. Education, information and follow-up training remain potent tools to change that situation.

While the scene regarding access to medicines is complex it is in essence well understood. It is also increasingly evident that ensuring access to medicines brings both social and economic rewards which at the very least provide a full return on the investment necessary to attain that ideal. There is no real doubt that, despite the extensive poverty in the world, the world community as a whole is economically well able to provide all its citizens with at least a basic range of the essential medicines. What is essentially needed to turn that ideal into reality is political and social will, wide community support, the readiness on the part of many parties in society to abandon entrenched attitudes which have had their day, and a determination to reset global and national priorities in order to serve the greater good.

TABLE 4
SUMMARY OF PRINCIPAL RECOMMENDATIONS
Numbers cross-refer to the full text of the recommendations

FIELD	National Recommendations	International Recommendations
5.2. GENERAL PRINCIPLES	Translate principles of human rights relating to drug access into enforceable rights for the individual	International organizations need to acknowledge access to medicines as a human right
5.3. BARRIERS TO AVAILABILITY		
5.3.1. Inadequate innovation	<ul style="list-style-type: none"> • Encourage advocacy for appropriate innovation and priority setting • Provide policy, funding and infrastructure for research for national priority health needs • Promote R and/or D for indigenous medicines 	<ul style="list-style-type: none"> • Promote public investment in research for priority health needs of developing countries • Create environment that mandates private sector to contribute to innovation in public health. • Ensure international standards for ethical research are applied in all countries
5.3.2. Unreliable supply systems	<ul style="list-style-type: none"> • Promote all effective supply channels (public, private, NGO) giving priority to sustainable, reliable supply systems • Provide clear regulations for supply systems • Ensure judicial system enforces regulations 	<ul style="list-style-type: none"> • Promote information sharing on successful national and pooled supply strategies to enable innovation • Provide producers with reliable forecasts of priority product requirements • Promote international standards for procurement agencies • Prequalify procurement agents

<p>5.3.3. Unsafe medicines</p>	<ul style="list-style-type: none"> • Strengthen drug regulatory authority with political support, financing, and staff • Institute system for monitoring and redressing drug injury 	<ul style="list-style-type: none"> • Enforce compliance with international GMP • Share information about poor quality products and producers • Set up system for sharing information on benefit-risk assessment and regulatory decisions (e.g., withdrawals) • Prequalify and monitor priority products and suppliers and share this information (e.g., white list)
<p>5.4. BARRIERS TO AFFORDABILITY</p>		
<p>5.4.1. Unfair financing</p>	<ul style="list-style-type: none"> • Increase public sector budget for essential medicines and ensure equity of access • Promote prepayment and insurance schemes including employer schemes • Phase out user fees for essential medicines in favour of more equitable drug financing • Institute performance based payment for providers • Promote good donation practices as per international guidelines 	<ul style="list-style-type: none"> • Increase total international financing for essential medicines targeting the poor • Loans should not fund recurrent drug expenditures • Provide comparative health and other sectoral accounts and pharmaceutical expenditure to encourage fair financing • International financial assistance should support national health policies and systems

<p>5.4.2. High prices</p>	<ul style="list-style-type: none"> • Promote generic and therapeutic competition • Monitor and regulate the prices of essential medicines • Remove inappropriate tariffs and taxes and reduce inappropriate distribution and dispensing margins and informal payments • Adapt and use national legislation to take advantage of TRIPS flexibilities and suspension of pharmaceutical patents for LDCs as per Doha declaration 	<ul style="list-style-type: none"> • Develop strategies to insure production and availability of generic medicines after 2005 and beyond the options that are currently available. • Promote equity pricing through company discounts, bulk purchasing, voluntary licensing, compulsory licensing, etc. • Promote company differential pricing for public health priorities • Monitor impact of pharmaceutical trade agreement on access to medicines and take action if negative • Share information on producer prices, mark-ups, tariffs and taxes, fees and other charges • Support a competitive international pharmaceutical environment that includes generic and therapeutic competition • Ensure that international understandings that support access to medicines are not undermined though regional and bilateral negotiations
<p>5.5. BARRIERS TO APPROPRIATENESS</p>		

<p>5.5.1. Inappropriate prescribing & dispensing</p>	<ul style="list-style-type: none"> • Create essential medicines list based on evidence-based treatment guidelines for prevalent conditions • Implement national coordinating policy on activities to improve rational drug use • Ensure responsible and ethical drug promotion and availability of independent and impartial information for continuing education of prescribers and dispensers • Separate prescribing and dispensing profits • Use evidence-based treatment guidelines in teaching, monitoring, and evaluation • People prescribing and dispensing medicines should be trained, regulated and monitored 	<ul style="list-style-type: none"> • International donor agencies should coordinate to support country efforts to promote rational use • Update and enforce WHO ethical guidelines for drug promotion and drug information (e.g., internet) • WHO should share, disseminate, and translate independent information on treatment of priority conditions for national adaptation
<p>5.5.2. Inappropriate use by households</p>	<ul style="list-style-type: none"> • Promote culturally appropriate health literacy and community support • Ensure availability of independent and impartial information for households through culturally appropriate means • Mobilize and engage communities to improve use of medicines • Control direct to consumer promotion 	

5.6. CROSS-CUTTING ISSUES		
5.6.1. Human resources	<ul style="list-style-type: none"> • Ensure sufficient numbers of trained pharmacy workers of different levels • Develop, support, and involve the communities' own resource persons • Continuously update and adapt to needs training curricula for prescribers and dispensers 	<ul style="list-style-type: none"> • Increase financing for health human resources in low income countries • Institute international agreements and cooperation on health worker migration
5.6.2. Gender	<ul style="list-style-type: none"> • Ensure women have access to accurate drug information • Involve women in policy setting on medicines • Promote innovative and outcome research in women and children • Collect and disaggregate by gender data on access and utilization gender as a basis for informed policies • Ensure women and children have access to medicines that is equal to men 	
5.7. INSTITUTIONAL STRUCTURES	<ul style="list-style-type: none"> • Create and maintain in efficient operation those national institutions required to implement law and regulation, inspection and financing in the field of medicines 	<ul style="list-style-type: none"> • Maintain international institutions capable of supporting the development of stable drug access systems in member states

SUPPLEMENT:

National case studies
(to be added to definitive report)

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APPENDIX 1
**Ten recommendations to improve use of medicines
in developing countries**

(adapted from Laing 2001b)

- (1) Establish procedures for developing, disseminating, utilizing and revising national (or hospital-specific) guidelines
- (2) Establish procedures for developing and revising an essential medicines list (or hospital formulary based on treatments of choice
- (3) Require hospitals to establish representative Pharmacy and Therapeutics Committees with defined responsibilities for monitoring and promoting quality use of medicines
- (4) Implement problem-based training in pharmacotherapy in undergraduate medical and paramedical education based on national STG's
- (5) Encourage targeted problem-based in-service educational programmes by professional societies, universities and the Ministry of Health, and require regular continuing education for licensure of health professionals.
- (6) Stimulate an interactive group process among health providers or consumers to review and apply information about appropriate use of medicines.
- (7) Train pharmacists and medicine sellers to be active members of the health team and to offer useful advice to consumers about health and medicines.
- (8) Encourage active involvement by consumer organizations in public education about pharmaceuticals, and devote government resources to support these efforts.
- (9) Develop a strategic approach to improving prescribing in the private sector through appropriate regulation and long-term collaboration with professional associations
- (10) Establish systems to monitor key pharmaceutical indicators routinely in order to track the impact of health sector reform and regulatory changes.

APPENDIX 2

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RESPONSE OF THE RESEARCH-BASED PHARMACEUTICAL INDUSTRY TO THE INTERIM REPORT OF THE TASK FORCE ON ACCESS TO ESSENTIAL MEDICINES

Introduction

The members of Task Force Five who represent the research-based pharmaceutical sector, in collaboration with colleagues from other pharmaceutical companies, are pleased to have the opportunity to respond to the December 2003 draft Interim Report of the United Nations Millennium Development Task Force on Access to Essential Medicines (ATEM). This Task Force was formed to identify the principal barriers preventing access to essential medicines in developing countries, and the best means of surmounting those barriers. The research-based pharmaceutical sector fully supports the Millennium Development Goals, especially relating to expanding access to innovative medicines. We wish to see those Goals advanced as effectively as possible.

As Secretary General Kofi Annan has pointed out, success in achieving the Millennium Development Goals depends on partnership, inclusion, transparency, and collaboration among all stakeholders. We applaud the Interim Report's recognition that the problem of insufficient access to essential medicines has a variety of causes, and that consequently it cannot be adequately resolved by any one group in isolation. The access problem arises from the weakness of basic healthcare infrastructure in many developing countries, misplaced national budgetary priorities, poverty, and civil conflict, among many other causes. Effectively addressing these conditions requires partnership among national governments, physicians, academic alliances, non-governmental organizations, international and multilateral institutions, and private industry. Research-based pharmaceutical companies are an essential element of this coalition, as Secretary General Annan acknowledged in calling for work on the Millennium Development Goals pertaining to essential medicines to be conducted "in cooperation with pharmaceutical companies."

Unfortunately, the Report as currently written does not adequately reflect that spirit of cooperation, transparency, and partnership, either in its substantive recommendations or the manner of its preparation. The pharmaceutical industry was granted only limited representation on Task Force 5, and the current Interim Report as written does not reflect industry's recommendations. We have thus felt it necessary to submit this document, which reflects substantial input not only from the industry members of the Task Force but also from scientists, policy, and technical experts from a large number of other companies.

In addition to responding specifically to points of significant dispute, the present document addresses two requests made of the pharmaceutical industry on page 19 of the Interim Report:

1. "...assist the public sector in identifying ways in which progress towards the essential goal of access to medicines can benefit from private and competitive initiatives," and
2. "...find approaches to the market which serve the broad public interest in a manner which is compatible with the maintenance and expansion of its business."

Background

The research-based pharmaceutical sector is composed of people who have freely chosen to devote themselves to providing healthcare products and services that extend life and enhance its quality. This industry originated and grew, over the better part of a century, in an environment characterized by certain specific economic characteristics and dynamics. Its business model has evolved in response to societal needs as defined by that environment.

Today all of us in healthcare – not just the pharmaceutical sector – face the daunting challenge of ensuring access to essential medicines for people who live in very different environments than the one which gave rise to the pharmaceutical industry – indeed, the healthcare industry – of the developed world. Our companies share the concern expressed by many observers about difficulties faced by patients in poor countries in gaining access to innovative medicines. The developing world confronts a variety of public health problems – ranging from both age-old and new epidemic diseases to an upsurge in chronic illnesses long common in industrialized countries – that threaten to set back economic development by decades. We are overwhelmed and energized by the extent of suffering in the developing world, and we recognize that many patients cannot obtain innovative medicines that they desperately need. There is no lack of desire to respond – rather a lack of knowing how to respond in the most effective and sustainable way. Herein lies the tension between the different groups and organizations that rally around the ATEM challenge. That tension must not lead to impugning of others' motivations – that would only distance us further from each other and hinder the discovery of effective solutions.

Finally, we must acknowledge the need to recognize, understand, and overcome the cultural and "language" differences among us. We work in different sectors and reside in different countries with distinct political cultures and economic structures. This diversity allows us to bring very different mindsets and approaches to this discussion. These differences can either polarize us or strengthen our response to the challenge we face. For the sake of millions in the developing world who look to us for answers, we must assure that it is the latter. We must find ways to step back from the emotions we all hold, understand that we all care about this challenge, and recognize that involvement of all sectors is essential if we are to find and implement workable solutions.

The most significant contribution our companies make to the goal of expanding access to essential medicines – and one that we are uniquely qualified to provide – is to discover and develop new cures and treatments for the diseases affecting developing countries. However, our companies are also fully committed to working in partnership with others to ensure that our medicines are available as broadly as possible, consistent with preserving our ability to innovate.

The Interim Report reflects many concerns shared by research-based pharmaceutical companies, but it also contains erroneous assumptions or incomplete factual statements regarding the pharmaceutical industry. A specific response is absolutely critical in order to correct faulty perceptions or misconceptions explicitly stated or implied in the Interim Report, and to ensure an accurate understanding of the realities of the research-based pharmaceutical sector.

The most common criticisms of the pharmaceutical industry reflected in the Interim Report relate to:

- “Western spectrum of innovation”;
- “the high prices generally demanded by the innovative industry for its products”;
- “the high proportion of its earnings which industry devotes to promotion and administration rather than research”; and
- “various means used by some innovative manufacturers to extend the protection of their intellectual property beyond normal period of patent validity or otherwise impede the introduction of low-cost generic equivalents”

[Interim Report, p. 18, Sec. 1.5.4]

The industry response to these criticisms can be broken down into the following major topics: innovation, pricing, investment in research, intellectual property, costs and quality of manufacturing, and appropriate use of medicines.

Innovation

Perception. Regarding the discovery and development of innovative medicines, the Interim Report states:

- “A medicinal substance which is required must exist. A fundamental problem is that the medicinal treatments required for many purposes do not exist and that, in the case of diseases prevalent in developing countries, therapeutic innovation has largely been lacking (MSF 2001). This in turn reflects the fact that industrial research has been preponderantly directed towards treatments for diseases of the western world, including the diseases associated with affluence (Trouillier 2002).” *[Page 23, Sec 2.2.1 “Failure to Innovate”]*
- “At the national level, governments should determine the correct priorities in medicinal innovation in accordance with the most basic and unfulfilled needs of their populations, and bring these priorities emphatically to the fore in their domestic

policies and in the global fora in which they participate.” [Page 58, Sec 5.3.1 “Improving the Rate and Relevance of Innovation”]

- “At the international level, much can be done to define an expanded role for public investment in medicinal research to meet the most pressing needs of developing countries and poor populations. Within industrialized countries an environment should be developed which is conducive to the private sector making a greater contribution to innovation in public health, including the creation of medicines attuned to developing country needs” [Page 58, Sec 5.3.1 “Improving the Rate and Relevance of Innovation”]

Reality. Recent advances in pharmaceutical science have produced a revolution in the state of global public health. Health-related technology improvements led by the introduction of new medicines and vaccines have contributed importantly to treating and curing diseases and improving patients’ quality of life. Innovative medicines are estimated to have reduced human mortality by more than 50 percent between 1960 and 1990, saving tens of millions of lives and enhancing the quality of life for millions of additional patients in developed and developing countries alike.

Patients have benefited directly from access to new cures for previously untreatable conditions. The first treatment to ameliorate symptoms of AIDS was launched in 1987, only four years after the discovery of HIV. Since then, private-sector pharmaceutical firms have developed four new classes of antiviral medicines, and more than 80 new treatments are currently in clinical trials. According to the UK Medical Research Council, death rates from AIDS have plunged by 80 percent since the middle 1990s, when advanced antiretroviral therapies were introduced and achieved widespread use in the United States and Europe. A laudable goal for 2015 would be to see a similar reduction in death rate due to HIV/AIDS across the developing world.

The role of health innovation in keeping patients one step ahead of the changing profile of disease is even more critical today, as global demographic changes lead to older populations suffering from the twin burden of chronic non-communicable ailments and new infectious pathogens resistant to established therapies. Forms of HIV/AIDS, tuberculosis, and malaria that are resistant to currently available treatments are rapidly increasing, especially in the developing world. This fact underscores the need for a policy environment that encourages additional innovation.

The Interim Report’s recommendations for increased public-sector involvement in setting pharmaceutical research priorities and monitoring sales and marketing practices would, if adopted, threaten prospects for future innovation. Abundant experience in recent decades indicates that governments should restrict themselves to activities that cannot be performed more efficiently by the private sector. This emphatically does not include pharmaceutical discovery and development. Indeed, the Interim Report’s emphasis on government-led solutions for expanding access to medicines is incompatible with the

indispensable role of the private sector in discovering and developing new cures and treatments.

Private research-based pharmaceutical companies have produced the overwhelming majority of new medicines now on the market and available to patients in all countries. Fully 77 percent of patented products added to the WHO Essential Drugs List (EDL) between 1977 and 2002 originated and were substantially developed by the private sector.

Pharmaceutical innovation is a difficult, lengthy, expensive, and high-risk process, and the business model that makes it possible is fragile. Scientific, financial, and political factors all affect the ability of innovative pharmaceutical firms to create new medicines. This is very important, as the private sector has the unique specialist skills and broad knowledge base to successfully bring a promising compound to regulatory approval. Indeed, only pharmaceutical companies are uniquely capable of managing the entire R&D chain, starting with early discovery and research and continuing with testing, manufacturing, distribution, and marketing.

In addition, large diversified pharmaceutical companies have the ability to commercialize the bioscience research taking place in small companies that are satellites to academic research “hubs” or “clusters.” These smaller firms have very narrow fields of research, and their product portfolio is often limited to just a few compounds. Investment and risk capital from big pharmaceutical companies help these firms develop and refine their products and bring them to market, not only commercializing useful products for the benefit of the public, but also creating revenue streams for these small biotech firms to invest in further innovation.

Turning to in-house capabilities, major pharmaceutical firms remain unchallenged when it comes to broad product portfolios and the consequent ability to generate a sustainable flow of new medicines. These unique capabilities enable pharmaceutical companies to strike a balance between ambitious, high-risk projects – which, if successful, would create a radical new approach to treatment – and lower-risk projects that offer an incremental gain in an established therapy. One of the key challenges involved in this process is the constant adjustment of the research portfolio to maintain this balance throughout the ten to fifteen years that elapse between initial discovery research and final regulatory submission. Again, large pharmaceutical firms can minimize the risks through development alliances with other companies and in some cases universities linked to licensing and contract research.

Pharmaceutical companies also make substantial capital investments in their own R&D capacities on a regular basis just to keep up with emerging technology. High-throughput screening and combinatorial chemistry are just two examples of technologies that can enhance the efficiency of identifying useful drug targets. In practice, no single company can invest in all available technologies. Consequently, pharmaceutical companies have developed a unique sense of how to tap into the latest process innovations. This skill cannot be easily replicated by an industry outsider. The vast libraries of compounds

made possible by these new technologies form an important element in the industry's expanding knowledge base.

Another strong capability of the R&D industry is its ability to organize and manage large-scale, internationally-based clinical trials. Indeed, major pharmaceutical companies are almost unique in having sufficient funding, facilities, and human resources to successfully run complex clinical trials (Box 1). In 1998 alone the industry spent \$7 billion on clinical trials, constituting more than one third of the total R&D budget. Leading pharmaceutical companies have each established twenty or more clinical trials centers around the world. This part of the R&D process can last as long as 7-8 years, and may require as many as 40,000 patients to participate (e.g. for cardiovascular diseases and vaccines), with no guarantee that regulatory authorities will approve the final clinical trial report or the product dossier based on the trial data.

Box 1. The Pharmaceutical Industry's Capacities in Clinical Trials

- **Production of clinical trials materials (and projecting the scaling-up of the production for commercial purposes)**
- **Financial capacities to fund clinical trials**
- **Technical and organisational capacities to conduct huge international trials on different patients' groups**
- **Logistical set-up**
- **Project management (combining technical, safety, medical, regulatory and commercial issues)**
- **Programming and conducting the whole process of clinical trials (4 very different phases)**
- **Dealing with regulatory authorities (experience, knowledge, know-how)**
- **Preparation of regulatory dossier (up to 100,000 pages)**
- **Very specific and diversified human resources: medics, state-of-the-art statisticians, IT specialists, quality managers, technicians, etc.**

Likewise, private research-based pharmaceutical firms have the unique ability to prepare a product dossier for submission to regulatory authorities, the final stage of development process before regulatory approval. This element is crucial since it determines the end result of years of R&D efforts. Pharmaceutical companies, as originators of medicines and vaccines, need advanced access to the skills and resources needed to fulfill all these requirements – in notable contrast to generic producers, who simply rely on existing data from earlier clinical trials financed by the innovative companies. The difference in underlying costs is very significant – on the order of hundreds of millions of dollars.

In view of the unique capability of the private research-based pharmaceutical sector to discover and develop new medicines, the Interim Report errs by calling for a dominant role for governments in providing healthcare products and services. Although the public sector can make important contributions in basic research, it has no comparative advantage in developing innovative medicines. This task can be done far more effectively by the private sector, which has superior capacity to deliver innovation in

health products and services. It would be a grievous mistake to adopt the Interim Report’s recommendation that governments – rather than markets – set medical research priorities for private companies. In particular, it would be a grave error to adopt recommendations urged by some industry critics for a new R&D treaty giving governments primary responsibility for funding and managing pharmaceutical research and development.

In addition, the Interim Report echoes the misguided accusations of anti-industry activists that the research priorities of private industry ignore the needs of developing countries. Such criticism assumes that virtually all diseases prevalent in developing countries are “neglected,” and that private pharmaceutical firms invest almost nothing in R&D for these diseases. Some health activists even argue that the entire R&D paradigm needs to be changed in order to address health problems of the poor.¹

The issue of pharmaceutical R&D for diseases prevalent in developing countries indeed deserves more attention, as it is directly linked to the core objective of private research-based companies, i.e. pharmaceutical innovation. For instance, some industry critics allege erroneously that only about 10 percent of the global health research budget (private and public) is used for research into 90 percent of the world’s health problems.² In fact, non-communicable diseases such as cardiovascular diseases, cancers, neuropsychiatric disorders, and diabetes account for 55 percent of global deaths. It seems reasonable to conclude that the bulk of pharmaceutical R&D should be focused on these indications (Table 1).

Table 1. The Focus of Pharmaceutical R&D

DISEASE	% of Global Deaths / DALYs	Number of New Chemical Entities (NCEs) approved in 1975-99	As a percentage of all NCEs
Infectious and parasitic diseases	19.3 / 24.5	224	16
Malignant neoplasms (cancers)	12.6 / 5.2	111	8
Neuropsychiatric disorders	1.8 / 13	211	15
Cardiovascular diseases	29.3 / 9.8	179	13
Respiratory diseases (asthma)	6.3 / 4.3	89	6
Other	31.7 / 43.2	579	42
TOTAL	100	1393	100

Source: Trouiller P., Olliaro P., Torreele E., Orbinski J., Laing R., Ford N., Drug Development for neglected diseases: a deficient market and a public health failure. *The Lancet*, 2003.

Furthermore, as shown in Table 2, the very same diseases have gained importance in developing countries, where they cause 46 percent of deaths (33 percent in least developed countries). Regarding infectious diseases, which remain the greatest health problem in developing countries, analysis of the pharmaceutical sector pipeline over the past six years reveals a rather different situation than the one described as the “10/90 gap”. For example, based on a January 1999 issue [#75, R.Currie] of Scrip Magazine, in 1998 alone, 11 percent of the 11,054 global R&D projects of private research-based companies focused on infectious diseases.

¹This proposal advanced by MSF, CPTECH, and other leading health activists assumes the establishment of a multilateral convention (R&D Treaty) in order to shift the R&D paradigm from a market-base process to a need-based one.

²This is so-called 10/90 gap, brought to the fore and advocated by the Global Forum for Health Research.

Table 2. Diseases Profiles in Developed and Developing Countries

% of deaths in developing/developed countries caused by	High mortality developing countries	Developing Countries	Developed Countries
Infectious and parasitic diseases	34.6	24.8	2.1
Respiratory infections	9.9	8.0	3.7
Perinatal conditions	6.7	5.6	0.4
Maternal conditions	1.7	1.2	0.0
Nutritional deficiencies	1.3	1.1	0.0
Malignant neoplasms (cancers)	6.3	9.9	21.2
Diabetes	0.6	1.5	1.7
Neuropsychiatric disorders	1.3	1.4	2.9
Cardiovascular diseases	18.9	23.4	47.8
Respiratory diseases (asthma)	4.0	6.7	5.0
Digestive diseases	2.7	3.4	3.7
Injuries	8.4	9.5	7.5
Other	3.4	3.4	3.7
TOTAL	100.0	100.0	100.0

World Health Report 2002, WHO

The truth is that effective treatments already exist – or at least substantial R&D efforts are underway – for the great majority of disorders. HIV/AIDS, malaria, and tuberculosis illustrate how private-sector R&D efforts (undertaken individually or in collaborations) can address the most important diseases of the poor. The industry’s response to HIV/AIDS has not only been immediate but broad-based, with a new class of treatments coming on stream in the 1990s that have allowed patients a virtual reprieve on what was formerly a certain sentence of death. Today, twelve pharmaceutical and biotechnology companies are working on an HIV vaccine, which is generally considered the only possible solution to the AIDS problem in developing countries. Even for diseases such as malaria and tuberculosis, which are economically less attractive targets, pharmaceutical companies have recently engaged either alone or in public/private partnerships to deliver new treatments. (Table 3 and Box 2).

Table 3. Malaria Initiatives by Pharmaceutical Companies

Industry Efforts	Results
<p>Drug development within individual companies over last 10-15 years</p>	<ul style="list-style-type: none"> ○ Roche introduced <i>Larium</i>, Wellcome (now GSK) introduced <i>Malarone</i> (both are entirely novel approaches to both the prophylaxis and, importantly, the treatment of uncomplicated malaria). ○ Novartis, in collaboration with pharmaceutical companies from China has developed <i>CoArtem</i>, a combination of natural and semi-synthetic products. ○ Currently, GSK has two anti-malaria drugs in development (Phase I and III of clinical trials)
<p>Drug development through public private partnerships</p>	<ul style="list-style-type: none"> ○ In just three years since its establishment in 1999, MMV (Medicines for Malaria Venture) has managed to create what is widely viewed as ‘the largest antimalarial drug research portfolio since World War II’ comprising of 15 projects. Currently, 8 biopharmaceutical companies from developed countries and 3 companies for developing countries are involved in MMV. ○ A new combination product, <i>Lapdap</i>, has been developed by GSK, which has specific activity against the malaria parasitic infections of Africa. The drug is now being registered
<p>Vaccine development through public private partnerships</p>	<ul style="list-style-type: none"> ○ GSK has been actively involved in the process of R&D for malaria vaccine since 1983. Early clinical studies of different projects started in 1990s and have continued ever since. Company’s projects are now considered the most advanced for protecting children in Africa against the <i>Plasmodium falciparum</i> strain of the malaria parasite. In the meantime GSK signed an agreement with MVI (Malaria Venture Initiative) to accelerate development of malaria vaccine for children in Africa. Currently the vaccine candidate is in Phase II Clinical Trials.

Box 2. Pharma Companies Investing in Tuberculosis

Three pharmaceutical companies have recently set up new R&D plants to develop new drugs for tuberculosis:

- AstraZeneca has created new Discovery Research Facility, worth \$11 million, in Bangalore (India) which will focus exclusively on TB. The facility has been equipped and designed accordingly and it is hoped that a strong drug candidate will be developed by 2006.
- Novartis has set up Novartis Institute for Tropical Diseases, a \$122 million research institute which will focus on R&D into TB and Dengue fever.
- GSK is conducting R&D into diseases of developing world in its research facility at Tres Cantos in Spain. Among diseases researched, TB remains a substantial target. GSK also cooperates in a project called the TB Vaccine Cluster, a joint academic-industry consortium working conducting early stages of TB vaccine R&D.

Another interesting initiative comes from Eli Lilly, which has established a partnership under which it will *inter alia* transfer its technology to manufacture two antibiotics necessary for treatment of multi-drug resistant TB, establish Centre of Excellence for the training of medical personnel, and create comprehensive surveillance program of TB treatment. The value of Eli Lilly’s contribution is some \$70 million.

For a small number of diseases of the poor, there is a need to create additional mechanisms to incentivize R&D. Such diseases can be referred to as the truly “neglected diseases.” The list of diseases of the poor that cannot be effectively addressed by privately-based research efforts alone is much shorter than is often asserted (see Table 4). Moreover, the diseases in question do not in fact represent the principal health problems of the countries concerned.

Table 4. Identifying “Neglected Diseases”

NEGLECTED DISEASES	Health Burden as a Percentage of Deaths/DALYs		
	Global	Developing Countries	High Mortality Developing Countries
Trypanosomiasis Chagas disease Schistosomiasis Leishmaniasis Lymphatic filariasis Onchocerciasis Dengue fever Leprosy	0.2 / 0.9	0.32 / 1.04	0.46 / 1.37

Source: World Health Report 2002.

Some of these diseases urgently call for substantial R&D investment, since no effective and safe treatments currently exist for them. For others, medicines exist but the mechanism of their application should be reconsidered, as should the whole strategy of controlling the disease. Various attempts to prioritize the need for R&D among “neglected” diseases ³ have led to a unanimous conclusion that efforts should be focused on the three kinetoplastid diseases: African trypanosomiasis, Chagas disease, and leishmaniasis (Box 3 below).

It is worth noting that the research-based pharmaceutical sector has already developed currently-available medicines for all of the diseases listed in Table 4. For example, there are two available medicines (Merck’s ivermectin and GSK’s albendazole) that can cure lymphatic filariasis. Both companies donate these medicines under a joint initiative with the WHO Global Alliance to Eliminate Lymphatic Filariasis.

Effective medicines and similar programs exist for other so-called neglected diseases, including onchocerciasis (the Mectizan Donation Program), leprosy (the Global Alliance to Eliminate Leprosy) and African trypanosomiasis (an initiative between WHO and three pharmaceutical companies – Aventis, Bayer, and Bristol-Myers Squibb). Also, two other diseases described in Box 3 have attracted the attention of pharmaceutical

³ WHO-IFPMA Working Group on Priority Infectious Diseases, Working Paper, July 2001; Remme J.H.F. et al, Strategic emphasis for tropical diseases research: a TDR perspective. *Trends in Parasitology*, Vol. 18, No. 19, October 2002; Depoortere E., Legros D., Torrele E., Developing a Needs-Based and Rational

companies. There are several products available for leishmaniasis, all developed by private-sector companies in collaboration with the WHO TDR. The same is true for Chagas disease, for which Roche has donated rights and technology to manufacture Benzonidazole (the most effective drug for Chagas disease) to the Brazilian government.

**Box 3. R&D Priority Neglected Diseases:
African trypanosomiasis, Chagas disease, leishmaniasis**

All three diseases are caused by kinetoplastid protozoa and present significant scientific challenges. The existing drugs are parenteral in use, need multiple administrations, have serious side effects and are increasingly becoming ineffective due to rising resistance.

African trypanosomiasis (Sleeping sickness)	Endemic in 36 countries in Sub-Saharan Africa of which 7 countries are highly endemic and 4 endemic. Number of people at risk: 60 million Number of people infected: 300,000-500,000 Annual death toll: 50,000
Leishmaniasis	Endemic in 88 countries. Visceral leishmaniasis (VL) is the most serious form of the disease which is fatal if untreated. 90% of all cases are found in Bangladesh, Sudan, Brazil and India. Cutaneous leishmaniasis (CL) is the most common form. 90% of all cases occur in Iran, Afghanistan, Syria, Saudi Arabia, Brazil and Peru. Number of people at risk: 350 million Number of people affected: 12 million Annual death toll: 59,000
Chagas disease (South American trypanosomiasis)	Endemic in 21 countries of Latin and Central America. Number of people at risk: 100 million Number of people infected: 16-18 million Annual death toll: 13,000

Source: <http://www.who.int/tdr/diseases/default.htm>; <http://www.who.int/health-topics/idindex.htm>

In the case of the three diseases listed in Box 3, populations affected may represent a large number of potential patients. However, because these disorders affect almost entirely the poorest populations of the world, the market of potential medicines as well as healthcare infrastructure are virtually nonexistent. Also, most of the concerned countries do not grant patent protection for pharmaceuticals, which further deters R&D investment in these areas. The absence of these vital stimulants to private-sector research helps to explain why pharmaceutical companies have not yet delivered a sufficient number of needed medicines in these specialized cases.

Despite the substantial achievements of research-based pharmaceutical firms, there is a dramatic ongoing need for new and innovative medicines and vaccines to fight current, emerging and evolving health challenges. The World Health Organization estimates that there are at least 2,000 current medical conditions whose origins are unknown and for which adequate treatments are lacking. Furthermore, emerging and evolving health threats are a continual challenge, as the SARS crisis illustrates.⁴

Health needs of developing countries are also changing with time. For example, disease patterns are converging between rich and poor countries. Cardiovascular disease is already the leading cause of mortality in many developing countries, and diabetes is not far behind. This convergence is closely related to the global trend toward aging populations. Chronic conditions that afflict the aged disproportionately require substantial R&D efforts in order to provide satisfactory treatments.

Pharmaceutical innovation is also required to address resistance to existing therapies. In the United States and Europe, resistance of HIV to antiretroviral medicines can reach as high as 30 percent in some populations.⁵ Resistance is also growing in developing countries plagued by infectious diseases such as malaria and TB. Counterfeiting exacerbates the problem, and is particularly dangerous for the anti-retroviral therapies used to treat AIDS. Nigeria was recently forced temporarily to suspend imports of a number of essential medicines after discovering up to 70 percent of the imported volume was counterfeit.

⁴ SARS has also proven the critical role of pharmaceutical companies in finding new cures. Just months after the outbreak of the epidemic there were nine biopharmaceutical companies working on drug/vaccine candidates for SARS. *Scrip*, 7-9 May 2003.

⁵ Gallo R.C., Montagner L., Débats et Opinions. *Le Figaro*, No. 18293, 2 June 2003

Box 4. What is the Need for Innovation?	
Major Disease Categories	Demand for Innovation
Infectious and parasitic diseases	Ever increasing number of infections (over 25 new diseases identified since 1973); new antibiotics and other improvement treatments needed; the growing fear of bioterrorism
<i>HIV/AIDS</i>	Despite a significant number of medicines no "cure" is available; great need for medicines and especially vaccines
<i>Malaria</i>	Counterfeits, lack of compliance, and mutations have all contributed to ever increasing resistance to existing medicines; given the vulnerability of children vaccine is most desired as well as safe drugs with pediatric applications
<i>Tuberculosis</i>	Similar explosion of resistance and the severity of HIV/AIDS - TB co-infection; need for simplified treatment
<i>Tropical diseases</i>	Existing products often ineffective and with important side-effects
Malignant neoplasms (cancers)	Despite huge progress in the area of anti-cancers this remains one of the most urgent therapeutic categories for pharmaceutical R&D
Neuropsychiatric disorders (e.g. Alzheimer, Parkinson diseases)	These diseases represent some of the most disabling and most expensive disorders; these conditions by and large remain chronic and incurable at this point
Cardiovascular diseases	Cardiovascular diseases are the leading cause of death in the world; there is need for better treatments and prevention tools
Respiratory diseases (e.g. asthma)	Asthma is a huge unmet medical need; drug R&D is essential for progress
Digestive diseases	Existing regimens for peptic ulcer are unsatisfactory; obesity is becoming important health problem worldwide

Source: Kaitin K.I., The importance of innovation in pharmaceutical research. *Pfizer Journal*, 2001; 4(5).

In summary, innovation in the pharmaceutical sector is often taken for granted, yet is just as often misunderstood. Popular perceptions of research and development of pharmaceutical products are often superficial and greatly underestimate the complexity of the discovery and development process. Even more unsettling, however, is the lack of understanding of the fragility of the innovation process. Indeed, at times short-sighted government policies aimed at reducing health costs actually cut away at the very basis of pharmaceutical innovation, paradoxically increasing overall health costs and depriving patients of the benefits of innovation. The most important drivers of innovation are:

- market-based pricing;
- intellectual property protection;
- sustained public support for basic research;
- a policy environment that protects current complementary and synergistic roles of public and privately funded research; and
- a predictable, expeditious regulatory climate based upon sound science and innovative leadership.

Government policies which support these principals encourage innovation. On the other hand, if policies do not support them, then innovation is dramatically slowed or even stopped. The ultimate denial to access is to have no new drugs and vaccines.

Market and Pricing Strategies

Perceptions. The Interim Report makes the following statements about the pharmaceutical industry's marketing and pricing strategies:

- "...the world market prices of many medicines, especially those supplied only by research-based companies, are attuned to the purchasing power of wealthy nations, and may be out of reach of even moderately poor countries." [*Final Draft Interim Report, Dec 2003; p. 30 Sec 2.3.1 "Resources for Procurement"*]
- "Whatever the prices at which medicines are procured, they are still likely to be out of reach of many consumers in poor countries. The state of internal government finance in many developing countries is too parlous to permit subsidizing pharmaceuticals when they are supplied to the population at large or providing them entirely free of charge to patients with no significant family income." [*Ibid, p.30 Sec. 2.3.2 "Affordability for the Individual"*]
- "While the Task Force appreciates the costs of maintaining the operations of research-based innovative firms must ultimately be borne by the world community, it would seem no less than equitable that those expenses should be borne primarily by the nations with the broadest shoulders, i.e. western industrialized countries with a strong economy which are capable of paying relatively high prices for the medicines which they require." [*Ibid. p. 31 Sec 2.3.3 "Problems posed by issues of Intellectual Property Rights"*]
- "There is no general trend for the manufacturers of specialties to reduce their worldwide prices...the essential question is whether multinational industry will be prepared to move from differential pricing to "equity pricing." [*Ibid. p. 43 Sec 4.1.2 "Price Reductions"*]

Realities. The research-based pharmaceutical sector shares the concern expressed in the Interim Report that many patients in developing countries cannot afford innovative medicines they desperately need. We recognize that many least-developed countries lack the resources to purchase the latest cures and treatments, and we are committed to working in partnership with governments, international organizations, philanthropic institutions, and others to overcome that obstacle. Nevertheless, the Interim Report errs in identifying lack of affordability as a principal obstacle to pharmaceutical access in developing countries. In fact, price is not a significant barrier to access in the developing world, in view of the industry's differential pricing practices and its many philanthropic access and donation programs. Indeed, efforts to reduce public spending on medicines threaten to worsen rather than ameliorate public health conditions.

The Interim Report errs in urging governments and other payers to push for the lowest price possible for medicines. The preoccupation of many governments with reducing spending on medicines is counterproductive – it threatens to drive up spending in other areas of the healthcare system, while making it harder for patients to obtain the latest therapies. This misguided approach is especially prevalent in industrialized countries

outside the United States, most of whose pharmaceutical markets are dominated by the public sector. Availability of medicines to patients in these countries is affected by the adequacy of health funding, budget allocation systems, and the process of price negotiation between pharmaceutical companies and all-powerful government agencies. Healthcare policymakers in these countries tend to view pharmaceuticals as the source of budgetary savings. Unfortunately, modern healthcare systems are characterized by a very complex cost structure in which many costs tend to be indirect or at least uneasy to identify. Medicines expenditures are the easiest cost factors to identify, and thus are the most tempting targets for cost-reduction policies.

In fact, price controls on pharmaceuticals have become more prevalent around the world, and in several cases have jeopardized the ability of pharmaceutical companies to continue discovering and developing new medicines. In Japan and some European countries, where price controls are a long-standing tradition, pharmaceutical companies prefer not to launch certain products because it would be uneconomical to do so. In addition, many government administrations now pay considerable attention to regulatory regimes in other national markets and, more specifically, have taken to “benchmarking” actual prices of medicines across groups of similar countries, despite the difficulties of making accurate comparisons.

Furthermore, new monitoring mechanisms and national guidelines based upon cost as well as clinical effectiveness have induced physicians to use cheap generics as widely as possible, and to be cautious in using expensive new products. In this case, patients are refused specific treatments that would otherwise significantly reduce underlying economic and social costs. Such developments clearly have serious negative repercussions for patients and society.

Such an attitude is also explained by the prevalent tendency among policymakers to look for short-term benefits and savings that may bring immediate relief to overcharged healthcare budgets, working in favor of political agendas. Paradoxically, these short-term benefits imply substantial costs over the long term, increasing the vulnerability of the whole healthcare system to financial pressures. Systemic healthcare reforms which are based on thorough analysis of the cost structure, and which prioritize well-being of patients as a central policy objective, would be more effective in promoting quality health care than short-sighted budget cuts.⁶

Cost-containment initiatives aimed squarely at pharmaceutical budgets, together with loss of confidence within the financial community, raise questions about the sustainability of the business model that generates innovation – and leave little room to address the special needs of the poor in countries with neither infrastructure nor the financing to capture the benefits of new medicines. Indeed, the Interim Report makes no connection between the prices paid in advanced industrial countries and the capacity of the research-based sector to meet the need for medicines in poor developing countries, many of which have no capacity to pay at any price.

⁶ See NERA. Global Principles for Better Health Care: A Guide for Policymakers. A Report for the IFPMA prepared by National Economic Research Associates. December 2002.

When government officials understand the value of pharmaceutical innovation for their domestic healthcare systems, they will tend to spend more on pharmaceuticals, not less. Such governments will also tend to be more open in allowing access to state reimbursement and formularies for newer medicines as well as more flexible in price negotiations with pharmaceutical companies. By doing so, they can create a win-win situation whereby both national healthcare systems and pharmaceutical companies gain clear benefits. The former improve the health status of patients while generating financial savings in the long run. The latter can recoup the costs of R&D and continue the process of innovation. Such arrangements are crucial for the whole system of pharmaceutical innovation, which is largely financed through the sale of existing products and where success or failure is determined by payers and physicians. They also enable pharmaceutical firms to generate the returns that are used to fund philanthropic access initiatives and research into new treatments for diseases of the poor.

Market factors affecting innovation are not limited to the national scale. Indeed, one effective market mechanism – which the Interim Report does not adequately acknowledge – is the ability of companies to charge different prices in different countries. Many factors influence price variations for pharmaceutical products across countries, including the size of the market, the development of the national economy, per capita income, local medical usage patterns, taxes and other mark-ups on prices, inflation, and fluctuation of exchange rates.

The existence of price variations has the following significant effects on the availability of medicines among different markets:

- Consumers (countries) who are charged the lower prices would be unable to purchase at a higher price. In other words, differential pricing gives consumers in a much greater number of markets access to new medicines.
- Patients consume a larger total volume of medicines overall, so a larger proportion of the global patient population base has access to new products.

International price variations for pharmaceuticals have an important positive impact on research-based pharmaceutical companies, as these variations allow the cash flow and resources that finance continued innovation. To recoup the high costs of R&D, companies must strive to launch new products simultaneously in many countries – a practice facilitated by price variations. Differential pricing also enables firms to sell products at low prices in lower-income countries, provided that safeguards exist to prevent the reimportation of these low-cost medicines into higher-priced markets.

In summary, developing countries clearly have a primary need for access to safe and effective medicines at prices they can afford, with distributions systems and healthcare infrastructures in place to assure effective use. Continued pharmaceutical innovation is essential for ensuring that developing countries can obtain new medicines to treat diseases unique to their environments. Dr. Patricia Danzon of the Wharton School has summarized the challenge as follows:

The standard means to encourage innovation in any industry, including pharmaceuticals, is to provide patent rights. But patents work by enabling originator firms to charge prices above marginal cost, in order to recoup their investments in R&D. Thus prima facie it appears that patents inevitably lead to high prices and that there is an inherent conflict between the objective of encouraging R&D and the objective of assuring access at affordable prices.

Danzon notes that options exist for ensuring this access – notably differential pricing, confidentially applied between originator firms and individual countries or perhaps original firms and regional procurement systems. If differential pricing is to provide a sustainable solution, however, it must be implemented in a way that addresses known problems with parallel trade and reference pricing. Those practices have already helped to drive much of Europe’s pharmaceutical research base to the United States. If adopted in developing countries, such measures would also undermine the foundations of innovation there.

Danzon’s analysis of differential pricing concludes that policies enabling pharmaceutical prices to vary across markets based on differences in true price elasticity will lead to higher overall social welfare and greater equity than policies encouraging narrow price bands or uniform prices across countries. Her recommendations include:

1. Defining patents based on national boundaries, including the right to bar parallel trade;
2. Implementing differential pricing through country-specific contracts with confidential rebates; and
3. Barring higher income countries from reducing their prices by referencing lower prices in low-income countries

(For additional insights on the challenges of pricing and possible solutions see various articles by Patricia M. Danzon, Ph.D., Jacob Arfwedson, et.al.)

The vaccine industry provides a number of lessons and cautions that must be kept in mind when considering solutions. According to the Institute of Medicine Report, “Microbial Threats to Health” released in 2003, the world faces a serious crisis with respect to vaccine development, production, and deployment. Concern has increased over the inadequacy of vaccine research and development efforts, periodic shortages of existing vaccines, and the lack of vaccines to prevent diseases that disproportionately affect developing countries. In contrast to the vast complex of institutions and individuals involved in basic medical research related to vaccines, only four leading companies worldwide have developed new vaccines during the past two decades. This concentration of responsibility for vaccine innovation did not result from mergers and acquisitions. Instead, firms were driven out of the vaccine business by the rising costs of innovation, production, and distribution and the shrinking margins allowed by monopsony, or the concentration of buying power in the hands of a relatively small number of public agencies. In the United States, several large companies ceased vaccine production because the total world market for vaccines was so much smaller than that for

pharmaceuticals; because government purchases allowed only narrow profit margins; and because liability continued to be an issue. The current economic situation surrounding vaccine innovation has not changed, and thus will not encourage the entry or reentry of large pharmaceutical companies with extensive resources to dedicate to vaccine innovation. If anything, the economic situation has deteriorated further. The increasing costs associated with discovery have become a major barrier. Under political pressures to hold down costs, many government agencies place downward pressure on margins, which make it difficult to sustain the needed level of innovation and production.

Pre-emptive regulatory and political pressures on the industry can wreak havoc, simply because conditions that shape the initial research and development process are set in motion one to two decades before the results are apparent at the final product stage. A host of intervening economic, technological, and socio-political factors can affect pipeline flow in the interim.

Only the developed nations can afford a pricing system that favors innovation. The manner in which vaccines are priced in the U.S. market cannot be applied to markets in Africa, Latin America, and Southeast Asia. In Japan and Europe, government-controlled markets have long prevailed. The IOM report also warned about an emerging crisis in the antibiotic industry for many of the same reasons. The challenges related to vaccine and antimicrobial development are many and complex. New solutions must be sought to alleviate some of the political pressures against differential pricing in the United States. Solutions will require a novel, coordinated approach among government agencies, academia, and industry. Issues that must be examined and addressed in a more meaningful and systematic fashion include the identification of priorities for research, the determination of effective incentive strategies for developers and manufacturers, liability concerns, and streamlining of the regulatory process.

Investment in Research

Perception. The Interim Report refers to “...the high proportion of its earnings which the industry devotes to promotion and administration rather than research” [*Final Draft Interim Report, Dec 2003, Sec. 1.5.4. The Situation and Perspective of the Pharmaceutical Industry*“]

Reality. The United States serves as the best source of data to put into perspective the pharmaceutical sector’s research investment. Biomedical research investment in the United States has steadily increased over the past forty years. This trend has accelerated recently with an infusion of public funds into NIH and to a lesser extent other federal agencies. The federal government still sponsors the vast majority of biomedical research carried out in academia and, in fact, has doubled the funding of NIH over the past five years (from \$13 billion in 1998 to \$27 billion in 2003).⁷ What is less evident, however, is that private sector investment in internal and sponsored biomedical research has not

⁷ Rosenberg, L.E. Exceptional Economic Returns on Investments in Medical Research. *Med. J. Aust.* 177:368-371, 2002.

only kept up with the public sector but now equals or even exceeds it (\$35 billion from the pharmaceutical industry and approximately \$5 billion from the biotechnology and medical device industry).⁸ On average, the innovative pharmaceutical industry spends approximately 17 percent or more of its sales on R&D—three times more than the telecommunications sector, four times more than the average aerospace and defense industry, and four times more than the average of all other U.S. industries.⁹ In 2003, the combined investment in biomedical research in the United States by both the public and private sectors exceeded \$70 billion.

The unprecedented scientific and medical advances of the last four decades have resulted from a sustained commitment to biomedical research by governments, as well as by the innovative pharmaceutical and biotechnology industries. No one questions that the resulting advances in both basic and applied research have provided a return to the taxpayer in the form of many newly discovered medicines that have greatly improved the health and quality of life of our citizens, extended life expectancy and saved billions of dollars in healthcare costs. What is generally not appreciated, however, is the essential, unique, and complementary roles that both industry (private sector) funded and federally (public sector) funded research play in translating these advances into tangible new treatments and the interrelatedness and synergies between the two. Although scientists in research based pharmaceutical and biotechnology companies contribute significantly to basic research and thus to increasing our fundamental understanding of disease, it is also true that federally funded investigators have traditionally conducted the bulk of basic biological research. However, the pharmaceutical industry continues to lead the way in the more applied research activity that ultimately results in the discovery and development of most new medicines, i.e., the actual compound or biological entity that is the drug. In fact, an analysis by the NIH of the top 47 selling FDA-approved drugs in 1999 (drugs with annual sales of \geq \$500 million) revealed that 43 or $>90\%$ were discovered and developed primarily by the pharmaceutical industry and only 4 or $<10\%$ were discovered primarily by the public sector.¹⁰ However, the exact (and often unrecognized) contribution(s) to drug discovery and development made by both the research based pharmaceutical industry as well as the federally-funded research enterprise are far more complex than these numbers indicate, and the numbers alone do not reveal the critical and complimentary roles that both the public and private sectors play in the drug discovery and development process.

Increasingly, research-based companies are valuable partners with researchers from academia and the public sector on basic research projects. However, companies that license inventions from universities pay the majority of the innovation's final cost and pay for all the failed efforts and blind alleys and the promising drugs that prove not to be sufficiently safe and sufficiently effective to gain approval for marketing from the

⁸ Pharmaceutical Industry Profile 2003. www.pharma.org

⁹ Ibid

¹⁰ DHHS, NIH, Report to the United States Congress, NIH Response to the FY 2001 Conference Report. <http://www.nih.gov/news/070101wyden.htm>

regulatory authorities. Each dollar invested in an academic invention or discovery can fuel upwards of \$10,000 of private capital to translate the invention into a useful product and bring it to market.^(11, 12) When a private sector investment does succeed, the average time for drug approval from the original scientific idea can be 10 to 15 years, or even longer. As indicated earlier, the average cost of discovering and developing a single drug depends on investing more than \$800 million in research and development – and this figure has steadily and dramatically risen over the past two decades. Applied pharmaceutical research and development is a very high-risk venture, with a failure rate from beginning to end that is in excess of 90 percent. Moreover, even if successful, seven of every ten regulatory-approved medicines fail to generate revenues that meet or exceed average R&D costs despite their therapeutic value.^(13, 14) This is exacerbated by the necessity to occasionally withdraw approved medicines from the market based upon subsequent data about risks versus benefits. Consequently, drugs selected for development within a given company must undergo stringent prioritization -- otherwise the current pharmaceutical model would not be economically sustainable.

Extension of Intellectual Property

Perception. The Interim Report refers to “Various means used by some innovative manufacturers to extend the protection of their intellectual property beyond normal period of patent validity or otherwise impede the introduction of low-cost generic equivalents.” [*Ibid. Sec. 1.5.4*]

Reality. Pharmaceutical companies generate innovation in health needs not only through inventing new treatments for previously untreated health problems (radical innovation) but also by developing new and improved uses for or new and improved forms of existing therapeutics (incremental innovation). The latter is crucial because the process of pharmaceutical innovation, just like any other innovative process, is built on constant improvements, and these incremental innovations significantly improve health and quality of life. The old unimproved uses or forms of existing drugs do not receive increased patent protection, and become available to the public at the end of the original patent term. This situation is exactly analogous to other fields of technology, where most patents are granted for improved forms of existing products, rather than breakthrough products, the result of radical innovation. Nevertheless, critics of the pharmaceutical industry have seized on these attempts to provide improved products for the public by spreading the myth that in some way this patenting of new and improved forms amounts

¹¹ Economist.com 4/21/03.

¹² Edwards, M.G., Murray, F, Yu, R. Licensing and commercialization: How is value created and shared among universities, Biotech, and Big Pharma? *Nature Biotech*, 2003. 21:618—625.

¹³ Grabowski, H., Vernon, J., and DiMasi, J. Returns on research and development for 1990s new drug introductions. *Pharmacoeconomics*. 20 (suppl. 3):11-29, 2002.

¹⁴ Pharmaceutical Industry Profile 2003. www.phrma.org

to "evergreening" of the original, unimproved, patented invention. This is simply incorrect. The patent for the old unimproved pharmaceutical product expires in the normal way, and the inventions disclosed therein become freely available to generic companies.

The benefits arising from incremental innovation are often underestimated. R&D companies use the limitations of even the most cutting-edge products as opportunities to develop related compounds that are more effective, more selective, and less toxic. By generating such incremental innovations, the industry has managed to significantly improve original products, creating therapeutic classes that offer multiple agents that provide for alternative treatments in case of failures of other existing drugs, or product back-ups in case of drug withdrawal from the market.¹⁵ The results in terms of efficiency, patient responsiveness, reduced side-effects, add up to one outcome: better value for money and lives saved.

Manufacturing Quality and Costs

Perceptions. The Interim Report makes the following statements about pharmaceutical manufacturing:

- "... it is an incontrovertible fact that once a medicine has been taken into mass production, the costs of manufacturing it are generally very low, perhaps less than 3% of the overall expenditure." [*Final Draft Interim Report, Dec 2003; p.12 Sec. 1.3 "An Economic Approach to Access"*]
- "Where these standards [GMP] have not yet been attained, the decision will have to be taken from case to case whether a particular product or supplier offering lesser standards can as a temporary measure be regarded as tolerable...some flexibility may be tolerated for certain simple remedies with a broad safety margin." [*Ibid. p.28 Sec. 2.2.6 "Issues of Quality"*]
- "...those medicinal products which prove to be a seriously inadequate standard of quality because of negligence or dishonesty on the part of the manufacture...constant vigilance is needed..." and Sec. 5.3.3 "Promoting the Safety of Medicines", Even more serious is the phenomenon of spurious and counterfeit medicines...superficial copies of well-known items but having little or no content of the active component...they represent a danger to public health..." [*Ibid. Sec. 2.2.7 "The Challenges of Sub-Standard and Counterfeit Drugs", p. 59*]

¹⁵ Wertheimer A., Levy R., O'Connor T., Too many drugs? The clinical and economic value of incremental innovations. Investing in Health: The Social and Economic Benefits of Health Care Innovation, Vol. 14, 2001, pp 77-118.

Reality. Once a product has been developed and approved, quality manufacturing is required to bring it to consumers. The Interim Report properly emphasizes the importance of good manufacturing practices (GMP) in producing medicines. Research-based pharmaceutical companies have unique advantages in manufacturing medicines according to high standards of quality and safety, since they alone have mastered the tasks of assuring quality control, designing and implementing manufacturing processes and plants, and constructing and commissioning primary and secondary manufacturing plants. All these activities, while linked to post-development processes, need to be organized during the development phase. Given that a failure in adhering to the highest quality standards may result in direct and immediate wide-scale damage to human health, the importance of perfecting high-quality, efficient manufacturing processes must not be underestimated.

Pharmaceutical companies not only invest substantial amounts in modern, integrated and multi-purpose plants, but they must also manage properly the logistics of such plants, in order to adapt the production capacities to changes in demand (both downward and upward). The leading R&D companies are uniquely qualified to ensure quality manufacturing, reliable marketing and distribution, and post-marketing surveillance – consistently, on a worldwide basis.

In addition to improving access to medicines, we must do everything possible to ensure that medicines are both safe and effective. To do otherwise would be to promote practices and standards below those expected in the developed world, which would clearly be at odds with basic human rights. Here are the facts: we know that medicine safety and efficacy are a direct result of implementing quality manufacturing practices. These practices, in turn, have implications for manufacturing costs and ultimately price; those connections and consequences are undeniable and unavoidable. Furthermore, as originator firms scale up to production-level manufacturing, some economies of scale will drive the per-unit cost down. However, many medicines are simply difficult to manufacture from a scientific and/or technical standpoint; and those manufacturing challenges, with their associated costs, are not diminished simply by an increased scale of production. Unfortunately, this reality results in the pursuit of manufacturing practices at odds with both safety and effectiveness – manifest in both sub-standard and counterfeit manufacturing operations – either or both with disastrous results for patients.

A recent *Lancet* article (“Pharmacopoeial Quality of Drugs Supplied by Nigerian Pharmacies”) makes clear the stark and deeply troubling reality of this problem:

The quality of medicines available in some less developed countries is inadequate in terms of content of active ingredient (...46% of locally manufactured preparations and 31% of imported products failed to meet set standards). Reasons for the poor quality of drugs include widespread counterfeiting of medicines in less developed countries, excessive decomposition of active ingredients as a result of high temperature and

humidity, and poor quality assurance during the manufacture of medicinal products.

The conclusion of the article sums up the challenge very well:

The potential health implications for the use of anti-infectives of poor quality are of concern. Where the amount of active drug is well below stated amounts, use of these preparations could lead to therapeutic failure and select for drug-resistant organisms. Around a quarter of all deaths in children aged 5 years and younger are associated with acute respiratory infections. WHO's regimen for the management of acute respiratory infections in childhood includes pediatric formulations of amoxicillin and ampicillin. Of the 13 syrup samples analyzed, the mean active drug content was 63% of the stated dose, and the use of these preparations could effect the successful outcome of treatment. The global burden of malaria is estimated at over 300 million cases and 1 million deaths, and of tuberculosis at more than 8 million new cases and 8 million deaths yearly. One sample of pyrazinamide was devoid of active drug and, when used for the treatment of TB, could contribute to both therapeutic failure and resistance in the patient. Widespread use of substandard drugs would contribute greatly to microbial drug resistance in standard therapeutic drug regimens. An excess of active content could also have serious consequences such as toxicity and side-effects, especially in pediatric formulations.

Evidence is building that the extent of problems associated with medicines safety and efficacy (e.g., second- and third-world manufacturing quality) is large and growing in the developing world. Whether due to poor local or regional manufacturing practices or the manufacture and/or importation of counterfeit products, the results are the same. Furthermore, if we wait for absolute confirmation of this alarming trend, the proof will be the thousands of individuals who have needlessly died for lack of successful treatment and/or due to the insidious, silent threat of microbial resistance.

Sustainable solutions to this challenge must include, but are not limited to the following:

1. Improve regulatory oversight and increase financial investments directed toward manufacturing quality in developing countries;
2. Develop robust interdiction, with financial and legal remedies assessed against substandard and/or counterfeit manufacturing operations;
3. Establish programs for technology transfer and the sharing of best practices and lessons learned between pharmaceutical manufacturing operations of the developed and developing worlds; and
4. Identify and make available any excess pharmaceutical manufacturing capacity in the developed world to manufacture priority medicines for use in the developing world.

Intellectual Property Rights and Data Exclusivity

Perception. Regarding intellectual property protection and data exclusivity, the Interim Report states:

- “It has been recognized for centuries – and is today virtually unquestioned – that, if enterprise and innovation are to be encouraged, the innovator must be in a position to exploit his discovery so as to reap his due reward and finance future work.” [*Final Draft Interim Report, Dec 2003; p.30-31 Sec. 2.3.3 Problems Posed by Issues of Intellectual Property Rights*”]
- “A restrictive approach may however be actively encouraged or demanded by the original manufacturer, advancing a claim of “data exclusivity”...If accepted, this policy would impede the entry of low-cost generic products to the market or obliging their manufacturers to repeat the original studies in animals, and man.” [*Ibid. p.25 Sec 2.2.4 “Regulatory and Fiscal Obstacles”*]
- “The most important tool for use by the government of developing countries in dealing with obstacles presented by patents is however Article 31, which sets out the procedures for compulsory licensing and government use of a patent...Countries are free to determine what they consider a national emergency and do not need to follow any official procedures... [*Ibid. p.45 Sec 4.1.3 “Interpreting the TRIPS Agreement”*”]

Reality. Many critics identify pharmaceutical patents as a principal barrier to making existing medicines affordable and available to poor populations.¹⁶ Some decision-makers assume that high prices for medicines are attributable to patents, and they promote policies to weaken patent protection or reduce the effective patent life of a product in a short-sighted attempt to reduce healthcare costs. Unfortunately, the Interim Report also appears to view patent protection as a barrier to access to essential medicines. Policies intended to weaken intellectual property protection ignore the fact that (1) patents are in force on only about 30 to 40 percent of global prescription volume and (2) nearly all patented products in use today face competition from anywhere between two and ten close substitute molecules able to treat the same condition – and frequently do so at a lower price than the originator. R&D companies are thus subject to competitive rivals from both the innovative (during patent life) and generic (after patent expiry) ends of the commercial spectrum. Thus, weakening patent protection will further reduce the innovators’ capacities to finance further research into new and innovative products.

¹⁶ In reality, the absolute majority of medicines needed in developing countries (i.e. medicines which are on the WHO Essential Drugs List) are not patented in the countries concerned. Of the 325 WHO essential medicines, at most 19 are patentable anywhere in the world (including 12 antiretrovirals and one antifungal), yielding an overall frequency of granted patents and pending applications of 1.3% for all the cases studied, with most of that accounted for by the antiretrovirals of one company. From an abstract by Attaran A., published at the 2nd IAS Conference on HIV Pathogenesis and Treatment in Paris, 13-16 July 2003.

Moreover, most essential medicines are already available in generic form. The research-based pharmaceutical sector recognizes the legitimate role of generic manufacturers in producing medicines once their patents have expired. But it is worth remembering that a robust research-based pharmaceutical sector benefits a vigorous generic industry. Generic firms gain the right to manufacture a medicine developed through private-sector pharmaceutical R&D immediately following expiration of the patent – and often before. The financial value of such products is enormous. Blockbuster patented products selling over \$1 billion worldwide for which patents will expire within the next five years are worth \$80 billion.¹⁷ Furthermore, the effective patent life is shorter due to tougher regulatory approval requirements before launch, and the time an inventor actually benefits from a patent – while the product is available for sale – is as short as 6.5 years today, compared with 10.8 years in 1997.

Likewise, the period of market exclusivity when the inventor has no other competition in his therapeutic class has decreased dramatically – to just one or two years for most products. Thus, generic companies able to manufacture such medicines on a quality basis have fantastic growth opportunities. This opportunity would not be possible if pharmaceutical companies had not developed a business model that actually invents these medicines and through extensive testing brings them forward for safe use in humans.

Intellectual property protection transforms the intangible capital generated by pharmaceutical companies during the R&D process into financial flows indispensable to continue the cyclical process of innovation. As such, it should be regarded as the heart of the whole system of pharmaceutical innovation. The pharmaceutical sector's dependence on intellectual property protection – and in particular on the temporary marketing exclusivity granted by patent protection – is arguably the highest among all industries.¹⁸

In the chemical and biological sciences, it is relatively cheap and easy to imitate manufacturing processes and commercialize generic copies of medicines, once the innovator has established the value of a molecule for treating a particular disease and satisfied regulatory requirements.

Patents for products last nominally for twenty years from the time of filing in national patent offices in all WTO members who have implemented the TRIPS Agreement. However, meeting the exacting technical regulatory requirements of the product licensing authorities now takes, on average, ten years from the point at which a patent is filed for an invention, which is the effective starting point for the product development process (Box 5). The already shortened effective patent life is further reduced by government policies designed to weaken patent protection and other intellectual property rights in

¹⁷ Important Facts and Figures. *R&D Directions*, November/December 2002, 8(10):11.

¹⁸ Mansfield, E, (1986), Patents and Innovation: An Empirical Study, *Management Science*, (February) 173; See also Mansfield, E, (1993), Unauthorised use of intellectual Property: Effects on Investment, Technology Transfer and Innovation, in “Global Dimensions of Intellectual Property Rights in Science and Technology”, Eds. Wallerstein M, Moge, M and Schoen R, National Academic Press, Washington DC, USA.

order to speed the entry of generics into the market. For example, the “Bolar” provisions in some countries, allowing early working of a patented invention, allow generic companies to perfect their manufacturing processes during the product’s patent life, and jump start their regulatory approval process even before the patent has expired. These otherwise prohibited commercial acts reduce the value of a pharmaceutical patent in a manner not permitted for patents from other technology sectors.

Box 13. Average Patent Exclusivity Periods for NCEs Approved During 1997-2001		
Year	Shortest Duration ^a	Longest Duration ^b
1997	10.8	13.4
1998	13.0	15.0
1999	8.6	10.2
2000	8.3	11.9
2001	6.5	9.1
Average, 1997-2001	9.8	12.3

^a Average number of years between the NDA approval and the earliest possible patent (or exclusivity) expiration.

^b Average number of years between the NDA approval and the latest possible patent (or exclusivity) expiration.

Sources: US Food and Drug Administration, Drug Approvals; List, 1997-2001. US Food and Drug Administration, Electronic Orange Book.

Data exclusivity is another form of intellectual property protection independent of patent protection. Developing a patented discovery into an approved saleable product requires amassing large amounts of data over many years on pharmacology, toxicology, clinical trials, manufacturing processes, and product quality. These data are submitted in confidence as a single dossier to the relevant technical regulatory approval body in national (or EU) jurisdictions to gain a license to sell the product by the innovator. Article 39(3) of the TRIPS Agreement obligates WTO Member States to ensure that this data package cannot be used by a generic copier to facilitate its regulatory approval for a fixed period from the date at which it was submitted to the government authorities.

Regarding Compulsory Licensing, Patricia Danzon offers the following analysis in “Differential Pricing for Pharmaceuticals: Reconciling Access, R&D, and Patents”:

The risk of permitting compulsory licensing is that this approach may expand beyond the circumstances where it is justified by real cost advantage for essential drugs for the most needy populations, to a broad range of drugs and countries that seek to use compulsory licensing as a way to avoid making any contribution above marginal cost to pay for R&D.... Thus many countries could make a hardship case for compulsory licensing of a wide range of drugs. In the absence of clear criteria to define which drugs and countries/populations should be eligible, the

compulsory licensing approach is at risk of undermining the function of patents over broad markets and therapeutics. This approach may seem to offer cheap drugs to needy people in the short run, but at the risk of undermining incentives to develop new drugs in the long run. Moreover, even the short run benefits may be illusory since there is no guarantee that generic companies will price at marginal cost. Even if they do, wholesalers and pharmacies often add high distribution margins, exploiting their local monopoly power. Given the risks inherent in the compulsory “solution”, it seems best to first try the approach of strengthening market separation, in order to make it possible for originator firms to maintain differential pricing. In these instances, originators may offer prices comparable to the prices that a local generic firm would charge, which eliminates the need for compulsory licensing.

A contentious issue regarding IPR is the concept of international exhaustion of patents. The rule in most countries is national exhaustion, where import can be stopped by the patent-holder. In contrast, if governments decide to promote international exhaustion of patents, then the patented products can be imported into the market without the authorization of the patent-holder, a process known as “parallel trade.” Within the European Union, international exhaustion exists and patented medicines can be traded freely within and across national borders but not into the EU from non-EU states. On the other hand, in the United States the law permits contracts that prevent parallel trade into the United States.

Parallel trade is sometimes seen as an important tool to reduce prices, as a purchaser could theoretically buy drugs at the lowest prices around the world. However, promoting such a policy would lead to negative effects internationally. As parallel trade always diverts products from low-price markets to higher-priced ones, it thus diverts needed medicines away from poor populations. Furthermore, parallel trade distorts the pricing strategy of pharmaceutical companies based on international price variations, reducing the access to medicines for poorer countries and depriving innovators of revenues needed for further innovation. Parallel trade thus works against patients and pharmaceutical companies themselves – and the key beneficiaries of parallel trade practices are in fact parallel traders, who keep the profits for themselves.

The pharmaceutical industry offers the following recommendations regarding intellectual property rights:

1. Work with public and private sector constituents to promote an understanding and adoption of IPR in the developing world as a tool for driving economic development;
2. Utilize IPR as a motivation in the second world countries for shifting pharmaceutical firms from “imitation to innovation,” with a particular focus on “essential medicines”;
3. Assist the governments of developing countries in institutionalizing appropriate mechanisms for securing IPR for their own indigenous system of patents and other property protections; and

4. Work with public and private sector stakeholders – in both the developed and developing world – to develop and implement IPR strategies that will promote the more rapid discovery and access to essential medicines for the most critical diseases and/or the most at-risk populations.

Appropriate Use of Medicines

Perceptions. Regarding appropriate use of medicines and the need of patients for healthcare information, the Interim Report states:

- “Prescribers should be protected from temptations to over-prescribe, such as may arise if they also dispense products for profit, or if they are subject to irresponsible advertising and promotion.” [*Final Draft Interim Report, Dec 2003; p. 7, “Executive Summary”*]
- “To ensure well-informed use of medicines in the home, understandable information on their use must be made available through appropriate channels.” [*Ibid.*]
- “A particularly evident problem is the pressure which can be exerted by advertising, generally amounting to intensive persuasion to prescribe newer and more expensive remedies even in situations where these offer no advantages over older products available much more cheaply.” [*Final Draft Interim Report, Dec 2003; p.33 Sec. 2.4.2 “Inappropriate Prescribing”*]
- “WHO ethical guidelines for the promotion of medicines should be updated and at the same time extended to deal with newer issues, including the trend to promote prescription drugs to the public at large and the publication of promotional material on the internet.” [*Final Draft Interim Report, Dec 2003; p.62 Sec.5.5.1 “Better prescribing and dispensing”*]

Realities. The Interim Report correctly stresses the need for appropriate use of medications, both by physicians in their role as prescribers and by patients at home. It also properly acknowledges that inappropriate use can result from poor prescribing or patient non-compliance. The goal of any healthcare system should be to expand the appropriate use of medicines, as determined by physicians themselves. It can only be achieved if governments acknowledge and protect the fundamental right of physicians and patients to healthcare information. Occasional poor use or misuse of medicines points to the need for more extensive education of both physicians and patients about the latest cures and treatments for disease.

The Report wrongly casts suspicion on information provided by research-based pharmaceutical companies about their own products. Such information is an invaluable resource for physicians, who frequently lack time to search it out on their own. In most markets, governments carefully regulate product information provided by pharmaceutical firms to physicians or the general public to ensure its accuracy and reliability. Physicians, who are typically among the most highly educated members of their societies,

are unlikely to absorb such information uncritically or naively, or to let it affect their decisions inappropriately. In any case, pharmaceutical firms have little incentive to undermine trust in their own products through “irresponsible advertising and promotion.”

Achieving optimal health outcomes requires patients to become full partners in their own healthcare. To do so, they need access to a wide variety of sources of healthcare information about disease states, treatment options, and prevention. Consumer-directed information provided by pharmaceutical firms – which goes well beyond traditional product advertising – plays a vital role in familiarizing patients with new treatment options for disease, and in motivating them to see their physicians. Disease-management and health literacy programs carried out by pharmaceutical firms are other essential sources of healthcare information for patients and medical professionals. Besides helping patients take a more active role in their own healthcare, such programs can help physicians communicate more effectively with their patients. A good example is the educational campaign underway for improving appropriate use of antibiotics. Package inserts now include critical information about treatment of acute respiratory tract infection and differential diagnosis. The pharmaceutical industry has partnered with various professional organizations to develop educational information on appropriate use of antibiotics; not only for physicians but also parents and the general public.

Potential Solutions, Options, and Scenarios for Sustainable Access to Medicines

New and innovative approaches are required to meet the unique medicine needs of the developing world. Traditional market forces, which are prevalent in the developed world and drive innovation for the private sector, may not meet every need in these situations. Serious economic, legal, and political tensions result from attempting to apply *in toto* what has worked in one market-health care environment to another quite different market-health care environment. New approaches and business models must be considered and implemented which respond to the unique market dynamics and characteristics of the developing world. Thus, a key condition for innovation for these diseases in these markets is an active role for the public sector – for example, offering drug companies incentives for them to invest in R&D.¹⁹ It follows that the public sector should create proper frameworks that would build incentives for use of the invaluable assets of pharmaceutical companies.

The Interim Report calls upon the private, research-based pharmaceutical sector to:

1. “...assist the public sector in identifying ways in which progress towards the essential goal of access to medicines can benefit from private and competitive initiatives”; and

¹⁹ Peabody J.W., Ruby A., Cannon P., The economics of orphan drug policy in the US. Can the legislation be improved? *Pharmacoeconomics*, 8 (5), November 1995. This could be achieved either by adopting/amending existing orphan drug legislations (Bourgeois, Burns, 2001; Milne et al, 2001) or introducing a ‘neglected disease act’ (CPTECH, 1999).

2. "...find approaches to the market which serve the broad public interest in a manner which is compatible with the maintenance and expansion of its business." [*Draft Interim Report, Dec 2003 p.19 "The Situation and Perspective of the Pharmaceutical Industry"*]

This public-sector involvement can be facilitated either by creating a set of special "push" and "pull" mechanisms (with little or no direct up-front investment), or by establishing public-private partnerships in which the public sector provides financial resources (direct and substantial up-front investment).

Push and Pull Mechanisms: Transferable Exclusivity and Purchase Fund

One option is to award rights of market exclusivity that are not linked to a particular product.²⁰ Such a model has a precedent. Recently, the U.S. Food and Drug Administration suggested that in order to provide incentives to study medicines that do not qualify for exclusivity under the FDA's pediatric exclusivity provisions, a manufacturer awarded²¹ Thus, a company with a new leishmaniasis treatment could seek bids from other companies for its exclusive marketing extension right. This measure offers a way to harness the existing intellectual property system for the benefit of the poorest and their health needs by giving tangible rewards for the successful development of products for neglected disease indications. Also, such a solution does not require direct public funding, and the arising costs could be proportionally distributed among many developed and emerging markets.

Another option to incentivize pharmaceutical R&D in neglected diseases is a "pull" mechanism in the form of a separate purchase fund to fight these diseases. Two existing model examples, GAVI and the Global Fund, provide a good illustration of the opportunities and problems. Theoretically, a single purchase fund could create a market for future medicines and vaccines and thus give incentives for positive investment decisions by pharmaceutical firms. This option assumes that pharmaceutical companies can obtain the up-front money for research, and thus that the funds available through a purchase fund will only be spent upon arrival of a product. This option would place the investment burden on the industry.

²⁰ This is different from 'simple' market exclusivity granted within orphan drug legislations because the underlying conditions are also not the same – namely, there is no promising market for products for most neglected diseases, so market exclusivity would not be of any use.

²¹ www.fda.gov/orphan.

However, there seem to be a number of possible constraints that need to be resolved in order to make this option truly operable and effective.²² These include:

- Problems with mobilizing financial resources across the global community, particularly given the likelihood that governments and political commitments may change over the long period of R&D process (this might require the commitment of up-front funds from public authorities);
- A purchase fund would require active participation of authorities and bodies from recipient countries. This necessitates clear specification of responsibilities and prior commitments of such countries to purchase and co-pay for products developed and delivered through such fund.
- The procedure to be adopted in a situation when a follower product comes onto the market – who would get the award? Only the first innovator?
- Companies would be rewarded only after having developed a product which given the precedent points may not be sufficient to motivate them to start R&D in disease areas concerned.

It is clear that the two options described above relate to public policy measures that may serve as incentives for the private sector to conduct R&D in “neglected” diseases. These options are also not mutually exclusive and can be used as appropriate for the disease research in question.

Public-Private Partnerships

Another solution that could complement the two options described above or be introduced on its own is to create a public-private partnership (PPP). Among existing partnerships, the Medicines for Malaria Venture (MMV) is viewed as a pioneer of PPPs for product development. Consequently there have been several attempts to build on its success with the establishment of other PPPs like the Global Alliance for TB Drug Development (GATB).

MMV offers the most illustrative example of constructive and fruitful collaboration between pharmaceutical companies (as founder partners) and partners from other sectors. Established in 1999, MMV managed in just three years to create what is widely viewed as the largest antimalarial drug research portfolio since World War II, covering no fewer than 15 projects. Using public and philanthropic funds, the partnership manages a balanced portfolio of projects conducted by academic and pharmaceutical partners from developed and developing countries. Currently, eight biopharmaceutical companies from developed countries and three from developing countries are involved in MMV.

²² These points are consistent with the work of Kettler (OHE, 2000).

This approach offers prospects for both faster and cheaper pharmaceutical R&D, since it is based on a close collaboration of partners from both the public and private sectors, leading to in-house early development of new medicines. At later stages of development, partnerships generally tend to license out their candidates to pharmaceutical companies, which are better placed to complete the process and eventually deliver the end product.

Additionally, with the growth of global public-private partnerships there is a unique and timely opportunity to explore the application of new technologies and business processes emerging vis-à-vis the concept of virtual R&D.

Virtual R&D as a Potential Solution

Virtual R&D, as applied to drug discovery and development, would rely upon a technology infrastructure to enable a critical mass of life scientists, pharmaceutical developers, and clinical experts to collaborate effectively around the advancement of product opportunities. It is daunting to assemble, own, and simultaneously bear all the risk associated with this mass of science and operation necessary to advance a portfolio of product opportunities to successful realization. However, accessing this network of scientists, pharmaceutical developers, and clinical specialists could be achieved if the appropriate collaboration platforms were in place.

In this view, the goal is to create a platform that enables a virtual R&D network by effectively connecting and coordinating the appropriate capabilities for collaboration independent of organizational affiliation or geographic/temporal boundaries. This would have the potential to assemble a diverse array of scientists and professionals around a common goal of advancing candidate products down a clinical and development timeline to deliver products to customers. It would effectively exploit the distributed global laboratory structures as sources of ideas and collaborators, and would allow for the pooling of resources that would minimize the amount of capital needed to support the aggregate development portfolio.

Such a proposed venture would leverage a process model and e-R&D solutions to create a platform whereby scientists, clinical investigators, and developers can collaborate with each other, while the sponsoring entity or entities can monitor R&D progress and integrate data in a way that meets requirements. Such a platform will integrate information technology, knowledge management, and project management tools that are specifically needed in advancing product R&D. With these tools in place, a complicated pharmaceutical development program can be broken down into the appropriate array of specific components and the work distributed and coordinated throughout the network of experts and developers around the world, allowing the sponsoring entity or entities to tap into these external resources effectively and efficiently. (For further discussion, see Sawhney's "Innomediation Model," Sloan Mgmt. Review, Winter 2003.)

Prioritization

The Interim Report states that:

- “The priority accorded to health issues and the associated supply of medicines will generally need to be raised.” [*Draft Interim Report, Dec 2003, p. 38 Sec 3.4.2 “National Preconditions: (iii) Priority Setting and Political Will”*]
- “There will for the foreseeable future be a need to set priorities so that the most catastrophic aspects of a situation are dealt with first.” [*Ibid. p. 56 Sec 5.1.4 “The Need to Set Firm Priorities”*]

Industry Response

One of the most pressing needs regarding Access to Essential Medicines is to acknowledge and respond to clear and irrefutable priorities, e.g. focusing the most significant attention and resources on those most urgent and devastating needs. It is widely acknowledged that priority belongs to HIV/AIDS, tuberculosis and malaria. Millions die each year from these diseases, while millions more contract them, increasingly in even more deadly combinations. Both trend lines and absolute numbers for these three diseases continue to rise at alarming rates among the world’s populations, and the 2 billion poorest people in the developing world experience the most direct and deadly impact of this devastation.

First, to meet the overarching global health goals of the UN Millennium Project, we must do everything we can to support the priorities of the other task forces focused on HIV/AIDS, TB, and malaria. From an ATEM perspective, these disease states must remain the clear priorities for individuals and organizations working on global health issues and challenges. Given that resources are finite, we must take care not to diffuse them in a way that jeopardizes our success in meeting the priority challenges represented in the focus of these other task forces. If we are unsuccessful in addressing these three diseases, access to other medicines and related issues will unfortunately be a moot point in view of the rapidity with which these infectious agents are spreading and the rate at which antimicrobial resistance to them is developing.

With respect to AIDS, TB and malaria one of the highest priorities and most immediate needs is to ensure drug quality and appropriate prescribing due to the rapid increase of resistance. With respect to TB the issue is particularly urgent. In some locations, as many as 40% of strains are resistant to 10 or more antibiotics. Only four drugs remain that are efficacious against these strains and they must be used in combination. Due to increased use of these second-line drugs, resistance is rapidly increasing. New compounds are only in the very early stages of development and will likely not be launched for at least six to eight more years.

Second, we need to coordinate, where appropriate and feasible, our recommendations, action plans, and efforts with other ongoing or planned initiatives. Partnering with others will leverage the best efforts of all toward our common goals. To this end, we need to open clear lines of communication, including information and resource sharing, with other leading global health programs, e.g. Global Alliance for Vaccines and Immunizations, International AIDS Vaccine Initiative, Lilly MDR-TB Partnership, Strategies for Enhancing Access to Medicines (SEAM), etc.

Finally, we need to utilize fully all available means to enhance and extend the reach of our efforts. We must engage the broadest share of minds from the world's leading scientific, medical, and technical communities in solving these problems and addressing these crises. New platforms for collaboration, information exchange, knowledge sharing, and virtual R&D must be actively utilized to ensure that the world's largest, most qualified and creative community of problems solvers is directly engaged. We need all that the world can offer in the way of new insights and ideas brought to bear on the world's leading health problems. Simply put, we must match the scope and magnitude of the problem we face with a solution set of equal scope and magnitude. The process and means of solution discovery must be open, transparent, and able to attract innovative ideas and unique solutions from any person, anywhere, at any time.

In summary, by committing the Task Force, the UN, and the broader global health community to such a clear set of priorities and principles, we believe we ensure the best opportunity to reach shared goals of providing cures to millions of the world's poorest afflicted with these deadly diseases, and building the programs, infrastructures, and "know-how" that can then be utilized to address other important ATEM needs.