SPECIAL
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Access to Essential Drugs in Poor Countries
A Lost Battle?

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Drugs offer a simple, cost-effective solution to many health problems, provided they are available, affordable, and properly used. However, effective treatment is lacking in poor countries for many diseases, including African trypanosomiasis, *Shigella* dysentery, leishmaniasis, tuberculosis, and bacterial meningitis. Treatment may be precluded because no effective drug exists, it is too expensive, or it has been withdrawn from the market. Moreover, research and development in tropical diseases have come to a near standstill. This article focuses on the problems of access to quality drugs for the treatment of diseases that predominantly affect the developing world: (1) poor-quality and counterfeit drugs; (2) lack of availability of essential drugs due to fluctuating production or prohibitive cost; (3) need to develop field-based drug research to determine optimum utilization and remotivate research and development for new drugs for the developing world; and (4) potential consequences of recent World Trade Organization agreements on the availability of old and new drugs. These problems are not independent and unrelated but are a result of the fundamental nature of the pharmaceutical market and the way it is regulated.

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THE EFFECTIVENESS OF DRUGS depends on a long chain of factors: research and development (R&D) of an appropriate pharmaceutical agent, production, quality control, distribution, inventory control, reliable information for health care professionals and the general public, diagnosis, prescription, financial accessibility, drug dispensing, observance, and pharmacovigilance. At each level, those involved may have conflicting interests, and poor populations are the first to suffer the effects of frail links in this long chain. Today, entire populations lack access to essential quality drugs, and the situation appears to be deteriorating, further marginalizing much of the world's population.

Essential drugs are the foundation for nearly every public health program aimed at reducing morbidity and mortality in the developing world, and pharmaceutical expenditure can account for a high proportion of the total health expenditure of a country. Important health programs that rely on essential drugs include child survival programs, antenatal care, treatment of enteric and respiratory pathogens, and control of tuberculosis and malaria. Other major public health issues exist for which there is no effective pharmaceutical treatment.

This article focuses on 4 main issues associated with the inaccessibility of drugs for populations in greatest need: (1) poor-quality and counterfeit drugs; (2) lack of availability of essential drugs due to fluctuating production or prohibitive cost; (3) need to develop field-based drug research to determine optimum utilization and remotivate R&D programs for new drugs for the developing world; and (4) potential consequences of the recent World Trade Organization (WTO) agreements on the availability of old and new drugs. For all these issues, practical recommendations to improve the situation are proposed.

The lack of access to essential drugs or vaccines because of economic reasons raises new human rights issues in a world that remains divided among wealthy countries, developing countries, and the rest of the world. Yet, financial access to drugs does not necessarily mean correct use. Continuous training for health care professionals, dissemination of reliable pharmacological data, and improvement of the management of drugs are fundamental steps in improving the quality of care in the developing world.

THE PROBLEMS

Examples of problems related to development and access to drugs and the magnitude of the public health problems concerned are given in TABLE 1.

Counterfeit and Substandard Products

Drug products must be produced according to good manufacturing practices.[1] Unfortunately, many developing countries do not have the technical, financial, or human resources required for the application of such standards, and some developed countries may be less strict when the product being manufactured is destined for exportation. Today, the quality of drugs and, therefore, their effectiveness and safety are less and

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Table 1. 1996 Worldwide Accessibility to Drugs or Vaccines for 10 Diseases*

Diseases†	Deaths†	Incidence (I) or Prevalence (P)†	Drugs or Vaccines	Type of Problem
Acute lower respiratory tract infections	3.9	394 (I)	Ceftriaxone sodium (for severe cases in hospital)	Available but limited use, prohibitive price
			Anti-*Haemophilus* vaccine (Hib conjugates *Haemophilus*)	Available but limited use, prohibitive price
			Antipneumococcal vaccine (group A streptococci)	Clinical development (phase 1 trial)
Tuberculosis	3.0	7.4 (I)	Isoniazid, rifampicin, pyrazinamide, ethambutol hydrochloride, streptomycin, thiacetazone	Poor compliance with therapy and outbreaks of drug-resistant strains (isoniazid, rifampicin)
			Sodium aminosalicylate, ethionamide, capreomycin sulfate	Production not secured, toxic effects of drugs
			Rifapentine	Available but limited use
			BCG vaccine	Effectiveness disputed
Diarrhea	2.5	4000 (I)	Ciprofloxacin (shigellosis)	Available but limited use, prohibitive price
			Antirotavirus vaccine	Available but limited use, prohibitive price
			Anticholera vaccine (whole cell B)	Available but limited use
			Anticholera vaccine (103Hgr)	Available but limited use
			Antishigellosis vaccine	Clinical development (phase 2, 3 trials)
Malaria	2.0‡	300-500 (I)	Pyronaridine	Clinical development (phase 3 trial)
			Artemisinin derivatives	Available but production not secured for substandard products
			Coartemether	Clinical development (phase 2, 3 trials)
			Atovaquone-proguanil	Available but limited use
			Antimalaria vaccine (preerythrocytic)	Clinical development (phase 2, 3 trials)
			Antimalaria vaccine (asexual erythrocytic stage)	Clinical development (phase 2 trial)
Preventable diseases (pertussis, measles, diphtheria, polio, tetanus)	1.7	82 (I)	Pertussis whole cell, measles, diphtheria, oral polio, and tetanus vaccines	Substitution of classic formulations by new formulations, prohibitive price (eg, acellular pertussis)
Human immunodeficiency virus	1.5	3.1 (I), 22.6 (P)	Antiretroviral drugs	Available but limited use, prohibitive price
			Anti-HIV vaccines	Clinical development (phase 1, 2 trials)
Hepatitis B	1.2	200 (P)	Hepatitis B recombinant vaccine	Available but limited use
Human African trypanosomiasis	0.15	0.2 (I), 0.3 (P)	Suramin sodium	Production not secured (no commercial interest)
			Pentamidine isethionate	Production not secured (no commercial interest)
			Melarsoprol	Production not secured (no commercial interest)
			Eflornithine hydrochloride	No longer produced (no commercial interest)
Leishmaniasis	0.08	2 (I)	Meglumine antimoniate	Production not secured (no commercial interest)
			Amphotericin B lipid complex	Limited use
			Aminosidine	Old drug (production stopped)
Meningitis	0.04	0.4 (I)	Ceftriaxone sodium	Available but limited use, prohibitive price
			Oily chloramphenicol	Available but production not secured for substandard products
			Antipneumococcal vaccine	Clinical development (phase 2, 3 trials)
			Anti-*Haemophilus* vaccine (Hib)	Available but limited use, prohibitive price
			Meningococcal A-C conjugates vaccine	Clinical development (phase 2 trial)

*For these diseases, there were a total of 16.07 million deaths of 52 million worldwide. One third (17.3 million) were due to infectious diseases (>90% in developing countries).
†Data, in millions, are from the World Health Organization, *World Health Statistics Annual*, 1996.[17]
‡Data indicated in *World Health Statistics Annual* as 1.8/2.2.[17]

less certain, especially for the poorest populations, who are attracted by lower-priced drugs sold outside pharmacies.

Recent years have seen an increase in the prevalence of counterfeit and substandard drugs on the market. Counterfeit drugs are those that mimic authentic drugs; substandard drugs are those produced with little or no attention to good manufacturing practices.

For example, during the meningitis epidemic in Niger in 1995 (41 000 cases reported), Niger authorities organized an extensive vaccination campaign. In March 1995, Niger received a donation of 88 000 Pasteur Mérieux and SmithKline Beecham vaccines from neighboring Nigeria. A Médecins Sans Frontières (MSF) team working with local health authorities noticed that the vaccines from Nigeria had an unusual appearance (eg, difficult reconstitution, black filaments in the solution). Inquiries were made and Pasteur Mérieux laboratories confirmed that the batch numbers and expiration dates did not correspond to their records. The drugs supplied had been substituted with counterfeit drugs. Tests carried out found no traces of active product, confirming they were false. Bottles and labels were copied to perfection.[2,3] Pasteur Mérieux subsequently filed a counterfeit suit. Some of the false vaccines (approximately 28 000) were located by batch number and destroyed. According to estimates, approximately 60 000 persons were inoculated with false vaccines of a total 5 million vaccinated during the campaign. Such a production would have necessitated an industrial-scale manufacturing facility, and it is probable that the 88 000 vaccines identified as false did not account for the entire fraudulent production.

Médecins Sans Frontières teams have encountered similar field examples that lead to the following conclusions: organized illegal circuits seem inclined to manufacture copies with the appearance of known trademark drugs (counterfeit) than comparatively less-expensive generic products, whereas nonorganized illegal circuits (small production) increasingly manufacture drugs that are substandard or inadequate, including generic drugs.

Poor quality may be accidental, with no intention to deceive, but oversights in manufacturing or neglected controls can have tragic consequences. Such was the case in recent decades with acetaminophen syrups that contained, by mistake, a lethal ingredient.[4,5]

Fluctuating Production of Essential Drugs

Drugs necessary for the treatment of certain tropical diseases have begun to disappear from the market because they are commercially unprofitable. Many of these drugs were discovered in the 1950s and 1960s or earlier and are seldom or never used in wealthy countries.

An example is seen in the effort to treat epidemic bacterial meningitis, caused by *Neisseria meningitidis*, which is rampant in sub-Saharan Africa. Efficacy of treatment with chloramphenicol in oily suspension (1 intramuscular injection repeated after 48 hours) for bacterial meningitis is comparable with the traditional treatment with ampicillin (intravenous injections 4 times daily for 10 days).[6] The lower cost of chloramphenicol in oily suspension—only one tenth the cost of ampicillin—and its simple administration make it particularly suitable to the precarious conditions in developing countries.[6] This is particularly important during epidemics. In Nigeria in 1996, for example, more than 100 000 cases of *N meningitidis* infections were reported.[7] However, production and availability of chloramphenicol in oily suspension are no longer guaranteed. Roussel-Uclaf stopped its production in 1995 and transferred its technology to another laboratory, which began production last year. In the meantime, temporary solutions have ensured that a certain (but far from sufficient) amount of chloramphenicol is made available.

The circumstances described herein also apply to other serious illnesses, such as leishmaniasis and its treatment with meglumine antimoniate and African trypanosomiasis and melarsoprol (Table 1). The trypanocidal activity of eflornithine hydrochloride was discovered in 1985.[8] It is the only treatment proven effective in cases in which African trypanosomiasis shows resistance to melarsoprol, and such resistance is becoming more frequent (20% in Omungo, Uganda).[9] This drug was sold at an extremely high price and is now no longer manufactured. Only through a joint effort of the World Health Organization (WHO), nongovernmental organizations involved in fieldwork, cooperative bodies, and pharmaceutical companies could this drug become available and affordable again.

Prohibitive Costs

The prohibitive cost of antiretroviral drugs for treatment of people with acquired immunoeficiency syndrome is well known.[10] There are many other examples of drugs that are simply not affordable, most of which have been recently marketed and therefore are still patent-protected.

Shigella dysenteriae type 1 dysentery is extremely contagious and, without effective treatment, is lethal in 5% to 15% of cases.[11] Since 1979, this disease has been the cause of large epidemics in Africa (for example, in Malawi in 1992 and 1993[12] and in Burundi in 1994[11,13,14]). *Shigella dysenteriae* type 1 bacteria quickly became resistant to traditional treatments. The only effective antibiotic drugs today are fluoroquinolones (eg, ciprofloxacin and norfloxacin). However, treatment with these new drugs is 10 times more expensive than the traditional treatment using nalidixic acid (approximately $20 vs $2).[15] A special agreement was reached between Bayer Laboratories and MSF in 1997 to make available treatments with ciprofloxacin for 50 000 people for a unit price of $2 per treatment. This example shows that it is possible to find a short-term ad hoc solution with the pharmaceutical industry, yet no midterm solution is anticipated.

A recent study of bacterial meningitis caused by *Streptococcus pneumoniae* in children aged 2 months to 3 years demonstrated that use of ceftriaxone sodium could reduce mortality from 66% to 32% compared with treatment with chloramphenicol in oily suspension.[16] Both antibiotics have a sustained action and require very simple protocols (daily intramuscu-

lar injection for a short time) and therefore are equally easy to use in adverse conditions. However, ceftriaxone treatment is 10 times more expensive than chloramphenicol treatment.[16] *Streptococcus pneumoniae* infection is also one of the main causes of severe acute respiratory tract infections—the primary cause of child mortality in Africa.[17] Therefore, ceftriaxone is vital but financially inaccessible to those populations that need it most.

Prohibitive pricing also extends to prevention when new vaccines are not available for the population most at risk. For example, hepatitis B virus and anti-*Haemophilus* vaccines are not accessible because of their steep price. Vaccines for hepatitis B, a disease predominantly found in eastern Asia and sub-Saharan Africa,[18] are approximately 10 times more expensive than other vaccines included in the Expanded Programme on Immunization promoted by UNICEF.[19]

Essential Drugs Not Adapted to Field Conditions

Tuberculosis caused the deaths of 3 million people in 1997, but the current treatment regimen, known as *directly observed therapy—short course* (DOTS), is impractical and compliance is poor: only 23% of the world's population has access to the WHO tuberculosis control strategy.[20] Research to simplify or shorten the DOTS regimen is needed to make the treatment more widely available. Furthermore, the emergence of strains resistant to commonly used antibiotics has potentially devastating worldwide consequences. Current second-line treatments are too expensive, too complex, and too long, and therefore not realistic for field conditions. Priority should be given to simpler treatment guidelines that combine several antibiotics, which may not achieve the same level of efficacy of more complex protocols but are at least more practical for the field. Today, those with multidrug-resistant tuberculosis in countries with limited financial resources are not receiving treatment, which from a medical and humanitarian perspective is completely unacceptable.

Access to drugs for poor populations would be greatly improved by research into new forms of existing drugs (eg, sustained action or rectal formulation) and the development of simpler treatment guidelines (eg, "one-shot" or short treatments). This type of research cannot be developed unless technical and financial resources are made available and, more importantly, unless new efficacy criteria are applied to the treatment being studied.

Insufficient R&D for New Drugs

Increasing drug resistance, adverse effects, and the lack of feasibility of current protocols point to the need for greater R&D into new drugs for diseases found in the developing world. From 1910 to 1970, the pharmaceutical industry's contribution was crucial to the fight against endemic tropical diseases: trypanocides and antiamebic agents in the 1930s (Bayer, Rhône-Poulenc), chloroquine during World War II (Specia, Winthrop), and in the 1960s, the discovery of leading anthelmintics (Janssen). Since then, pharmaceutical companies have adopted a completely different strategy.[21]

Among the 1223 new chemical entities commercialized from 1975 to 1997, 379 (30.9%) are considered therapeutic innovations, but only 13 (1%) are specifically for tropical diseases (**TABLE 2**). Two of these 13 drugs are actually updated versions of previous products (new formulations of pentamidine and amphotericin B), 2 are the result of military research (halofantrine hydrochloride and mefloquine), 5 come from veterinary research (albendazole, benznidazole, ivermectin, oxamniquine, and praziquantel), and only 4 (0.3%) may be considered direct results of R&D activities of the pharmaceutical industry (artemether, atovaquone, eflornithine, and nifurtimox).[22]

Thus, it appears that pharmaceutical R&D is abandoning tropical diseases. There are 4 main reasons for this shift:

1. Costs and Risks of R&D Relative to the Low Purchasing Power of Developing Countries. A typical R&D program (from initial results to registration) would cost approximately $160 million and take between 8 and 12 years to complete.[23] Moreover, a successful outcome is not guaranteed (as was the case with oltipraz, an antibilharzial agent abandoned during clinical trials).

2. A Shift to More Profitable Production. To cope with large investments and reduce duplicate spending, pharmaceutical companies started an unprecedented cycle of industrial consolidation and mergers at the end of the 1980s (eg, Glaxo and Wellcome, Sandoz and Ciba-Geigy, Roche and Synthex). This consolidation focused on the most profitable segments of the market (infectious diseases, cardiovascular conditions, cancer, dermatology, and neurology), leaving tropical medicine largely out of the equation.

3. Competition and Counterfeiting of Drugs. Some drugs patented in the developed world are being copied in developing countries, where patent rights of pharmaceutical products are not protected. Such production competes, sometimes fiercely, with the innovating laboratory. For example, Bayer Laboratories, the patent holder of praziquantel, was outpriced by Shin Poong, a Korean laboratory that had developed a less-expensive manufacturing process.[24] In addition to copies of drugs resulting from a different notion of intellectual property rights, there are cases of pure and simple piracy (appropriation of the name and appearance of a trademark drug) that are frequent in countries where informal markets play a significant role.[25]

4. Cost of Adhering to Quality Standards. There has been a general trend toward heavier regulations with which companies must comply to obtain approval before marketing a drug product, which raise the costs of clinical development. The necessity of minimizing therapeutic risks leads to reinforcement of various quality standards (good clinical, laboratory, and manufacturing practices).[26] In practice, when clinical development incidentally identifies a promising product (eg, eflornithine for African trypanosomiasis) or a new indication (eg, atovaquone for malaria, ivermectin for onchocerciasis, and albendazole for lymphatic filariasis) for the treatment of tropical diseases, the manufacturer often decides not to market the drug,

knowing it would be too expensive. The company generally decides to either make exceptional arrangements (eg, donations in the cases of albendazole, atovaquone, and ivermectin) or takes negative action (eg, discontinued production of eflornithine).

GLOBALIZATION AND DRUGS: QUESTIONS AND CONCERNS

A discussion of the current landscape in the area of drug availability would not be complete without a consideration of the increasing globalization of the pharmaceutical industry and the potential implications of recent and upcoming world trade agreements.

Drugs: Another Industrial Product?

The General Agreement on Tariffs and Trade (GATT) was signed on April 15, 1994, and was replaced by the WTO agreement, signed in 1997.[27] This agreement ratifies the worldwide implementation of a free-trade economy. Its enforcement with regard to the pharmaceutical sector raises certain concerns. Two types of provision seem particularly important for pharmaceutical companies in developing countries: that which puts an end to protectionist measures and that which defines as mandatory the protection of patents on drugs and their respective manufacturing processes, such as the Trade Related Aspects of Intellectual Property Rights Agreement (TRIPS). This is important because many developing countries do not fully acknowledge patent protection rights for pharmaceuticals.

Newly Invigorated Research?

Directors of pharmaceutical companies in the developed world have stated repeatedly that the reason for not conducting research on tropical diseases is the lack of protection for innovations in some developing countries, which would also explain their limited investments in the countries concerned.[28] The moment the enforcement of patent protection becomes effective (in developing countries, no later than January 1, 2006) tropical disease research should logically start again, funded by Western companies or by manufacturers in developing countries.

However, it is unlikely that Western manufacturers will devote much of their effort to nonsolvent populations, with or without patents. Manufacturing companies in developing countries may actually be motivated to invest more in research for new drugs, but such investments will essentially respond to the need to shift their innovation capacity away from finding ways to copy the patented drugs of developed countries and toward discovering new drugs.[29] All things considered, tropical research may not have a more promising future, even if patents are widely enforced.

Table 2. Tropical Disease Drug Development Output, 1975-1997*

Indication	Product	Year Marketed or Approved	Development Context
Marketing Approval of New Chemical Entities for Treatment of Tropical Diseases			
Malaria	Artemether IM	1997	Chinese academy discovery; public/private collaboration (WHO-TDR/Rhône-Poulenc-Rorer); Rhône-Poulenc-Rorer/ Kunmig (China) agreement
	Atovaquone/proguanil	1992/1997	Glaxo-Wellcome antimalarial research; initially orphan product designation and approval for *Pneumocystis carinii* pneumonia associated with human immunodeficiency virus
	Halofantrine hydrochloride	1992	US Department of Defense discovery (WRAIR); public/private collaboration (WHO/WRAIR/SmithKline Beecham); US orphan product designation and approval for acute malaria
	Mefloquine	1987	US Department of Defense discovery (WRAIR); public/private collaboration (WHO/WRAIR/Hoffman LaRoche); US orphan product designation and approval for acute malaria
Human African trypanosomiasis	Eflornithine hydrochloride	1990	Hoechst Marion Roussel; US orphan product designation and approval for human African trypanosomiasis (*Trypanosoma brucei gambiense*)
	Nifurtimox	1984	Veterinary R&D (Bayer)
Schistosomiasis	Oxamniquine	1981	Veterinary R&D (Pfizer)
	Praziquantel	1980	Veterinary R&D (Bayer); public/private collaboration (WHO/Bayer)
Helminthic infections	Albendazole	1987	Veterinary R&D (SmithKline Beecham)
	Benznidazole	1981	Veterinary originally (Roche)
Onchocerciasis	Ivermectin	1989	Veterinary R&D (Merck); public/private collaboration (WHO/Merck)
New Indications for Chemical Entities			
Human African trypanosomiasis	Pentamidine isetionate	1950/1984	Rhône-Poulenc-Rorer; galenic reformulation (mesylate to isetionate); US orphan designation and new approval only for *P carinii* infection
Leishmaniasis	Amphotericin B lipid complex	1962/1996	NeXstar; galenic reformulation of amphotericin B in liposomes; US orphan designation and approval only for treatment of invasive fungal infections

*WHO indicates World Health Organization; TDR, Tropical Disease Research; WRAIR, Walter-Reed Army Institute of Research; and R&D, research and development. Products are listed by international nonproprietary names.

Increasingly Prohibitive Prices?

A study sponsored by US pharmaceutical companies shows that granting drug patents does not tend to increase the price of drugs on the market.[30] This study, however, does not examine the prices of new innovative drugs and declares that, logically, the price of these new drugs should be higher. Naturally, when the manufacturing company is assured that its product cannot be copied, it holds a stronger position to negotiate prices with public health authorities. Moreover, the liberalization of international pharmaceutical trade entails the development of parallel imports between countries where the same drug is sold at different prices. Pharmaceutical companies, which are consequently less inclined to grant significantly lower prices to less developed countries, may instead set unique worldwide prices or delay marketing their drugs in developing countries.[28] In either case, access to drugs is jeopardized.

RECOMMENDATIONS

WHO's Revised Drug Strategy and the essential drugs concept are still key strategies to help improve access to essential drugs and worldwide health. The essential drugs concept is evidence based, is simple, promotes equity, and is rooted in firm public health principles. WHO's assistance to countries and advocacy work to promote the essential drugs concept and support countries in the formulation and implementation of national drug policies has resulted in change for the better. This strategy is a proven success but it needs to be continued and strengthened, and new ways of implementation have to be explored, given the changing context. In this spirit, the following recommendations are made with respect to the 4 main issues that have been developed in this article.

Procurement of Quality Drugs

To improve the quality of existing drugs and their procurement, it is important to develop a permanent "Observatory of Drug Quality," established by WHO in collaboration with organizations involved in the provision of essential drugs (eg, UNICEF, World Bank, the European Union, and nongovernmental organizations), that would oversee the implementation of adequate and effective control procedures. The practical knowledge acquired by international organizations to ensure the quality of generic drugs must be shared with health authorities in developing countries. Invitations to bid, required by big sponsors such as the World Bank, European Union, and the US Agency for International Development, must combine quality criteria and lower costs. Furthermore, procurement of drugs should be centralized at a national level to reinforce the responsibility of governments to make procurement, quality control, stock management, and distribution of essential drugs a priority.

Increased Availability

To provide better access to effective treatments for people in greatest need, several initiatives must be launched now, even if their results will not be realized immediately. In the short-term, practical solutions involving the various partners must be found to maintain the production of essential drugs. By establishing public health priorities, new high-priced drugs must be made available to the poor through solutions similar to those implemented for Expanded Programme on Immunization vaccines, for which the supply is guaranteed by UNICEF. These drugs could be made available by creating centralized purchase funds whereby manufacturers would be guaranteed large sales volumes (financed by existing public and private funds). The funds would also set forth, by consensus, compliance with drug indications. Finally, operational research in the field must be promoted and developed in close collaboration with health care professionals in developing countries. Such research should produce simple, efficient, and low-cost protocols without losing sight of the risk-benefit factor for the poorest countries.

Restart of R&D

In an attempt to offset this costly structural evolution in the pharmaceutical industry, several public and private initiatives have attempted to introduce public health criteria in R&D strategies. The 1975 Special Programme for Research and Training in Tropical Diseases (sponsored by the United Nations Development Programme, World Bank, and WHO) has had outstanding results in strategic research (eg, entomology and pathogenesis) and has bolstered research potential (eg, epidemiology and training). However, strategies for product R&D that were actually launched in 1994 have yet to produce any convincing results.[31] Nevertheless, this program has succeeded in raising awareness and has promoted reflection on potentially effective tools, even if most projects focus exclusively on malaria (eg, Multilateral Initiative on Malaria). The US Orphan Drug Act implemented in 1983 also has produced significant results for rare diseases (157 new drugs were commercialized and 837 new indications were developed from 1983 to 1997), but no real impact has been seen with respect to tropical diseases.[32] We can therefore conclude that while such initiatives may occasionally boost the development of new drugs (eg, derivatives of artemisinine and pyronaridin), they are unable to significantly redirect R&D toward tropical diseases. In the midterm, a legal and fiscal framework must be developed to spur R&D on tropical diseases or related areas, similar to those developed in the United States for orphan drugs used in rare diseases.

Humanizing the WTO Agreements

On the whole, it is regretful that WTO agreements contain no specific provisions that would guarantee both funding for ambitious tropical pharmaceutical research and realistic pricing of potential drugs. However, some developed countries were able to protect vulnerable economic and business sectors (eg, textiles, agriculture, and culture). One can understand why wealthy countries demand that developing countries comply with regulations on unfair competition. It is obvious that to meet pressing public health needs, we need new essential drugs. To develop them, we need

innovative research and industry. To fund new research, industry needs commercially viable results. It is therefore vitally important that the pharmaceutical industry collaborates with organizations like WHO, UNICEF, and the World Bank to identify the challenges and get a clearer view of what they can achieve together in developing sustainable markets for new tropical pharmaceuticals.

It must be remembered that those developing countries that are the main sources of cheap copies of patented drugs[31] are nevertheless relatively poor. Enforcing the WTO regulations will remove a source of affordable copies of innovative quality drugs on which the poorest countries depend. Developing countries, particularly the less advanced, should be encouraged to take advantage of the limited alternatives offered by the WTO agreements. Specifically, they should be able to obtain compulsory licenses whereby national authorities allow local manufacturers to circumvent patent rights (with certain conditions and in return for the payment of royalties to the inventor, as stipulated in article 31 of the WTO agreements).[33] Judiciously enforced, such an alternative seems to be the only recourse to balance the interests of the developing and developed world.

WHO is in a unique position to argue the case for health at an international level. Health-related nongovernmental and consumer organizations certainly have a supportive role to play, but WHO is the only intergovernmental organization with a formal international mandate to protect and advance health internationally. While WHO's authority in this area has suffered in the last decades, part of WHO's strategy should now be to clearly and unambiguously put health first and provide leadership in promoting access to essential drugs.

CONCLUSIONS

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.

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