Increasing access to medicines

Civil Society Commentary on the IGWG draft Plan of Action

Increasing Access to Medicines: Civil Society Commentary on the IGWG draft Plan of Action

Alternate Solutions Institute, Pakistan
Asociación de Consumidores Libres, Costa Rica
Cediquifa, Argentina
Center for Science in Public Policy, Hudson Institute, USA
Centro de Investigaciones de Instituciones y Mercados de Argentina
Free Market Foundation, South Africa
Fundación Atlas 1853, Argentina
Fundación Libertad, Panama
IMANI Center for Policy and Education, Ghana
Initiative for Public Policy Analysis, Nigeria
Institut Constant de Rebeque, Switzerland
Institut für Unternehmerische Freiheit, Germany
Instituto de Libre Empresa, Peru
Instituto Ecuatoriano de Economía y Política, Ecuador
Instituto Liberdade, Brazil
Instituto Libertad y Progreso, Colombia
Instituto Veritas, Honduras
International Policy Network, United Kingdom
Institute of Public Affairs, Australia
Istituto Bruno Leoni, Italy
Jerusalem Institute for Market Studies, Israel
Liberales Institut, Switzerland
Liberty Institute, India
Minimal Government, Philippines

Increasing Access to Medicines

Civil Society Commentary on the IGWG draft Plan of Action

In July 2007, the IGWG released its draft Strategy and Plan of Action. Underlying this text are the assumptions that there is a dearth of R&D for diseases that specifically affect poorer countries, and that the international patent system – and concomitantly price – is a barrier which prevents access to existing medicines. Based on these assumptions, the text proposes an array of interventions which governments could undertake to address these perceived failures.

These underlying assumptions contradict WHO's own statements on these issues:

- During the World Health Assembly (WHA) in May 2006, WHO released a report on the pricing of drugs. A major finding was that "taxes and duties levied on medicines, as well as the mark-up applied, frequently contribute more to the final price than the actual manufacturers' price." WHO then went on comment: "There is evidence that some governments procure medicines efficiently, but charge markedly higher prices to patients, e.g., in Indonesia's public sector, patients paid 11 times the procurement price."
- In July 2006, the director for WHO's HIV division publicly stated: "Africa has been hardest hit by the AIDS epidemic … it is very obvious that the elephant in the room is not the current price of drugs. The real obstacle is the fragility of the health systems. You have health infrastructure that is dilapidated, and supply chains that don't exist."
- WHO followed up its May 2006 pricing report in July 2007 during a meeting in Vienna to launch Pharmaceutical Pricing and Reimbursement Information (PPRI), a project sponsored by the European Commission and the Austrian government. Using new data since the May study, WHO stated: "The mark-up on generic products can be considerably more than on originator products. Some countries have set prices to patients at levels which have the purpose of, for example, protecting the [local] industry, providing revenues for hospitals or funding the development of national health services."

Further, the notion that R&D for Type III diseases requires the intervention of WHO does not stand up to scrutiny:

- In January 2007, the IGWG asked Member States to comment on the Draft Global Strategy. Several Members, including the USA, Germany, and Japan asked the Secretariat to review existing R&D programmes (such as the WHO's TDR) before establishing a new forum, in order to avoid duplication. These requests were ignored.
- In reality, R&D for Type II and III diseases is now taking place at an unprecedented pace. A 2007 editorial in the British Medical Journal stated: "the long held belief that it is not economically feasible to develop drugs…specifically for tropical diseases has been shattered…we can expect to see eight or nine new drugs for neglected tropical diseases in the next five years."[1]
- The Annex to this Civil Society Commentary details some of the commercial work that is taking place globally to address Types II and III diseases. If the Secretariat had reviewed this inventory, the need for a new WHO forum would be less clear. Neither has the Secretariat indicated how the IGWG will avoid costly duplication of this work.

Similar to the concerns that we have voiced in the past, it remains far from clear that new medicines – whether

produced under the existing intellectual property system or under some hypothetical new system – will actually be delivered to those people who urgently need them. The track record on the delivery of existing medicines, whether protected by patents or produced by quality generics producers, is not encouraging. Although India did not enforce patent rights for over thirty years and the country also boasts a competitive medicines manufacturing industry, access to medicines is still less than 50 per cent in many areas. This suggests that delivery systems and infrastructure are far more important obstacles to achieving widespread health.

The draft Plan of Action, as it currently stands, ignores this evidence. Its overall strategy is to address a fictitious 'crisis' in the availability of treatments in developing countries for Type II & III diseases by overseeing a significant increase in the manufacturing capacity of the copy drug industry in developing countries. It is envisaged that this will be underwritten by the compulsory transfer of technology and intellectual property from wealthy countries to poorer countries. This could take the form of exploiting flexibilities in the TRIPS agreement, such as via compulsory licences, which were originally envisaged as a "last resort" policy option.

IGWG's current focus on technology transfer and local capacity building for drug production is a re-visitation of the discredited 'import substitution industrialization' policies promoted by the development community (including the World Bank) in the middle of the 20th Century.[2] By advising Member States to pursue strategies that have already failed, the IGWG will almost certainly fail to meet its objective of improving the quantity and quality of therapies for the diseases of poverty.

1 Patient safety issues

The draft Plan of Action misleadingly conflates the term 'generic' with copy drugs. The key regulatory requirement for a 'generic' drug is a reference product against which it can be compared for bio-equivalency. When a drug has not undergone bioequivalence testing verified by a rigorous drug regulatory agency, it is most probably a 'copy' drug. Among stringent regulatory authorities, such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMEA), a copy drug is by definition a substandard drug. The ARVs produced in India and de-listed by WHO in 2004 for lack of bio-equivalence were all copy drugs, although WHO had led UN procurement agencies and the activist community to understand that they were certifiably-tested generics.

Copy drugs can have several adverse effects on patients. If copy drugs are not interchangeable with the reference product they will likely lead to treatment failures. A critical adverse effect is drug resistance. Substandard copy ARVs that are not bio-equivalent to true generics could lead also to a mutation of HIV and create a new, drug-resistant strain of AIDS. Substandard anti-malarials may result in increased resistance to the malarial parasite.

The burden of adverse effects resulting from the use of copy drugs will fall on the poor in the developing world as current treatments are rendered useless, forcing use of more expensive second and third-line drugs. Substandard copy drugs for other types of diseases could lead to an increased incidence of clinical failure and death.

In 2007, WHO estimated that counterfeit drugs accounted for 30 per cent of all sales of medicines in Africa, "killing thousands."[3] It is likely that substandard drugs account for at least an equal percentage of drug sales. In Brazil, a testing of Amoxicillin and other medicines showed that every sector had procured substandard drugs: 14% by the public sector, 10% by NGOs, and 9% by the private sector.[4] *The Lancet* has projected that close to 40 percent of products in Thailand and Nigeria labeled as containing artesunate (an effective antimalarial) contain no active ingredient.[5]

This is extremely relevant if the IGWG envisages scaling up local production in developing countries. Currently, only 20 per cent of WHO's 191 Member States have well-developed regulation. Fifty per cent operate at varying levels of regulation and capacity, and 30 per cent have weak regulation or none at all.[6] The prospect of these countries producing true generics that have demonstrated bio-equivalence and met the stringent

standards demanded by bodies such as the FDA or the EMEA, is therefore remote.

WHO has responded to the lack of capacity within local National Drug Regulatory Authorities (NDRAs) by providing a Secretariat for the International Conference of Drug Regulatory Authorities (ICDRA). The ICDRA is supposed to be a tool for WHO and NDRAs to "harmonise regulation and improve the safety, efficacy and quality of medicines."[7] In reality, NDRAs take their lead from WHO, which then assumes *de facto* power as a collective regulatory authority. In principle, WHO holds NDRA members to standards of quality, safety and efficacy; but, in practice, it is powerless when members export and import drugs of substandard quality.

For example, the WHO Prequalification Programme was developed in 2001 to certify HIV/AIDS drugs for procurement by UN agencies. The two qualifications for entry into WHO's Prequalification Program are dossier evaluations and manufacturing site inspections. Dossiers are thoroughly evaluated for compliance with WHO recommendations and guidelines."[8] Site inspections are performed at the manufacturing site. In practice, however, WHO admits that in some cases dossier evaluations are substituted for site inspections. In addition, while WHO claims its standards are as stringent as those of the FDA, it issues a disclaimer for prequalified drugs stating that it does not warrant the products for safety or efficiency if used in the treatment of HIV/AIDS.[9]

Should the IGWG be passed in a Resolution, the WHO will become the *de facto* supranational regulatory authority for Type I, II and III diseases, using the authority granted by its running of the secretariat of the ICNDRA. Manufacturing standards which are not required to achieve bioequivalence will then be acceptable globally, because the principle of equity *above safety* will be extended to low cost producers.

As a result, patients in developing countries would be exposed to a wider array of suspect or substandard drugs. In addition to the individual tragedies faced by increasing numbers of patients who will then suffer drug resistance and clinical failure, this will increase the burden on health systems of developing countries.

2 Economic issues with local production

Local production underwritten by subsidy may not necessarily result in less costly drugs. Establishing a new local industry in this manner incurs efficiency losses that may never be recouped. The home market must pay on three separate counts: the start-up costs of establishing the industry, the costs of subsidising production, and the higher price of the finished product.

For anti-retrovirals (ARVs), it takes about two years to build a manufacturing plant that meets international Good Manufacturing Practice (GMP), and a further year to run through a validation process and train staff. By the end of these three years, the technology of ARV production will have become more sophisticated, as new products come onto the market. This would necessitate an overhaul or redesign of the plant. Commercial R&D companies make allowance for this in their forward planning. By contrast, the large cost of re-engineering a local government-owned plant will have to be met from public funds.

In addition, building plant capacity for one type of disease (AIDS, TB or malaria, for example) is risky. Commercial R&D companies mitigate this risk by having a large portfolio of different drugs under production, so that if one of their products is superseded by a superior competitor, they can continue to produce other products. Local production will not have this diversity, and therefore will always depend on subsidies from the donor community – and with no guarantee that their products will yield financial savings over products that are manufactured commercially. Moreover, it takes time and resources to develop the local capacity and expertise required to produce specific treatments. As a result, local patients will likely face an added risk: medicines hypothetically produced by local manufacturers could be less effective than new treatments that may emerge during that period of time, which would contradict the stated objective of the IGWG. Consider the following:

- In May 2007, the Clinton Foundation negotiated a procurement contract with an Indian company for a copy version of the ARV Lopinavir / Ritonavir. The Foundation's published price for Lopinavir is $695 per person per year. However, for the past five years, the rights holder has offered this same drug with assured quality, safety and efficacy to 69 poor countries at $500 per person per year.[10] In this case, the Clinton Foundation is paying a 29% premium for local production of a copy product that has not even been pre-qualified by WHO.
- In 2002, Thailand began production of GPO-Vir, a triple combination therapy including lamivudine, stavudine, nevirapine, without paying royalties to the originators. Since then, WHO has steadily refused to enter this drug into the Prequalification Programme, mainly for a lack of proof of bioequivalence.[11] The Global Fund to Fight HIV/AIDS, TB, and Malaria granted Thailand's Government Pharmaceutical Organization (GPO) $135 million to upgrade its plant and produce copy drugs to WHO standards. After three years of effort, the fund was forced to withdraw the remaining monies because of the GPO's failure to comply.
- In its analysis of a hypothetical local production plant in Nigeria, the U.S. National Academies of Science found that it would have initially cost 15 per cent more to grow, extract, purify and derive local artemisinin derivatives than to import them directly.[12]

The IGWG has not yet made clear how it intends to suspend the economic laws of comparative advantage in its pursuit of local production. It risks creating a series of domestic industries that will require permanent subsidy from either foreign donors, or the fiscal reserves of developing country governments. Additionally, their products are likely to be more expensive than the original, imported product – with none of the assurances of quality and safety. Resources used to create local production facilities could be utilised more effectively to address other health priorities, such as improving health infrastructure or retaining health personnel.

3 Compulsory licenses

As part of its promotion of local production, the IGWG envisages greater usage by developing countries of the flexibilities enshrined in the TRIPS agreement, particularly those which allow for compulsory licensing of patented pharmaceuticals.

Compulsory licenses have great populist appeal. However, experience to date has shown that the production of drugs of known quality, safety and efficacy is a costly undertaking, and that compulsory licensing is fraught with difficulties, as illustrated by a recent experience in Canada. In 2005, the Canadian Government offered a $100 million subsidy to its generic industry for the production of ARVs which would be made available to African countries through the Canadian Access to Medicines Regime. Doctors Without Borders (MSF) partnered with Canadian drugmaker Apotex to produce a drug that combines three patented AIDS drugs into a single dose.[13]

Three years into the partnership, however, Apotex ran into two problems. First, it couldn't produce the combination therapy to Canadian generic standards at a cost that would yield a profit – even with a subsidy. Second, by the end of 2007, Apotex and MSF concluded that the legislation to support this partnership "appears to have disappeared into the Ministry of Industry's office, with no sign that it will see the light of day in the near future."[14] They both agreed that regulatory hurdles were more complex than previously envisioned. Accordingly, on December 5, 2007, MSF announced that since not one pill had been produced and the legislation was bottled-up, it would abandon all future efforts and turn to India for ARVs.

Experts have voiced concern about drug production under compulsory licenses in countries without strong regulatory authorities, especially with regard to patient outcomes. Clinical pharmacologists and physicians from Stanford Medical School and Trinity College, Dublin, publicly stated: "Manufacturing standards must be monitored. Drug concentrations that are too low can cause the therapy to fail and, equally important, promote the emergency of resistant forms of the infectious agent … this failure can compromise the response of the patient to other medicines in the future."[15]

4 Cost of the Plan of Action

The WHO Secretariat for IGWG has not detailed the projected costs of its plan of action, though several Member States requested this information. Each of the eight Elements cut across many jurisdictional boundaries (for example those of WIPO and WTO) while intersecting with multiple drug regulatory authorities that always take their sovereignty seriously. If the Plan of Action is ratified at the May 2008 World Health Assembly, Member States would be unable to vote resultant increases in their dues to support the Plan of Action via the Regular Budget.

The likely cost of funding all eight Elements would consume an inordinate amount of the Members' Dues which make up the WHO's Regular Budget (now totaling $457 million per annum). Perhaps this explains why the Secretariat chose to ignore Members' request on detailed estimates for the Plan of Action.

Rather than a reliance on the Regular Budget, those Member States which have been most active in promoting the IGWG (e.g. Brazil) as well as the activist community, will provide WHO with Extrabudgetary funding to pursue discrete elements of the Plan of Action. These elements will include:

- developing countries to set research priorities;
- developed countries to devote a larger proportion of their health R&D budgets to the health needs of developing countries;
- develop systems in developing countries for the management of intellectual property;
- conduct research on appropriate products to combat Type I diseases;
- and (as Brazil has recommended), pursue "necessary legislation steps to allow compulsory licensing for exports consistent with the flexibilities of TRIPS."

While this Extrabudgetary funding will be insufficient to meet all eight Elements in the draft Plan of Action, the importance of their funding lies more in their ability to use all of the institutional authorities and legitimacies of WHO without the burden of having to be held accountable and responsible to its governance structure–which is tethered only to the Regular Budget.

WHO will take on the role of a hosting organization, much as it does now with UNITAID. This will permit it to form a Secretariat and extend to its new non-governmental members (e.g., MSF, the Clinton Foundation, the Rockefeller Foundation) all the privileges and immunities of the Organization. This means these groups can not be held accountable by law if the products they distribute have adverse effects on patients.

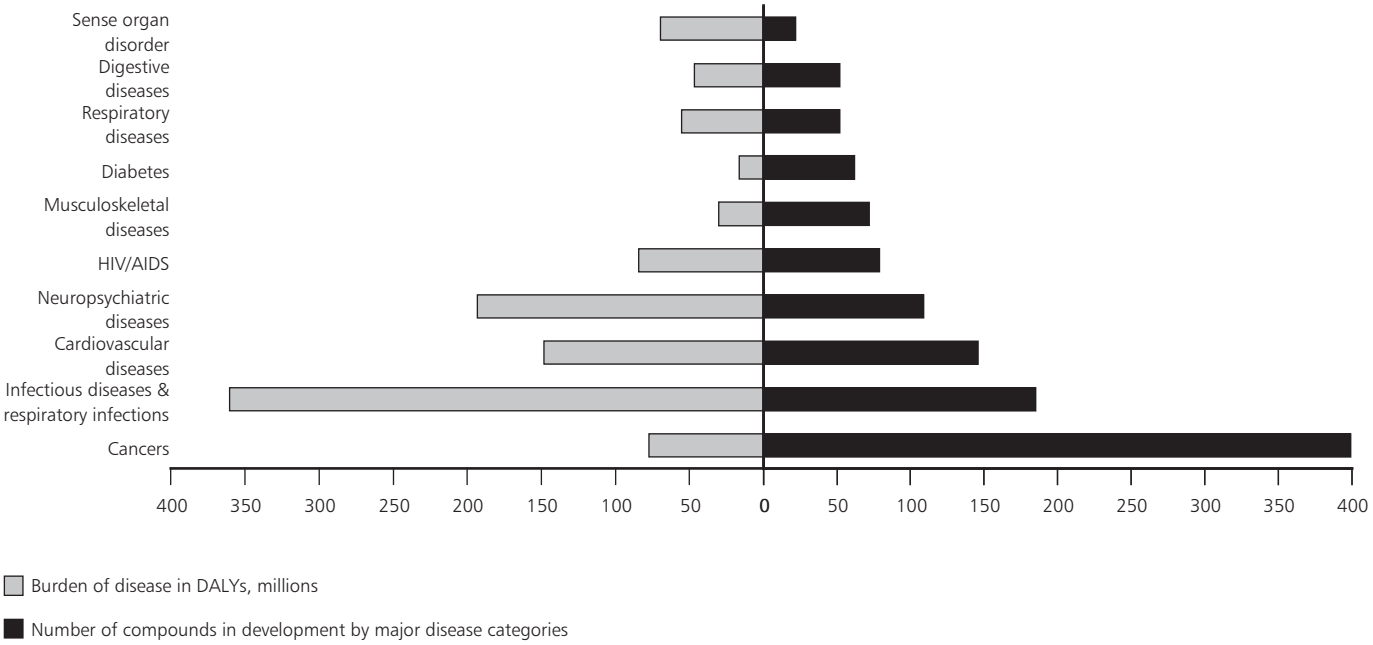
A "market failure"?

It is not clear how the IGWG can promote its agenda of local pharmaceutical production underwritten by compulsory licenses without damaging commercial incentives to continue investing in these areas. This is particularly true if the IGWG expands its remit to Type I diseases. Currently, the levels of innovation for these diseases by R&D companies generally reflect the global disease burden (see Figure 1), so it would be foolish to jeopardise this with the high-risk schemes proposed in the draft Plan of Action.

The assumption underlying IGWG is that the current system of market-based pharmaceutical R&D is a "market failure", in that markets have failed to produce drugs relevant to the needs of poor countries, and that the drugs that are produced are too expensive for those countries. The latter is often attributed to the notion that the international patent system drives up costs.

In any market, producers respond to the perceived demands of consumers. In wealthy countries the market for pharmaceuticals includes individuals, health agencies, insurance companies and governments. Such market demand constitutes a functioning market, which has driven – and continues to drive – producers to invest significant resources into the creation of a wide variety of drugs to combat the range of disorders suffered by patients. As demonstrated by lucrative markets in North America, Europe, and Japan, which together account for 85.6 per cent of the world pharmaceutical market, commercial R&D is allocated to those regions where companies believe they will recover their investments.[16]

Figure 1 **The global disease burden vs. number of compounds in development**



Sources: PhRMA (2005) and WHO (2004)

However, to classify the healthcare situation with regards to pharmaceuticals in developing countries as a 'market failure' is disingenuous. It is more accurately described as a limited and severely fragmented market: a lack of buyers able to pay the prices needed to drive entrepreneurs to pursue research and development for neglected diseases. This limited market makes it very difficult for private sector firms to justify the high-volume, low-price model advocated by certain NGOs.

The size of the market in lower income countries is constrained by a host of factors. As mentioned in the report of the Commission on Intellectual Property Rights, Innovation and Health, many of these factors exist irrespective of the retail cost of medicines. Among others, they include the weakness of distribution mechanisms (caused by inadequate health infrastructure), which necessarily leads to a concomitant decrease in supply.

If a medicine stands little chance of reaching its intended consumer, there is little point for a commercial venture to risk large amounts of capital in developing it. One World Bank study demonstrates that demand-side variables such as education, opportunity costs, distance and culture may actually be far more important determinants of access to healthcare than the price of medicines.[17]

Within the scope of the IGWG, the demand for medicines is reduced by a variety of factors, many of which are a result of poor governance. These include issues such as taxes and tariffs on medicines, weak health care systems (including a lack of personnel), and a lack of risk pooling mechanisms, which means that consumers must pay out of pocket. All of these factors reduce the demand for drugs, and therefore reduce incentives to risk capital in supplying the market.

Simultaneously, a range of governance factors constrain the supply of drugs. These include burdensome pre-market regulations; price controls on pharmaceuticals; weak or poorly enforced intellectual property rules in middle and lower income markets; slow and costly

patent registration; and overly complex registration procedures from local drug approval bodies.

Recommendations

The IGWG draft Plan of Action is unlikely to fulfill its stated objective of increasing the quantity and quality of medicines in the world's poorer countries. Based on the promotion of publicly-subsidised local pharmaceutical industries, it is likely the IGWG will lead to an increase in the supply of substandard medicines in developing countries, which will have subsequent deleterious health and macroeconomic impacts. It is also likely to increase the cost of medicines. Furthermore, attempts to de-couple 'price' and 'innovation', for example through the creation of a Medical R&D Treaty or an *ex ante* prize fund is fraught with risk.[18]

While better health in developing countries is generally a consequence of economic growth, there are several steps that Member states can take to improve access to quality medicines within the context of the IGWG.

To increase demand for medicines

- Improve healthcare infrastructure in developing countries by encouraging plurality and competition within the health sector. Competition should be permitted between public and private sector providers.
- Donors should consider making Development Assistance for Health (DAH) contingent on pre-determined outputs, and accordingly, allow private and public bodies to compete for contracts to deliver health service.
- Private sector management techniques should be adopted by public health systems in order to improve efficiency and minimize corruption.
- Reduce individuals' out-of-pocket healthcare expenditure by creating regulatory and legal environments that are conducive to the formation of viable insurance markets and other risk-pooling mechanisms.
- Eliminate price controls on drugs, so that companies can more easily segment the global market according to ability to pay.
- In order to incentivise price segmentation and marginal pricing strategies in the poorest countries, Member states, particularly middle income countries, should avoid the use of compulsory licenses.
- Remove all taxes, tariffs and other government mark-ups on health-related goods and services.

To increase the supply of medicines

- Currently, local National Drug Regulatory Authorities do not have the capacity to test and approve drugs as true generics, and simultaneously impose burdensome and unscientific requirements on potential registrants of drugs. This drives up the cost of drug registration. Member states should encourage the use of mechanisms such as the FDA's free Fast Track certification, in order to ensure the drugs they use are of proven efficacy and safety.
- The high cost of conforming to extensive pre-market regulations deters R&D into treatments for Type III diseases. High income countries should therefore consider 'Orphan Drug' type legislation and tax breaks for research into the diseases of poverty.
- Countries with slow and inefficient patent offices might introduce incentive-based pay schemes or contract out services to the private sector. It may be worth merging patent offices in certain regions to minimise redundant processing.
- Companies are more likely to incur the costs of marketing their products in countries that strive to comply with minimum standards of intellectual property protection, such as those set out in the TRIPS agreement.
- While the protection of IP is important for foreign companies seeking to distribute medicines to under-served markets, it is also crucial to help home-grown R&D industries to develop and flourish. Such local industries could serve as local partners to foreign rights-holders.

Annex I

A Brief Inventory of commercial R&D, treatment and licensing activities with Type III & II Diseases

Research and patient care facilities

1. AstraZeneca built and operates an Infectious Disease Institute in India, doing R&D on neglected diseases.
2. Novartis built and operates the Tropical Disease Institute in Singapore, focusing on TB, dengue and malaria. It announced on 26th February 2008 that it had tested an experimental dengue drug in animals and found it effective in killing all four serotypes of the virus.
3. Bristol-Myers Squibb built Africa's first Pediatric AIDS Hospital.
4. Pfizer built and now helps to operate Africa's first Infectious Disease Institute in Uganda, conducting basic research and training new cadres of physicians in infectious disease management and treatment via a partnership with a U.S. medical school in Utah.
5. GlaxoSmithKline built and operates the Tres Cantos R&D Facility in Spain, specifically targeting development on those essential medicines identified by WHO as needed for diseases which disproportionately affect poor countries.
6. Bristol-Myers Squibb built specialty clinics in pediatrics for ten countries in Southern Africa.
7. Bristol-Myers Squibb and Baylor Medical College jointly sponsor the Pediatric AIDS Volunteer Corps, now supplying more than 260 physicians to Southern Africa.
8. Lilly, through the MDR-TB Partnership Program, has transferred drug production technologies to:
   a. Aspen Pharmacare, South Africa. Its new oral solid dose facility in Port Elizabeth was approved by WHO in September and manufacturing of cycloserine is underway.
   b. Hisun Pharmaceuticals, China. Hisun will produce capreomycin vials from the new site in Fuyang. Hisun will supply final product from their biotech facility to local markets by mid-2009.
   c. Purdue University in the U. S. validated Shasun Chemicals and Drugs cycloserine capsules in its new facility, the Chao Center, and once approved by the FDA, the Chao Center will become the sole proprietor to the U. S. market.
   d. Shasun Chemicals and Drugs, India. It is now supplying cycloserine API to the Chao Center, which began in July, and to Aspen and to SIA International (Russia) which began in November 2007.
   e. SIA International, Russia. Is on schedule to supply cycloserine capsules to the local market by the first quarter of 2008 in time for the 2008 government tender. The manufacturing partner has already supplied the Russian Ministry of Health data on cycloserine API Registration.
9. Bristol-Myers Squibb built Africa's first AIDS Reference Laboratory, now operated by Harvard University in Botswana.
10. Pfizer in October 2006 provided a library of 12,000 compounds to WHO's Special Programme for Research and Training in Tropical Diseases. The purpose is to speed up the search for new drugs to combat some of the world's most deadly parasitic diseases.
11. The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) announced on 25th January 2007 a grant of $1 million to the Special Programme for Research & Training in Tropical Diseases at WHO/Geneva. The purpose is to develop new medicines to combat diseases that disproportionately affect poor people living in developing countries.

12. In 2003, Novartis funded the Singapore Dengue Consortium. Along with six other partners, the Consortium will explore ways to understand and better manage dengue infection, and ultimately minimize the incidence of dengue.
13. In 2004, Abbott Laboratories built a Children's Hospital in Tanzania and helps now to operate it, particularly for the prevention of mother-to-child AIDS transmission.
14. In February 2008, Novartis announced the opening of a new research institute in Siena, Italy "with a non-profit mission to exclusively focus on the development of vaccines for diseases of the developing world."
15. On March 7, 2008 GlaxoSmithKline and the non-profit organization, Drugs for Neglected Diseases announced a collaborative research effort targeting neglected tropical diseases which disproportionately affect the developing world. Research will focus on compounds that may have activity against the most neglected diseases of visceral leishmaniasis, human African trypanosomiasis, and Chagas disease.
16. Of the 176 AIDS therapies in various dosage forms and strengths on WHO's Prequalification list, 104 of them are being produced in India, either as copies or true generics via the FDA's Fast Track project. Right holders to the intellectual property of these products presented no legal challenges to the Government of India, making that country the largest supplier of AIDS therapies to the developing world. The Foreign Direct Investment (FDI) value of this transfer has not been calculated, yet it has arguably catapulted India into a major role as an emerging competitor in global drug markets

Patient treatment

1. In 2000, eight industry companies joined with WHO, the World Bank, UNICEF, UNAIDS, and the United Nations Population Fund to form the United Nations Accelerated Access Initiative Program (UN/AAI). As of June 2007, more than 694,000 people living with AIDS in the developing world were receiving treatment with at least one ARV medicine provided by the AAI companies.
2. Under the FDA's Fast Track Program to approve ARV applications from developing world manufacturers for certification as 'true generics', PEPFAR (President Bush's Emergency Plan for AIDS Relief) reports that at least 70% of the 1.4 million patients being treated now receive a true generic ARV, purchased with U.S. foreign aid funds. This is more than one-half of the 2 million patients under ARV treatment in the developing world. The rights-holders were given an opportunity to challenge these applications. None did so.
3. Novartis sponsors the Glivec International Patient Assistance Program through partnerships with NGOs, physicians and local health organizations. Initiated in 2002, it provides Glivec at no cost to eligible patients with certain forms of a rare cancer in countries with no comprehensive reimbursement system or available generics. Patients must be properly diagnosed, and the delivery of Glivec to patients is by their physician. By the end of 2006, Novartis provided $362 million worth of Glivec to more than 21,000 patients who otherwise would not have been able to afford treatment in 80 countries.
4. Merck and the Bill and Melinda Gates Foundation have been operating since 2000 a comprehensive AIDS treatment program in Botswana for seven years, providing care to more than 85,000 patients. Their contributions have exceeded $150 million, and the Government of Botswana has more than matched this value.
5. Bristol-Myers Squibb has been operating since 1999 its Secure the Future Program in twelve Southern African countries, funded at $140 million, and comprehensively treating more than 105,000 AIDS patients. Its prevention and education programs work with thousands more.
6. Pfizer has been collaborating with governments and non-governmental organizations since 2000 to donate its antifungal medicine Diflucan to HIV/AIDS patients. The medicine is free of charge and without time limits to public health clinics for distribution to patients. As of December 2006, Pfizer had donated medicines worth more than $500 million in 47 countries, enough to treat 200,000 patients.
7. Since the AIDS virus was first identified in 1982, industry has developed 96 different therapies to treat

this disease. At an average R&D cost of $800 million per therapy, industry's contribution amounts to $76.8 billion. Most of these therapies are being produced as copy products by non-R&D companies in the absence of any legal challenge by their rights-holders. According to WHO, more than 2 million AIDS patients are now on these life-extending therapies.

Licensing arrangements

1. Boehringer Ingelheim offers a non-asset declaration to all WHO pre-qualified manufacturers, stating that it will not enforce its nevirapine patent rights in low-income countries in order to ensure supply at lowest possible cost.
2. Bristol-Myers Squibb has had a policy of not enforcing its patents for HIV products in sub-Saharan Africa and has immunity from suit agreements for stavudine and didanosine with five African generic companies. In February 2006, it concluded technology transfer agreements with generic companies Aspen PharmaCare (South Africa) and Emcure Pharmaceuticals (India), for its newest antiretroviral, atazanavir. BMS has transferred intellectual property and technical know-how related to manufacturing, testing, packaging, storage and handling of the active pharmaceutical ingredient and finished dosage form.
3. Gilead has partnered with Aspen PharmaCare in South Africa to manufacture and distribute Viread and Truvada in Access Program countries. In 2006, Gilead also entered into non-exclusive licensing agreements with 11 Indian companies. Gilead allows them to distribute generic versions of Viread in 95 countries, as well as Thailand. The agreements include technology transfer to allow production of high quality products, and the generic companies are free to establish their own pricing for their products.
4. GlaxoSmithKline granted its first license in 2001 and now has negotiated eight licensing agreements for its ARVs in Africa. In 2006, GSK-licensed manufactures significantly increased their manufacturing capacity to supply larger quantities of ARVs at lower prices. In that year alone, its manufacturers supplied 120 million ARV tablets.
5. Merck in 2005 granted a non-exclusive, royalty-free patent license for the manufacture and supply of a generic version of its antiretroviral Stocrin to Aspen PharmaCare in South Africa.
6. Roche has committed not to file any new patent or enforce existing patents for any of its medicines in UN-defined Least Developed Countries. Nor will it file new patents or enforce existing patents for its antiretrovirals in sub-Saharan Africa. As a result, generic versions can be produced in these countries, encompassing 87% of all people living with HIV, without a license. In September 2006, Roche announced technology transfer agreements with three companies in Africa, which allow them to supply saquinavir to any sub-Saharan or UN-defined Least Developed Country.

Notes

1. Gavin Yamey, Peter Hotez, "Neglected Tropical Diseases", *British Medical Journal*, 11th August 2007, Vol. 335.
2. For more on the perils of Import Substitute Industrialisation, please see Salgado, G., "Unsustainable development, Latin Style", *Sustainable Development*, Profile Books, 2002
3. WHO Press Release, World Health Organization, Geneva, October 17, 2007.
4. U. S. Pharmacopeia, Matrix of Drug Quality Reports in USAID-assisted countries, Rockville, Maryland, Pharmacopeia, October 15, 2007.
5. Penetration in Nigeria is estimated at 36 percent and in Thailand at 40 percent. See Paul N. Newton, Michael D. Green, Facundo M. Fernández, Nicholas P. J. Day, and Nicholas J. White, "Counterfeit Anti-Infective Drugs," *The Lancet Infectious Diseases* 6, no. 9 (September 2006): 602–613.
6. WHO, "General information on counterfeit medicines" fact sheet
7. International Conference of Drug Regulatory Authorities, WHO web site, http://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/en/index.html (accessed Feb. 11, 2008.
8. World Health Organization, Marketing Authorization of Pharmaceutical Products with Special Reference to Multisource (Generic) Products: A Manual for Drug Regulatory Authorities, WHO, Geneva, May 1998.
9. World Health Organization, Access to HIV/AIDS Drugs and Diagnostics of Acceptable Quality, Prequalification Programme, World Health Organization, Geneva, all editions since 2002 and through February 1, 2008.
10. "AIDS Healthcare Foundation Lauds Landmark Drug Pricing Deal Negotiated by Clinton Foundation", *Drug Week via News Edge Corporation*, May 18, 2007.
11. Ten Kate, Daniel, "Thailand's Generic AIDS Drugs Don't Meet International Standards", Asia Sentinel, January 24, 2007.
12. National Research Council, Committee on Creation of Science-Based Industries in Developing Countries, *Mobilizing Science-Based Enterprises for Energy, Water, and Medicines in Nigeria* (Washington, DC: National Academies Press, 2007), 110.
13. Jeff Davis, "Aid Group Abandons Drug Access Program", Canadian Embassy, no date.
14. Ibid.
15. Terry Blaschke, Concepta Merry, "Generic Drugs for HIV/AIDS is good news, but manufacturing standards must be monitored", The Financial Times, October 6, 2003.
16. WHO, *Public Health: Innovation and Intellectual Property Rights*.
17. Ensor, T., & Cooper, S., (2004), "Overcoming barriers to health service access and influencing the demand side through purchasing"
18. See e.g. Farlow, A., "A Global Medical Research and Development Treaty: An Answer To Global Health Needs?" International Policy Press, 05/2007.