

estimated two billion people have no access to essential medicines, effectively shutting them off from the benefits of advances in modern science and medicine.

A complex – and vexing – problem

In recent years, the need for uninterrupted supplies of medicines has become more urgent. The importance of preventing stock outs has been underscored by the advent of antiretroviral therapy for HIV, the long duration of treatment for multidrug-resistant tuberculosis, the ability of artemisinin-combination therapies to prevent malaria deaths if administered quickly, and the need for life-long treatment of chronic conditions such as hepatitis B infection and diabetes. Lack of access to medicines is one of the most complex – and vexing – problems that stand in the way of better health. The agenda for improving access is exceptionally broad. Affordability is the cornerstone of access, but many other factors also determine whether people get the medicines they need. Gaps in local health systems and infrastructures hamper the delivery of medicines to millions of people. Access also depends on procurement practices, tax and tariff policies, mark-ups along the supply chain, and the strength of national drug regulatory authorities. Apart from being affordable and of good quality, medicines must also be safe; a system for pharmacovigilance needs to be in place. Secure supply chain management is likewise needed to protect populations from substandard or falsified medical products. International conventions for the control of narcotic drugs can be another barrier to access. They place a dual obligation on governments: to prevent abuse, diversion and trafficking, but also to ensure the availability of controlled substances for

medical and scientific purposes. Many controlled substances play a critical role in medical care, for the relief of pain, for example, or use in anaesthesia, surgery, and the treatment of mental disorders. Unfortunately, the obligation to prevent abuse has received far more attention than the obligation to ensure availability for medical care. WHO has estimated that 80% of the world's population lives in countries with zero or very little access to controlled medicines for relieving moderate to severe pain. Efforts to improve access are complicated by a number of economic issues. Affordability matters for households and health budgets. WHO estimate says that up to 90% of the population in low- and middle-income countries purchases medicines through out-of-pocket payments. If a household is forced to sell an asset, like the family cow, or take its children out of school, this payment can be the final nail in the coffin that buries the family in intergenerational poverty. This is the pathology of poverty when no forms of social protection, such as those provided by universal health coverage, are available and even low-cost generic products are a heavy financial burden. For health budgets, staff costs usually absorb the biggest share of resources, with the costs of drug procurement following closely behind. The part of the budget devoted to medicines varies significantly according to a country's level of economic development. Medicines account for 20% to 60% of health spending in low- and middle-income countries, compared with 18% in countries belonging to the Organization for Economic Co-operation and Development. One of the most daunting economic issues comes from the fact that the research-based pharmaceutical industry is a business, and a big one. Multinational pharmaceutical companies, concentrated in

North America, Europe and Japan, are powerful economic operators. Economic power readily translates into political power. When ways to improve access are negotiated at WHO, a familiar polarizing tension surfaces. Which side should be given primacy, economic interests or public health concerns? As many have argued, letting commercial interests override health interests would lead to even greater inequalities in access to medicines, with disastrous life-and-death consequences. At the same time, the pharmaceutical industry is a business, not a charity. When prices are so high that they preclude profits, companies leave the market – and leave a hole in the availability of quality products, as happened with anti-snakebite venom. Economic factors shape another pressing public health concern. Many diseases mainly prevalent in poor populations have no medical countermeasures whatsoever, or only old and ineffective ones. In other cases, access suffers from the lack of products adapted to perform well in resource-constrained settings with a tropical climate. The patent system, with its market-driven R&D incentives, has historically failed to invest in new products for poor populations with virtually no purchasing power, resulting in a paucity of R&D driven by the unique health needs of the poor. Apart from having few new products that address their priority diseases, the poor are punished in a second way: the common practice of recouping the costs of R&D through high prices protected by patents means that those who cannot pay high prices do without. Recent shifts in the poverty map introduces another set of problems. An estimated 70% of the world's poor now live in middle-income countries which are losing their eligibility for support from

mechanisms like the Global Fund to Fight AIDS, Tuberculosis and Malaria and Gavi, the Vaccine Alliance. Will governments step in to make up for the shortfall in access to medicines and vaccines? If not, vast numbers of poor people living in countries that are rapidly getting rich will be left to fend for themselves.

Keeping substandard and falsified products out of the supply chain

WHO has recently stepped up its efforts to combat yet another threat to the life-saving and health-promoting power of medicines: the health harms caused by substandard and falsified medical products. These products flood the markets in countries with weak drug regulatory authorities, or circumvent regulatory controls through sales via the internet. The complex web that characterizes the global production and distribution of pharmaceutical products, including a long and convoluted supply chain, places all countries at risk. Products that enjoy lucrative commercial markets are particularly susceptible to falsification, as are badly needed medicines and vaccines that are in short supply. Substandard and falsified medicines not only steal income from consumers who pay for products that have little or no medical value. They cause harm by not resolving a medical problem and have sometimes caused hundreds of deaths, especially when the products contain toxic ingredients. The WHO Global Surveillance and Monitoring System for Substandard and Falsified Medicines was launched in West Africa in July 2013. Since then, more than 400 regulatory personnel from 126 countries have been trained to use this system for the rapid reporting of substandard or falsified products. Reports from national

regulatory personnel are immediately uploaded to a secure WHO website for general use . If investigation confirms harm to health, WHO responds within 24 hours, providing coordination and technical support in the event of an emergency. Ten years in public health 2007–2017 When warranted, WHO issues a global Medical Product Alert to warn countries and populations of the existence of a dangerous medical product. The alerts, which include photographs of falsified products, also encourage increased vigilance and regulatory action to protect populations and supply chains. In the past two years, alerts were issued for falsified yellow fever vaccines, hepatitis C medicine, meningitis vaccines, anti-malaria medicines, and treatments for epilepsy. Information gathered by the surveillance and monitoring system can have broader policy implications. For example, many anti-malaria tablets, sold at street markets in endemic countries, contain no active pharmaceutical ingredients at all.

[Building on previous innovations](#)

In 1977, on the eve of the Alma-Ata conference on primary health care, WHO issued its first Model List of Essential Medicines as the Organization's signature contribution to rational drug procurement. The concept that a limited number of inexpensive medicines could meet the priority health needs of a country's population was considered revolutionary at the time. Historically, the model lists gave priority to effective medicines that offer clear clinical benefits, while also paying attention to their costs and impact on health budgets. That position changed in the 1990s with the advent of expensive yet highly effective antiretroviral therapies for HIV. It changed again in 2015, after new medicines came on the market that

transformed hepatitis C from a barely manageable condition to one that could be safely and easily cured by all-oral treatment options. Those new direct-acting antivirals created an unprecedented dilemma for public health: the arrival of breakthrough drugs with tremendous potential to treat millions of patients with a potentially deadly liver infection, but at a price considered unaffordable, even in high-income countries. The 2015 list also included 16 drugs, including some with high prices, which can increase survival times for common cancers, such as breast cancer, or can successfully cure up to 90% of patients with rare cancers, such as leukaemia and lymphoma. The list further included second-line drugs for the treatment of multidrug-resistant tuberculosis. WHO anticipated that including these sometimes extremely expensive medicines in the list would stimulate efforts to get prices down through policies such as tiered pricing, voluntary and compulsory licensing, pooled procurement, and bulk purchasing. WHO was specifically asked to help countries negotiate lower prices and to rapidly introduce prequalified generic formulations, especially for the hepatitis C antivirals. In several countries, prices dropped significantly for hepatitis C antivirals, but less so for the newly listed cancer drugs. Of the options available, WHO prequalification of generic products held considerable promise as a proven way to increase affordable access. The concept of essential health technologies evolved further in 2017, when the Expert Committee on the Selection and Use of Essential Medicines approved the establishment of a complementary Model List of Essential Diagnostics. For essential medicines, inclusion in the model list was often necessary before large funders, like ministries of health,

funding agencies, and insurers, would invest in large-scale procurement of a given medicine. The establishment of a list of essential 17 Access to medicines: making market forces serve the poor diagnostics is expected to perform a similar role in guiding rational procurement decisions and improving population access to tests that will have the biggest impact on their health. Introduced in 2001, the WHO Prequalification Programme was equally revolutionary. The programme responded to an urgent need. Generic manufacturers, largely concentrated in India, were producing large quantities of low-cost treatments for HIV, tuberculosis, and malaria, but those products were coming on the market without authorization from a stringent regulatory authority. The WHO programme stepped in to meet the need for stringent assessment by sending expert teams to inspect manufacturing facilities and ensure compliance with WHO Good Manufacturing Practices and testing to see if the quality and efficacy of generic products matched those of patented originator products. The programme clearly satisfied an urgent and unmet need at a time when the three epidemics were still rapidly expanding. It eventually extended its remit to include the prequalification of active pharmaceutical ingredients and drug-testing laboratories. Today, the WHO “prequalified” stamp of approval means that medicines and vaccines are considered safe, effective and of high quality, and thus recommended for bulk purchase. After years of stepwise improvements urged by WHO, China’s National Regulatory Authority was assessed as fully functional for the regulation of vaccines in 2011, when WHO certified that the authority’s oversight of vaccine quality met rigorous international standards. That assessment paved the way for the prequalification of individual vaccines, and

opened the door to exports from the country that had the largest vaccine manufacturing capacity in the world. The first vaccine made in China, for Japanese encephalitis, was prequalified by WHO in 2013. The vaccine was not only less expensive than vaccines already on the market, it was also a better product. The vaccine is easier to administer, being effective after a single dose, and can be safely given to infants, greatly simplifying the logistics of vaccine delivery and cutting costs even further. The prequalification of this vaccine by WHO was welcomed as a true game-changer for a disease that is the leading viral cause of disability in Asia. Japanese encephalitis kills or causes neurological disabilities in 70% of those infected. In February 2017, WHO assessed India's National Regulatory Authority as fully functional, reporting 100% compliance with a roadmap, set out by WHO in 2012, for strengthening the national authority. That seal of approval is expected to go a long way towards securing international confidence in medical products manufactured in India, often referred to as the "pharmacy of the world". The programme's major contribution to the availability of life-saving medical products is now widely recognized. The initiative deserves much credit for the fact that more than 18 million people living with HIV in low- and middle-income countries have seen their lives turned around by access to antiretroviral therapy. It has had other successes as well. By allowing smaller manufacturers producing quality products to compete on an equal footing with multinational companies, it has increased supplies, improved their predictability, and used competition to get prices down, sometimes dramatically. Less well-known is the programme's contribution to capacity building. It conducts in-country training programmes, lets regulators in

developing countries learn from mature regulatory authorities, and uses expert inspections as an additional training and corrective tool. The programme 18 Ten years in public health 2007–2017 also operates a system of rotational fellowships at WHO for hands-on learning. In these ways, WHO helps countries move towards self-sufficiency in their regulatory capacity, also when serving the domestic market.

Partnerships: another route to new products

Public-private partnerships are the most visible manifestation of the power of collaboration to promote R&D for diseases that predominantly affect the poor. Products developed through these partnerships nearly always have clear and transparent strategies to ensure access, providing the best examples of specific features that can ensure broad and affordable coverage. Some of these partnerships have been remarkably successful. The Meningitis Vaccine Project, coordinated by WHO and PATH with substantial funding from the Bill and Melinda Gates Foundation, successfully developed a new conjugate vaccine for use in Africa's meningitis belt. It is arguably the best illustration of the ability of public-private partnerships to attract broad-based collaboration, and the best demonstration of the unique benefits of doing so. A consortium of academics and scientists developed the vaccine. Technology was transferred from the US and the Netherlands to the Serum Institute of India, which agreed to manufacture the vaccine at the target price of 50 cents per dose. African scientists contributed to the design of study protocols and conducted the clinical trials. Canada assisted the Indian National Authority in regulatory approval, and WHO pre-qualified the vaccine using accelerated procedures. The

vaccine, developed in record time at one-tenth the cost of a typical new vaccine, was tailor-made for an African need, priced for Africa, and developed with hands-on support from African scientists. For once, Africa was the first to receive a product that was the best that the world, working together, could offer. The impact has been significant. Since the vaccine's launch at the end of 2010, more than 230 million people in 16 countries in Africa's meningitis belt have been vaccinated against meningococcal meningitis serogroup A, with support from Gavi and the Bill and Melinda Gates Foundation. Given the added impact of herd immunity, the recurring outbreaks of meningitis A that devastated 26 African countries for decades have now been virtually eliminated. Following the Ebola outbreak in West Africa, WHO convened a series of expert consultations to develop a blueprint for the expedited development and regulatory approval of new medical countermeasures during public health emergencies. By setting up collaborative models, standardized protocols for clinical trials, and pathways for accelerated regulatory approval in advance, the blueprint aimed to cut the time needed to develop and manufacture candidate products from years to months. One of these consultations led to the establishment of the Coalition for Epidemic Preparedness Innovations, announced in January 2017 with initial funding of nearly \$500 million. The Coalition was further guided by a new WHO list of priority pathogens that have the potential to cause severe epidemics yet have no vaccines to slow their spread.¹⁹ Access to medicines: making market forces serve the poor The Coalition is building a new system to advance the development of safe, effective and affordable vaccines, ensuring that price is not a barrier to access for populations

most in need – a vital insurance policy against the growing threat from emerging and re-emerging diseases. Three diseases from the WHO list of priority pathogens have been initially targeted: Lassa fever, Nipah virus disease, and the Middle-East Respiratory Syndrome, or MERS. The Coalition is pursuing a proactive (“just in case”) and accelerated (“just-in-time”) vaccine development strategy for epidemic threats that moves vaccine candidates through late preclinical studies to proof of concept and safety in humans before epidemics begin, so that larger effectiveness trials can begin swiftly during an outbreak and small stockpiles are ready for potential emergency use. The strategy is also building technical platforms and institutional capacities that can be rapidly deployed against new and unknown pathogens. The Global Antibiotic Research and Development Partnership is another new initiative established to develop and deliver new antibiotic treatments with prices fixed to be sustainably affordable. Initiated in May 2016 as a collaborative project between WHO and the Drugs for Neglected Diseases initiative, the antibiotic R&D partnership responds to the call in WHO’s Global Action Plan on Antimicrobial Resistance for public-private partnerships designed to develop new antimicrobial agents and diagnostics. The partnership is supported by initial seed funding and pledges of \$5.33 million from the governments of Germany, the Netherlands, South Africa, Switzerland and the UK as well as from the medical charity Médecins Sans Frontières. A Scientific Advisory Group is overseeing the portfolio of priority R&D projects. Initial priorities include a new first-line antibiotic for the treatment of neonatal sepsis and a new second-line treatment for managing infants with drug-resistant infections. Antimicrobial

resistance is a major factor determining clinical unresponsiveness to treatment and rapid evolution of infections to sepsis and septic shock. WHO estimates that around 214 000 yearly neonatal deaths due to sepsis worldwide can be attributed to resistant pathogens. A second initial project aims to recover data, trial results and assets from R&D projects that were abandoned as large pharmaceutical companies closed down their work on antibiotics. The partnership views this project as a bridging measure aimed at recovering urgently needed replacement products while the search for new classes of antibiotics is being pursued. A third project will give urgent attention to new antibiotics to treat gonorrhoea, a widespread disease that may soon become untreatable as it develops resistance to all existing classes of antibiotics.

High ambitions enter a highly contentious area

While all of these initiatives are doing great good, they address only pieces of a much bigger – and deep-seated – problem: the way the patent system operates to preferentially stimulate innovation for wealthy markets, establish a 20-year minimum monopoly on high prices, and leave the poor – and their vast health needs – abandoned by the wayside. A 2002 WHO document expressed the situation well: “A significant proportion of the world’s population, especially in developing countries, has yet to derive much benefit from innovations that are commonplace elsewhere.” 20 Ten years in public health 2007–2017 WHO’s approach to access issues became far more ambitious in 2006, when the WHO Commission on Intellectual Property, Innovation and Public Health issued its report. The Commission concluded that, while governments

bear much responsibility, WHO must take the lead in promoting more sustainable funding mechanisms to stimulate innovation in cases where intellectual property acts as a barrier to access to medicines. In line with that conclusion, the report urged WHO to “develop a global plan of action to secure enhanced and sustainable funding for developing and making accessible products to address diseases that disproportionately affect developing countries.” WHO Member States promptly acted on that advice. Two years later, after tense and sometimes heated negotiations, the World Health Assembly approved the Organization’s first Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, an achievement immediately hailed as a milestone. WHO had taken a daring step into the potential minefield of the patent regime, with major implications. As one of its strengths, the strategy and action plan tackled the need for innovation and affordable access simultaneously. The resulting text did indeed contain some breakthrough proposals. It raised the prospect of managing intellectual property in a more responsible manner that maximized needs-driven innovation and promoted access to affordable medical products. It called for exploration of new incentive schemes that would delink the costs of R&D from the price of medical products. Financial prizes for R&D milestones or bringing a product to market were put forward as one way of doing so. And it scolded, drawing attention to the practice, often embedded in trade agreements, of stipulating more extensive intellectual property protection than required by the World Trade Organization’s Agreement on Trade-related Aspects of Intellectual Property Rights – the so-called TRIPS-plus measures. Commonly used measures include extending

the term of a patent longer than the 20-year minimum, introducing provisions that limit the use of compulsory licenses, and requiring data exclusivity, which blocks market entry by generic manufacturers. WHO was unquestionably taking a stand in contentious territory. With an agreed strategy and action plan in hand, the next step was to finance its implementation. As requested, WHO appointed expert working groups to explore innovative proposals for financing and coordinating R&D. The report of the Consultative expert working group, issued in 2012, critically and systematically assessed 15 proposals for financing R&D and recommended five as best meeting its established criteria: a binding R&D convention or framework, pooled funds, direct grants to companies, milestone prizes and end prizes, and patent pools. While the experts believed the time was right to initiate negotiations for a binding convention, Member States disagreed. By 2012, the impact of the 2008 financial crisis was being felt almost universally. The proposal to negotiate a binding convention did not resonate well in a climate of austerity. Governments were reluctant to accept any new instrument that committed them to substantial and sustained financial support. During discussions of the report in subsequent sessions of the World Health Assembly, WHO was asked to pursue several recommendations: to establish an R&D observatory, to appoint an expert committee to advise on R&D priorities and means of coordination, to elaborate a mechanism 21 Access to medicines: making market forces serve the poor for the voluntary pooled funding of R&D, and to conduct demonstration projects for designated diseases of the poor. The latter initiative was crippled by a significant funding gap. The proposal to negotiate a binding R&D

convention was revived in 2016, when the UN Secretary-General's High-level panel on access to medicines issued its report. That report also drew attention to the fact that many countries were not using fully the flexibilities under the TRIPS Agreement, for reasons ranging from capacity constraints to undue political and economic pressure from states and corporations. As the report noted, "Political and economic pressure placed on governments to forgo the use of TRIPS flexibilities violates the integrity and legitimacy of the system of legal rights and duties created by the TRIPS Agreement, as reaffirmed by the Doha Declaration." WHO works closely with the World Trade Organization, the World Intellectual Property Organization, and other UN agencies to support the unimpeded use of measures that can improve access, such as local production, giving least-developed countries a transition period, implementing patentability criteria that reward only genuinely innovative discoveries, and compulsory licensing. On request, WHO provides direct technical support to countries that intend to make use of these flexibilities.

Improving industry behaviors

By entering what had long been forbidden territory and publicly asking some hard questions, WHO opened up opportunities for others to act in novel ways. The Access to Medicine Index, launched in 2008 and published every two years since, holds the world's 20 leading research-based pharmaceutical companies accountable for making their products more accessible in low- and middle-income countries. The index gives particular attention to problematic industry behaviors identified in the WHO global strategy and action plan. WHO experts serve on the review committee and

technical subcommittees. Under public scrutiny, the behaviour of the pharmaceutical industry has progressively improved in some, though not all, ways. The 2016 index shows that intellectual property can indeed be managed in a more responsible way. Access-oriented approaches to intellectual property management include responsible patenting policies, transparency about existing patents, and a willingness to engage in non-exclusive voluntary licensing. On the negative side, the index exposed continued lobbying for TRIPS-plus measures and legislation, the breaching of laws or codes relating to corruption and unethical marketing, and several blatant instances of company misconduct. On balance, though, the situation is improving. Many of the problems addressed in the WHO global strategy and action plan have captured industry's attention and stimulated remedial action. The 2016 Access to Medicines Index gave high marks to companies that have negotiated licenses for antiretrovirals and hepatitis C medicines through the Medicines Patent Pool. The Medicines Patent Pool was set up in 2010 to improve access to antiretroviral therapy in low- and middle-income countries, with a remit later expanded to include hepatitis C and tuberculosis treatments. 22 Ten years in public health 2007–2017 It is sponsored and fully funded by UNITAID, a drug purchasing facility that draws substantial and sustainable funding from a levy on airline tickets. Patent pools were recommended in the WHO global strategy and action plan and strongly endorsed by the expert groups on the innovative financing of R&D. Since the first company joined the pool in 2012, it has operated as an independent driver of access-oriented licensing in the pharmaceutical industry. It is transparent as well as effective. Companies that engage with

the patent pool are obliged to disclose information about their patents, which the pool then makes public. Data exclusivity waivers are included in all agreements. Through the patent pool mechanism, licensing by patent holders has accelerated, with broader geographical coverage, greater competition, and improved terms and conditions, enabling more robust competition. The patent pool works well because it offers something for everyone. Patent holders are rewarded with fair royalties that accumulate as low-priced generics bring a surge in demand. Generic manufacturers benefit from the vastly simplified procedure of dealing with a single negotiating body, plus the ability to enter the market before patents expire. They further benefit from the waiving of data exclusivity and the market clarity that comes when details about patents are made publicly accessible. Innovation is facilitated by making it possible to produce fixed-dose combinations using medicines from different patent holders. Pediatric formulations are encouraged by an obligatory waiving of all royalties on all pediatric medicines. As companies have licensed their best-in class medicines to the patent pool, patients benefit from widespread geographical access to affordable quality-assured medicines that are the best the world has to offer.

[A model for fair pricing](#)

WHO is providing a platform to discuss the fair pricing of pharmaceutical products. The issue of fair pricing is framed by two extremes: prices so high they are unaffordable, even in the world's richest countries, and prices so low they drive high-quality manufacturers out of the market, leading to drug shortages. The SDG target for universal health coverage

depends on finding ways to tackle both extremes. The overarching objective is to find a model for fair pricing that makes essential medicines available in sustainable quantities at prices that are sustainably affordable for patients, third party payers, and health system budgets. The extremely high prices charged for newly approved drugs for the treatment of cancer and hepatitis C are indicative of a trend in which new medicines are nearly always more expensive. For some new drugs approved for various cancer indications, the high prices have not always been justified by studies of their therapeutic advantages over existing medicines. In addition, prices for older off-patent products can increase astronomically when a new company gains a monopoly on the market. Recent controversies in the United States – the overnight 5000% increase in the price of pyrimethamine and the price increase for epinephrine auto-injection devices – are the most egregious manifestations of this second trend. 23 Access to medicines: making market forces serve the poor In late November 2016, WHO convened an informal group of experts from governments, international organizations, research institutes and academia to gather advice on the full range of issues that determine whether the prices charged for pharmaceutical products are fair. The advisory group was also asked to identify issues that will need further exploration during a May 2017 Fair Pricing Forum being co-hosted by WHO and the government of the Netherlands. The ultimate aim, the experts agreed, should be a price that assures new medicines are affordable to all patients and health systems, allows for an acceptable profit margin, also as a stimulus for further innovation, and assures a stable supply of generic medicines. In working towards a model for fair pricing, the experts

identified a number of priority issues and information gaps, including the need for market transparency in prices actually being paid in different settings, the true costs of R&D for new product development, the costs of manufacturing a product, and the range of profit margins that result. The group looked with some scepticism at industry's common argument that rising prices reflect the escalating costs of R&D and found some evidence that prices are fixed according to what the market will bear. Although the report of the advisory group demonstrated that a range of factors influence medicine prices, it confirmed that more transparency around production and R&D costs would move the discussion forward during the Fair Pricing Forum.