# AIDS, DEVELOPING COUNTRIES AND PHARMACEUTICALS

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## The Underlying Healthcare Crisis in Developing Countries

Despite improvements in recent years, millions of people in developing countries still cannot access the most basic healthcare, including safe and effective medicines. This has led to a continuing healthcare crisis in these countries, many of which are amongst the least able to cope economically or administratively with the challenge of managing infectious diseases, such as HIV/AIDS, tuberculosis (TB) and malaria, as well as the growing problem of non-communicable diseases, such as diabetes, cardiovascular disease, respiratory conditions and cancers.

Poverty remains the single biggest barrier to improving healthcare in the developing world. In many countries people still do not have enough food, access to a clean water supply, hospitals or clinics in which to receive treatment, and healthcare professionals to care for them.

## THE HIV/AIDS Epidemic

- The first cases of AIDS were reported more than 35 years ago.
- 78 million people have become infected with HIV.
- 35 million people have died from AIDS-related illnesses.

The response to the epidemic has included working to provide access to appropriate medicines at little or no cost, developing new medicines to overcome disease resistance and provide simpler dose regimes for patients, giving financial and educational support to help develop the basic healthcare infrastructure within developing countries, and ensuring that transmission of the AIDS virus is minimised. Discrimination and social and cultural considerations relating to sexual behaviour continue to impede expanded success in addressing the AIDS epidemic in many developing countries.

In 2015, the global community committed to ending the AIDS epidemic as a public health threat by 2030 as part of the UN 2030 Agenda for Sustainable Development. It is an ambitious yet achievable goal but scale-up of the most effective services for preventing HIV infection and treating people living with HIV has already seen a 32% global decline in AIDS-related deaths and a 16% global decline in new HIV infections between 2010 and 2016[1]. The UN Joint Programme, UNAIDS, leads the global effort to end AIDS as a public health threat and has collected and published information on the state of the world's HIV epidemic for the past 20 years[2], helping shape and guide the global response to HIV infection.

In 2016, UNAIDS reported[3] that 36.7 million people worldwide were living with HIV. Of these, 19.4 million (53%) were in Eastern and Southern Africa with women and girls accounting for more than half [59%]. As of June 2017, 20.9 million people living with HIV were accessing antiretroviral therapy, up from 17.1 million in 2015 and 7.7 million in 2010. TB remains the leading cause of death among those living with HIV, accounting for around one in three AIDS-related deaths. Regrettably, almost 57% of the TB cases among those living with HIV were not diagnosed or treated, leading to 390,000 TB-related deaths in 2015.

## Patents on Pharmaceuticals – Rationale and Complexities

Patents are now granted for new pharmaceutical developments in much the same way as for other useful inventions i.e. they must be new and inventive. The availability of patent protection continues to stimulate and underpin the discovery and development of new improved medicines to treat diseases prevalent in developed and developing countries alike, including infectious as well as non-communicable diseases such as diabetes and cancer.

In addition to the cost and uncertainty of discovering a potential candidate molecule and producing and formulating it on a large scale, developing a new medicine includes extensive safety and clinical evaluation as well post launch monitoring, with the risk of failure at any point. In a recent study, the full, out-of-pocket cost per approved new medicine (including the cost of failures) has been estimated at 1.3B USD[4]. Further, for every 10,000 candidate molecules identified from an initial pharmaceutical invention, only one will make it all the way through to regulatory approval and become a successful medicine[5] and only one in three of those medicines will "break even" on the cost of its discovery and development. Accordingly, private companies are unwilling to undertake the long, risky and very expensive R&D process without the possibility of recovering the substantial investment costs through

adequate patent protection and the existence of a market for the new medicine.

The existence of intellectual property protection for pharmaceuticals, and patents in particular, continues to be blamed for the fact that many millions of people are denied access to the medicines they need. There are inevitably delays before a new medicine becomes commercially available in other countries, influenced in part by local regulatory and pricing factors as much as by the patent situation. These delays can often amount to several years, particularly in low income countries, before the public health benefits of a new medicine can be achieved[6].

Alternative models to patents such as prizes, government grants, tax-credits etc have been proposed as a means of encouraging innovation in development of medicines for diseases mainly prevalent in least developed countries[7]. However, so far, these have yet to make significant impact as alternatives to patents in stimulating innovation in pharmaceuticals.

# Comment

Focusing on patents as the main barrier to access to healthcare in the developing world is misleading and unhelpful when there are other significant barriers. The access problem stems primarily from poverty and an inability to pay for even the cheapest medicines, including patent free generic medicines. Thus, first line treatments for killer diseases such as malaria and TB are available as generic products at very low cost, and yet still many people are unable to access them. There is often chronic under-investment in healthcare infrastructure resulting in lack of clinics and hospitals, inadequate distribution networks, insufficient trained healthcare providers, and high levels of patient illiteracy. Other factors impeding access are local taxes and tariffs that raise prices unnecessarily, cultural factors such as stigma and discrimination in many parts of the world, as well as criminalisation, deterring those most at risk from seeking essential HIV services.

Relatively few patents exist in many African countries. A study published in 2002 which reviewed the patent position for fifteen anti-retrovirals in 53 African countries concluded that: "patents and patent law are not a major barrier to treatment access in and of themselves" [8]. Similarly, 95% of the 375 medicines on the 18th edition (2013) of the WHO List of Essential Medicines (provided as a model list for lower income countries to adopt) are not patent protected at all. Where there is protection, it is mainly in developed rather than developing countries[9]. Nevertheless, it is true that, unless licensed, a patent can also prevent production or sale of lower cost, generic medicines

or development of novel formulations. This is particularly the situation for the recently introduced anti-retroviral medicines and certain fixed dose combination products.

In addressing the access problem in developing countries, the pharma companies have adopted varying approaches to improve access, such as differential pricing, donations, voluntary licensing and capacity building. Some of these, such as differential pricing and capacity building, are relevant whether or not there are patents on the medicines concerned[10]. This is often the case in least developed and low-income countries. Several global companies have joined in patent pooling arrangements such as the Medicines Patent Pool[11]. This was set up under the auspices of UNITAID[12] working with a range of stake-holders to create a pool of relevant patents for sub-licensing and product development of key HIV therapies as well as fixed-dose combinations and paediatric formulations. There is now a searchable, public database, MedsPal[13], showing the regulatory, patent and licensing status of HIV, hepatitis-C, TB and other patented medicines on the WHO model List of Essential Medicines in developing countries.

The independent, non-profit Access to Medicine Foundation[14], analyses the progress of twenty leading pharma companies in improving access to medicine in developing countries, publishing the results regularly in a detailed Index[15]. The WHO and others have called for 45 diseases to be urgently prioritised for further R&D, including twelve pathogens that pose a critical risk of antimicrobial resistance; the 2018 Index will assess how pharma companies are responding[16].

More pharma companies are experimenting with innovative access-oriented business models, companies are granting more licenses for making and distributing generic versions of their products, and companies continue to improve their oversight of access policies and activities. Yet progress remains uneven. Companies still lack the ability to effectively coordinate their access efforts within key disease and geographical areas and have a coherent and consistent approach to their pricing policies.

The research based pharma companies, sometimes working in partnerships with their competitors, have developed new HIV/AIDS medicines including anti-retrovirals that have helped save millions of lives in the global fight against the disease. But there is a continuing need for R&D on innovative products targeting poverty-related diseases, and for products adapted for specific needs, such as new fixed-dose combinations, heat-stable formulations, and adaptations targeting new demographic segments. However, unless these disease areas and needs overlap with those affecting

populations in developed countries, the market incentives for companies to engage in the relevant R&D are limited.

Over the last two decades, product development partnerships (PDPs) designed to re-engage pharma companies with R&D for poverty-related diseases have been successfully introduced involving open collaborative sharing of intellectual property[17]. Examples of PDPs include, fixed-dose artemisinin-based anti-malarial combinations delivered by over a dozen companies, with over 200 million treatments shipped each year; and the safer nifurtimox-eflornithine combination for sleeping sickness, developed in a consortium led by DNDi and manufactured by Sanofi and Bayer.

The High Level Panel on access to medicines, convened by the UN Secretary General, released its consensus report in September 2016[18] with the simple yet powerful message: no one should suffer because they cannot afford medicines, diagnostics, medical devices or vaccines. It remains to be seen just how the various report recommendations will be taken up by the principal actors in concrete steps to address gaps in health technology innovation and access to medicines as part of the UN 2030 Agenda for Sustainable Development.

> *"The journey from concept to finished medicine can take up to 25 years. If there is significant uncertainty about returns being available for successful, value-adding products at the end of that period, investors and therefore companies would be much less willing to invest the significant levels of funding required to discover, research and develop new medicines. Innovation would be endangered for patients around the world."*
>
> **Sir Andrew Witty, member of the UN High Level Panel on access to medicines [19]**

## Suggested Further Reading:

- "Developing world health partnerships": International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)[20]
- "Towards zero infections" – UK position paper on HIV in the developing world - Department for International Development (DfID) – May 2011[21]
- "Patents versus patients: five years after the Doha declaration" – OXFAM paper - Nov 2006[22]
- "Evidence on access to essential medicines for the treatment of HIV/AIDS" – Charles River Associates - 2016[23]
- Global HIV statistics - UNAIDS factsheet – 2017[24]
- IFPMA policy position - patent licensing – Feb 2015[25]
- Intellectual Property & Access to Medicines in Developing Countries – Public policy statement – GlaxoSmithKline – Jan 2014[26]

- Perspectives on access to medicines and IP rights – WIPO magazine, Dec 2017[27]
- UN High Level Panel report on access to medicines – factsheet[28]

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[1] Michel Sidibé, UNAIDS Executive Director
[2] http://www.unaids.org/en/whoweare/about
[3] http://www.unaids.org/en/resources/documents/2017/2017_data_book
[4] DiMasi, Grabowski, and Hansen (2016) surveyed the R&D costs of 106 randomly selected new drugs from 10 companies to estimate average pre-tax cost of new drug and biologics development; Innovation in the pharmaceutical industry: New estimates of r&d costs, Journal of Health Economics 2016, 47, 20 – 33; https://www.ncbi.nlm.nih.gov/pubmed/26928437
[5] https://www.efpia.eu/about-medicines/development-of-medicines/
[6] See recently reported study of 642 new medicines in 76 countries over the period 1983-2002: Schankerman M et al (2016), Patents and the global diffusion of new drugs; American Economic Review, 106 (01). pp. 136-164; http://eprints.lse.ac.uk/65415/
[7] For example, see James Love, WIPO Expert Forum Tech Transfer, Feb 2015: http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_inn_ge_15/wipo_inn_ge_15_p014.pdf
[8] Attaran and Gillespie-White (2010), http://iipi.org/wp-content/uploads/2010/07/Antiretroviral_Article.pdf
[9] Beall RF (2016), Patents and WHO model List Essential Medicines - IP and Access; http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_gc_ip_ge_16/wipo_gc_ip_ge_16_brief.pdf
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[16] https://accesstomedicineindex.org/news/new-methodology-for-2018-access-to-medicine-index-6/
[17] Cole and Iyer, June 2016: https://accesstomedicinefoundation.org/media/atmf/2016-Ensuring-sustained-incentives-for-pharma-to-develop-medicine-for-the-poor.pdf
[18] http://www.unsgaccessmeds.org/final-report/
[19] Commentary in report of UN High Level Panel on access to medicines, Sep 2016; http://www.unsgaccessmeds.org/resources-documents/2017/7/19/report-of-the-united-nations-secretary-generals-high-level-panel-on-access-to-medicines.
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