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Achieving the impossible to finance R&D for neglected diseases

A Question of Social Justice

Von Susanna Hausmann-Muela

When Ebola severely hit West Africa last year, the global community was largely unprepared – almost no drugs, no diagnostics, no vaccines – despite knowing of the disease's existence for almost 40 years. The Ebola crisis made the global community wake up to the fact that in our interconnected world infectious diseases concern us all. New challenges lie ahead of us, with the (re-)emergence of communicable diseases and antimicrobial resistance on the rise worldwide. Investing in Research and Development (R&D) for health products against communicable diseases has increasingly become a matter of global security, and it is in everyone's interest to have well prepared responses to emerging risks.

Kenyan Researchers (Photo: Anna Wang/zVg)

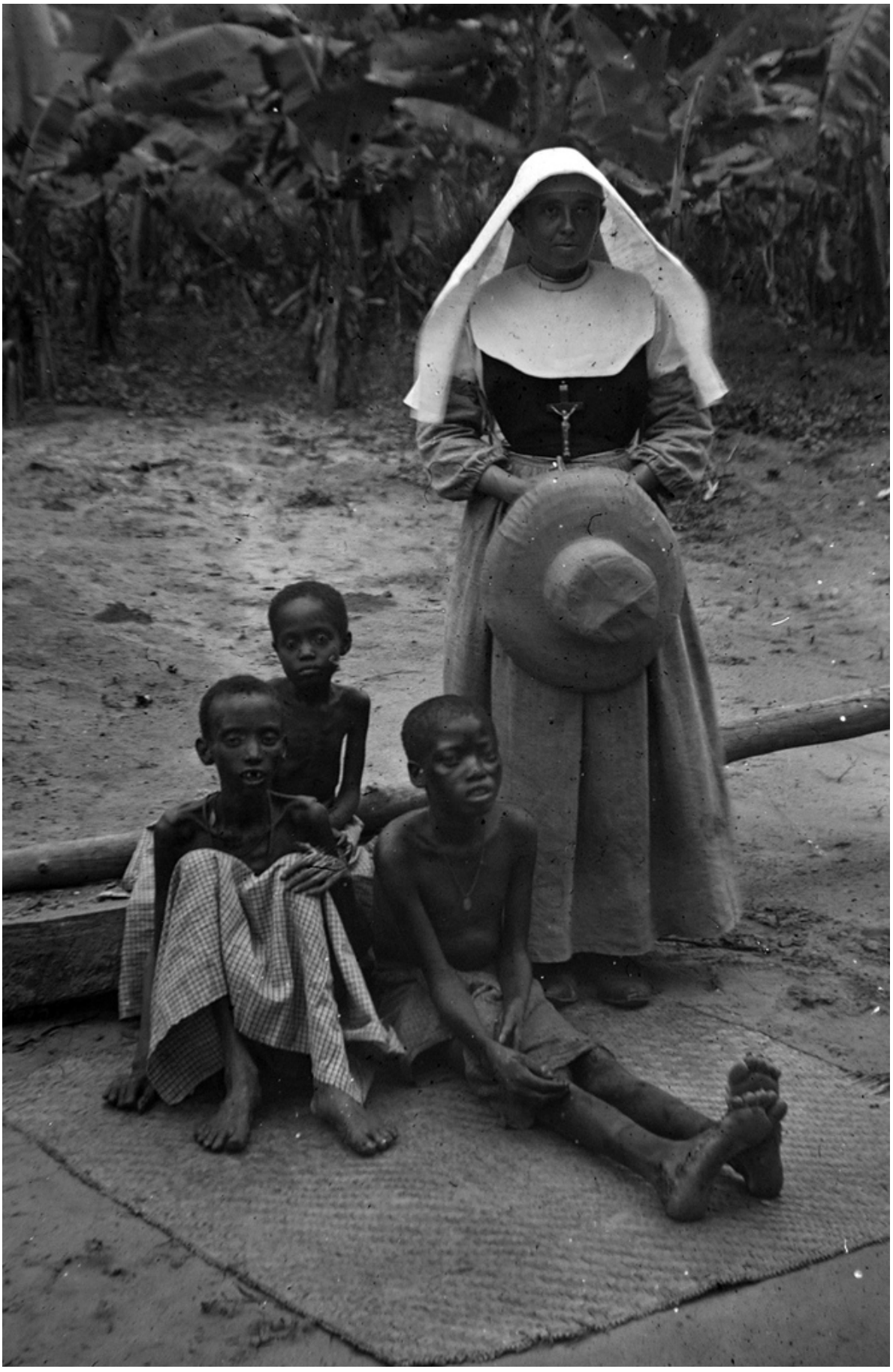
Neglected diseases as problems for security and social justice

Global needs and market failure

It is true that not every communicable disease threatens to become a global problem. Investing in Research and Development (R&D) for diseases that disproportionately affect the poor is also a matter of social justice and equity. As early as the 1990s, the Commission on Health Research for Development reported on the 10/90 gap to highlight the imbalance in research investment, estimating that less than 10% of the worldwide resources for health research were put towards health in developing countries, where over 90% of preventable deaths worldwide occurred. Although progress has been made, we are still far from correcting this imbalance. This is because the current drivers behind R&D investment simply do not work for poor people's diseases. Globally, patents are the main policy tool driving investments in medical products R&D. Lack of investment is inherent in this system, since private companies are by nature profit-oriented. Industry has no market incentive to invest in products defined by global health needs or public priorities and targeted to populations with poor purchasing power.

Sleeping beauty or sleeping sickness? – Profit versus patients' needs

R&D in drugs against African sleeping sickness speaks volumes of the consequences of patent and not patient-driven investment. For decades, there was only one treatment for the late stage of the deadly disease. Intravenously administered *melarsoprol*, an arsenic compound developed and introduced in 1949, is highly toxic and killed between 3% and 10% of patients treated (Robays *et al.*2008). The good news was that another drug, *eflornithine*, developed in the 1970s as a potential anti-cancer drug, was found in the 1980s to be active against late stage gambiense sleeping sickness and registered for treating the disease (Ollivier & Legros 2002). However, despite the life-saving properties for patients on the African continent, patent holder Aventis ended production in 1995 when the drug was found ineffective against cancer (MSF 2001). Profit-driven production resumed five years later, when the US Food and Drug Administration (FDA) granted a new drug application to *eflornithine cream*, for use in cosmetics as a prescription medication applied to the skin for the reduction of unwanted facial hair in women. After years of intense international pressure, in 2001, Aventis, supported by Médecins Sans Frontières, signed a long-term agreement with the World Health Organization to manufacture and donate the drug (MSF 2001). Today, *eflornithine* is used in combination with *nifurtimox*, a drug originally used to treat Chagas disease in Latin America. Since 2009, *Nifurtimox-eflornithine combination therapy* (NECT) is on the World Health Organization's List of Essential Medicines as the first-line treatment option for patients infected with advanced stages of gambiense sleeping sickness. Bayer Health Care (*nifurtimox*) and Sanofi-Aventis (*eflornithine*) promised continued support in the 2001 donation agreement, and in the London Declaration, signed in 2012 (pdf) by some of the biggest pharmaceutical companies, pledging to control ten NTDs including sleeping sickness. A new orally administered drug, *fexinidazole*, which is currently under clinical testing, is a promising future breakthrough that would take the treatment closer to the communities.



People with sleeping sickness, Congo, probably 1901 (Marc Lambrechts/flickr)

The pharmaceutical golden era

The story of R&D investment against sleeping sickness culminating in the absurdity of drugs used as cosmetics rather than to save lives reflects the history of public and private R&D engagement and investment throughout the 20th century.

The rise of industrial research programmes originated in the early 20th century discoveries that specific synthetic chemicals could selectively kill disease-causing microbes. Early successes and an emerging highly profitable market for medical products led to the "pharmaceutical golden era" (Daemmerich & Bowden, 2005), with rapidly growing levels of investment by private companies.

From private to public to public-private: The Special Programme for Research and Training in Tropical Diseases (TDR)

Private industry invests in products for which there is a potential for high return on investment. The diseases that disproportionally affect poor populations are unattractive for companies as they are likely to result in high investment but low profit.

The 1960s and 70s, against the backdrop of an increasingly strengthened and enlarged WHO and a changing political context with the decolonisation of Africa, marked a public sector awakening. The global health community expressed growing concerns that private sector driven biomedical advances, as impressive as they were for the industrialised world, were not reaching people in developing countries, and that products needed by the poor – as in the case of sleeping sickness – were not being developed. A resolution at the 27th World Health Assembly in 1974 endorsed the need for intensified research on parasitic tropical diseases which led to the establishment of the Special Programme for Research and Training in Tropical Diseases (TDR). TDR was set up as a partnership with an independent joint coordination board of representatives from public donors, endemic country governments and civil society, and was co-sponsored by the United Nations Children's Fund, United Nations Development Programme, the World Bank and the World Health Organization, with the latter as the executing agency.

TDR's original programme sought to obtain "effective new vaccines, diagnostic tests, drugs and measures of vector control through R&D and concurrently to help the tropical countries to improve their own research" (Goodman 1995). TDR primarily focused on defining research needs and invested in upstream basic biomedical and compound discovery research, but it did not have the experience, understanding or resources to directly engage in the downstream product development activities of registration and commercialisation, which remained the remit of the pharmaceutical industry.

In the 1990s, it became increasingly clear that the well-intentioned efforts made on the basis of this division of labour between public and private sectors – with totally different institutional cultures – were not yielding the expected results. The tedious discussions leading up to the

2001 donation agreement for eflornithine between Aventis and the WHO is just one example of the awkward collaboration between public and private sectors.

At the same time, private industry's growing tendency to close down their remaining tropical medicine programmes created a pressing need for alternative collaborations. This was the birth of the "Era of Partnerships" (Mahoney 2011) and the important stepping in of philanthropic organisations. Drug development projects for diseases of poverty moved increasingly from the public domain to newly established public-private partnerships, which became known as product development partnerships (PDPs).

Product Development Partnership (PDPs) – offering alternatives to patent-driven R&D

Product Development Partnerships (PDPs) seek to coordinate the contributions of the private, public, academic and not-for-profit sectors to address the scientific, economic, legal and political challenges that exist in developing new health technologies for use in developing countries, and in ensuring their rapid and widespread use. Over the past 15 years, PDPs have gained increasing relevance in accelerating R&D for diseases of poverty. Today, there are around 20 PDPs focusing on vaccines, drugs, diagnostics, and insecticides. It has been estimated that the PDP model supports 40% of the overall neglected disease pipeline (Ponder & Moree 2012). According to the G-FINDER 2014 survey (Moran *et al.* 2014), the public sector played a key role in neglected disease R&D, providing two-thirds of funding ($2,128m, 66%), predominantly from high-income country governments. The philanthropic sector contributed $688m (21%) while industry invested $401m (12%).

The contribution of Switzerland in financing neglected diseases R&D

The Government of Switzerland has been prominent in supporting neglected disease R&D over the past decades. Since the launch of TDR, the SDC has always been a reliable source of funding. When TDR drug development projects were transferred to the new PDPs the SDC was actively involved in their establishment. The new style of partnership accorded well with Switzerland's desire to engage in partnerships with the private sector in order to gain access to knowledge and expertise, mobilise resources and promote innovation, an approach later promoted in the Swiss Health Foreign Policy. The Medicines for Malaria Venture (MMV) was launched as one of the first PDPs in 1999 with initial seed money from the SDC, the UK Department for International Development, the Government of the Netherlands, the World Bank and the Rockefeller Foundation.

The SDC is supporting two other PDPs focusing on drug and diagnostic R&D for specific neglected diseases, including sleeping sickness, the Drugs for Neglected Disease Initiative (DNDi) since 2003 and the Foundation for Innovative New Diagnostics (FIND) since 2013. Together with MMV, these two Geneva-based PDPs are also leading the way in addressing the

critical issue of access to health products for the poor in developing countries. In 2014, the Innovative Vector Control Consortium (IVCC), focusing on R&D of insecticides was added to the SDC's portfolio.

Substantial progress has been made in recent years to establish a voluntary, sustainable R&D fund and mechanism as part of the lengthy and difficult political process to negotiate a global framework for R&D financing and coordination for diseases that disproportionately affect the poor. Switzerland is heavily engaged in this process, and has supported a pragmatic approach of implementing demonstration projects to provide evidence of the feasibility of global priority-setting and coordination as well as innovative financing mechanisms.

PDPs – with their extensive experience in neglected diseases R&D and innovative financing – are spearheading a global framework by actively implementing projects based on 'open' innovation not intellectual property, and by de-linking R&D costs from end-product prices. Two of the three demonstration projects selected by WHO-mandated expert panels are run by Swiss-based and supported PDPs, namely MMV and DNDi.

Together with its strategic partners, Switzerland is well positioned to play a pivotal role in accelerating neglected diseases R&D and to advance the global policy discussion towards a global health R&D framework.

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