

SDC ENGAGEMENT IN PRODUCT DEVELOPMENT PARTNERSHIPS: WHEN PUBLIC MEETS PRIVATE



Vaccines, diagnostics, medicines and insecticides are critical medical tools for preventing and treating diseases around the world. But for many diseases, these tools are partly ineffective, toxic or not suited to patients' needs – or not even available. While investments in medical innovation are huge for diseases mainly prevalent in high-income countries, diseases that disproportionately affect poor populations in low and middle-income countries are under-researched and the development of medical products is under-financed. These are neglected diseases occurring in countries with insufficient commercial market to stimulate research and development by private industry. This health brief provides an insight into global research and development needs and current responses, focusing on public-private collaboration through product development partnerships and the Swiss approach to it.

DISEASES OF THE POOR: THE SDC'S FOCUS ON MEDICAL INNOVATION

There are two categories of diseases with insufficient market drive for research and development: those that occur in high, middle and low-income countries, but with a substantial proportion of the cases in the latter (e.g. HIV/AIDS and tuberculosis); and diseases that are predominantly or exclusively prevalent in low- and middle-income countries (e.g. dengue, malaria, sleeping sickness, Chagas disease, river blindness, leprosy). Globally, 36.9 million are living with HIV/AIDS, and 1.2 million die each year of AIDS-related causes, two thirds of which alone in Sub-Saharan Af-



rica. More than 2 billion people are infected with tuberculosis, and annually 1.5 million die of the disease. Some 3.3 billion people worldwide are at risk of a malaria infection, with children and women being disproportionately affected, and an estimated 600,000 annual deaths. Apart from these big three killer diseases - HIV/AIDS, tuberculosis and malaria - neglected tropical diseases (NTDs) alone affect more than 1 billion people worldwide, mainly in sub-Saharan Africa and mostly living in remote rural areas, urban slums or conflict zones. NTDs account for a major part of the national disease burden, resulting in approximately 534,000 deaths worldwide every year and 57 million years of life lost due to premature

disability and death. In addition to causing severe physical and emotional suffering, these devastating diseases hamper a person's ability to work, keep children out of school, and prevent families and communities from thriving.

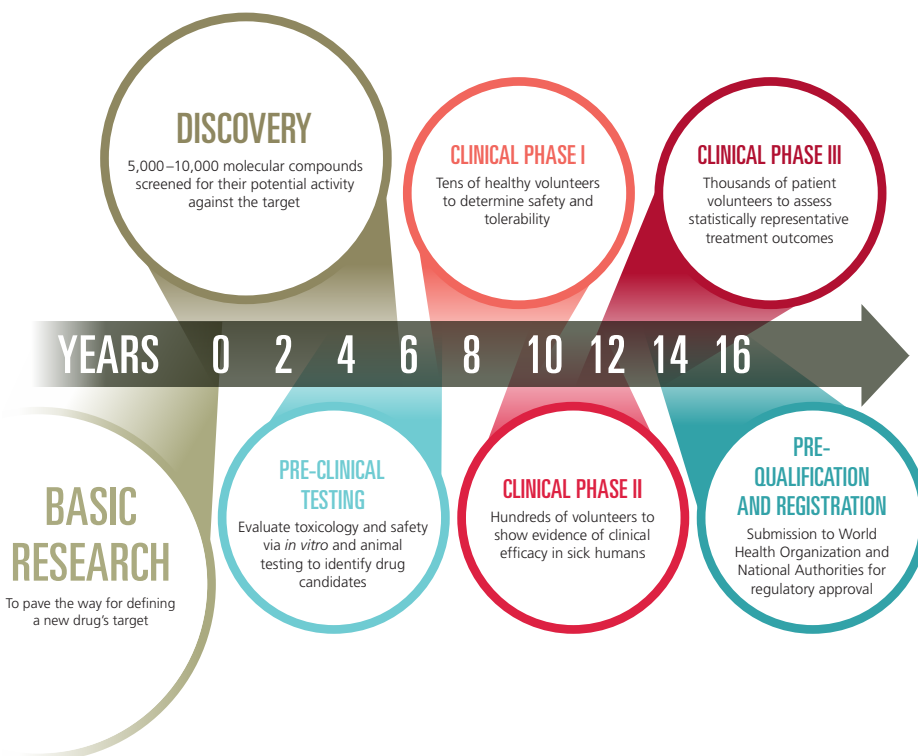
As early as the 1990s, the Commission on Health Research for Development reported on the 10/90 gap to highlight the imbalance in research investment, estimating that less than 10% of worldwide health research resources were dedicated to health problems found in low- and middle-income countries where over 90% of deaths occurred. Although progress has been made, we are still far away from striking a balance.

With its core mandate of poverty reduction, the Swiss Agency for Development and Cooperation (SDC) is firmly committed to helping reduce the disease burden of poor people. The SDC's engagement in medical innovation for diseases of the poor builds on Swiss excellence in the research-based pharmaceutical industry and academic organisations.

A MATTER OF SOCIAL JUSTICE AND GLOBAL SECURITY: THE SDC'S COMMITMENT

Investing in research and development for diseases of the poor is a matter of social justice and equity. But we are increasingly being made aware that it is also a matter of global health security. When Ebola ravaged West Africa in 2014, the global community was largely unprepared – almost no medicines, diagnostics or vaccines were available – 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: we cannot rule out the possibility of deadly communicable diseases such as malaria and dengue expanding to new areas as a result of climate change, migration and uncontrolled urbanisation. Antimicrobial resistance is on the rise worldwide, threatening the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. It is in everyone's interest to have well prepared responses to global health risks. The SDC's commit-

FROM MOLECULE TO MARKET: THE LENGTHY ROAD TO NEW DRUGS



Once a 'molecular drug target' is identified through basic research, a vast range of compounds is screened for their potential activity against the target. This is like finding a needle in a haystack. The best compounds are selected for pre-clinical studies to evaluate toxicology and safety via *in vitro* and animal testing. In clinical testing phase I, the drug candidates are tested in a few healthy volunteers to assess safety and tolerability in humans. The next phase, phase II, tests clinical efficacy and aims to identify the optimal dose, exposing a selection of a hundreds of patients to a range of dosages. Only in phase III are drug candidates tested on a large number of patients in randomised clinical trials, requiring access to participating trial sites in disease-endemic countries and involving several thousands of patients, for assessing statistically representative treatment outcomes. Before a drug can be launched, comprehensive documentation from pre-clinical and clinical testing needs to be submitted for regulatory approval. Manufacturers of medical products targeted for low- and middle income countries usually seek approval with the World Health Organization pre-qualification programme before they seek approval at the National Medicines Regulatory Authorities of the target countries.

ment to research and development for neglected diseases is consistent with the Swiss Health Foreign Policy, which fosters a human rights-based approach by promoting equal access to health care for all worldwide and greater social justice by considering the needs of poor and vulnerable population groups within countries.

PATENT SYSTEM: A DEAD END FOR POOR PEOPLE'S DISEASES

Investing in new medical products is a huge financial undertaking and bears high risks of failure. One of the main arguments put forward by industry in favour of Intellectual Property Rights is the high cost of research and development for new medical products. According to an investigation undertaken by the Tufts Center for the Study of Drug Development, developing a new prescription medicine that gains marketing approval, a process often lasting longer than a decade, is estimated at USD 2.6 billion. However, these costs include failures and capital costs, and alternative calculations estimate research and development costs of around 40 to 50 million USD per new drug, i.e. around 60 times less than the Tufts Center estimates. In any case, what is clear is that the road from molecule to

market requires vast resources and expertise alongside the drug research and development process.

The justification for a time-limited monopoly granted to the developer is based on the assumption that without patent protection, an uncertain return on investment compromises innovation and, as a result, reduces benefits for patients and society as a whole. Patents as drivers for research and development investment simply do not work for poor people's diseases. Industry has no market incentive to invest in developing products targeting populations and governments with low purchasing power.

Switzerland recognises the importance and merit of the intellectual property regime and, in particular, the role of patents in stimulating research into and the development of new health products and medical devices. But – in the absence of a viable market, as is typically the case with neglected tropical diseases and the specific medical product needs of developing countries – Switzerland also believes it necessary to find financing mechanisms that complement the patent system. In this context, Switzerland promotes research and development for new, affordable medicines and diagnostics through public-private partnerships.

SWISS SUPPORT FOR THE PROCESS OF ESTABLISHING PRODUCT DEVELOPMENT PARTNERSHIPS (PDPs)

In the 1990s, it became increasingly clear that the public sector alone or publicly-driven collaborations with the private sector could not yield expected results. At the same time, private industry's growing tendency to close down their remaining tropical medicine programmes created a pressing need for alternative modalities. This was the birth of the 'era of partnerships' and the important involvement of philanthropic organisations. Drug development projects for diseases of the poor moved increasingly from the public domain to newly established public-private partnerships, which became known as product development partnerships (PDPs).

The Government of Switzerland has been prominent in supporting neglected diseases research and development in recent decades. When drug development projects were transferred from the public sector to the new PDPs the SDC was actively involved in their establishment. The new style of partnership dovetailed nicely 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 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.

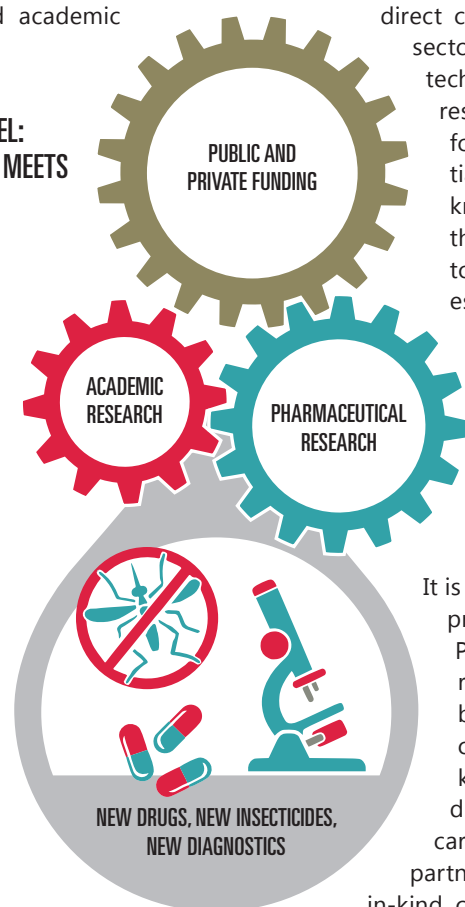
PDPs – A SUCCESSFUL COLLABORATION BETWEEN PUBLIC AND PRIVATE SECTORS

PDPs seek to coordinate the resources of the private, public, academic and philanthropic sectors to address the scientific, economic, legal and political challenges that exist in developing new health technologies for use in low- and middle-income countries, and in ensuring their rapid and widespread use. Importantly, PDPs provide the drive and scientific and technical leadership to promote research and development programmes through



the product development process. Most PDPs do not have their own laboratories, but channel funding through partners from the pharmaceutical industry and academic institutions.

THE PDP MODEL: WHEN PUBLIC MEETS PRIVATE



The PDP model works with the private sector because many of the starting compounds necessary for the research and development process are stored in large libraries owned by pharmaceutical companies. But the skills and resources that only private companies have amassed are also crucial. Having the public sector replicate the system would be totally inefficient and exceedingly costly. Thus matching public interests of promoting health research and development for diseases of the poor with private sector skills and knowledge is the PDPs model for effectively and efficiently using public and private philanthropic investments.

Over the past 15 years, PDPs have gained increasing relevance in accelerating research and development 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 pipeline¹.

¹ Ponder E. and Moree M. *Developing New Drugs & Vaccines for Neglected Diseases of the Poor: The Product Developer Landscape*. Bio Ventures for Global Health. 2012.

From a government's standpoint, contributing to PDPs' pooled funding approach is clearly an advantage over research and development by public institutions or direct collaboration with the private sector. PDPs have the scientific and technical know-how for stringent research and development portfolio management, with negotiated access to private sector know-how and facilities but at the same time are accountable to global public health interests. PDPs have an important role to play in overcoming bottlenecks at all stages in the product development process, not with a profit focus but with the aim to get products to those who need them.

It is difficult to assess the value of private sector contributions to PDPs. PDPs generally do not receive direct financial contributions from pharmaceutical companies, but receive in-kind contributions. MMV conducted an internal analysis and carried out a survey with project partners in order to estimate these in-kind contributions. The results of this assessment showed that for each dollar invested, MMV received on average an additional USD 2.5 from its pharma partners, including pharma matched funding and in-kind support.

CAN PDPs ENSURE ACCESS TO PRODUCTS?

Newly developed vaccines, drugs, diagnostics and insecticides will only be useful if they reach the patients who need them. In fact, ensuring access must be considered early on in product development, as early as clinical development phase II, when issues around regulatory affairs, manufacturing and financing need to be addressed. Most PDPs recognise access as an important aspect of research and development, and in recent years they have been developing effective access strategies. Experience is still scarce since the first products were launched relatively recently. Achievements include the supply of 250 million treatments of Coartem® Dispersible – the fixed-dose artemisinin-based dispersible combina-

tion therapy (ACT) tablet tailored for children, launched in 2009 and developed by Novartis and MMV - to 50 countries at a not-for-profit price. Another success is the DNDi developed and launched treatment for sleeping sickness (NECT), included on the WHO Essential Medicines List in 2009 and used in nearly all endemic countries as a first-line treatment for second-stage sleeping sickness. FIND has been involved in upgrading laboratory infrastructures, training laboratory and medical staff and implementing new tests to develop diagnostic capacity in 27 multi-drug resistant tuberculosis high-burden countries. PDPs are increasingly engaged in collecting market intelligence in order to better understand the target markets into which the products under development would be launched.

SWISS SUPPORT TO PRODUCT DEVELOPMENT PARTNERSHIPS (PDPs)

Besides MMV, the SDC has been supporting two other Geneva-based PDPs focusing on drug and diagnostic research and development for specific neglected diseases, the Drugs for Neglected Disease Initiative (DNDi) since 2003 and the Foundation for Innovative New Diagnostics (FIND) since 2013. In 2014, the UK-based Innovative Vector Control Consortium (IVCC), focusing on research and development efforts for insecticides was added to the SDC's portfolio. The short portraits of the four SDC-supported PDPs on page 5 provide further details on the main achievements.

A recent example for the SDC support is FIND and WHO partnering to develop an Ebola Diagnostics Access Collaboration. Against the backdrop of the acute emergency situation during the Ebola epidemic, early and rapid diagnosis is essential for controlling the spread of the disease. The SDC acknowledged that co-ordination was critical to accelerating the process along the entire value chain, from research and development to registration and implementation. The collaboration helped to guide the right investments and to deliver the right diagnostic tools to the right places.

PORTRAITS OF SWISS-SUPPORTED PDPs

The SDC supports four PDPs, tackling the need of new drugs, diagnostics, and insecticides for neglected diseases:

MEDICINES FOR MALARIA VENTURE (MMV):

Mission: MMV is dedicated to reducing the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective, and affordable antimalarial drugs.

Location: Geneva

Target disease: Malaria

Foundation: MMV is one of the first PDPs launched in 1999, with seed money from the Government of Switzerland, Department for International Development (UK), the Government of the Netherlands, The World Bank, and Rockefeller Foundation.

Financials: MMV expenditure 2014: USD 67.2 million, **Swiss contribution:** 2000-2016: CHF 17.8 million

Achievements: 5 new antimalarial drugs launched, 250 million Coartem® Dispersible treatments delivered to 50 malaria-endemic countries, 36 million vials of injectable artesunate delivered for treating severe malaria, 9 new medicines in clinical development. MMV launches the pathogen box for 400 diverse, drug-like molecules active against neglected diseases for early stage drug discovery.

Website: www.mmv.org

DRUGS FOR DISEASES INITIATIVE (DNDi):

Mission: DNDi is dedicated to developing new drugs, or new formulations of existing drugs, for patients suffering from the most neglected communicable diseases.

Location: Geneva, with regional offices in India, Kenya, Malaysia, Brazil, Japan

Target diseases: Sleeping sickness, visceral leishmaniasis (kala-azar), Chagas disease, paediatric HIV, specific helminth infections and Mycetoma. The malaria portfolio was recently transferred to MMV

Foundation: In 2003, seven organisations established DNDi: the Oswaldo Cruz Foundation from Brazil, the Indian Council for Medical Research, the Kenya Medical Research Institute, the Ministry of Health of Malaysia, France's Pasteur Institute, and Médecins sans Fron-

tières (MSF); with the UNICEF/UNDP/World Bank/WHO's Special Programme for Research and Training in Tropical Diseases (TDR) as permanent observer.

Financials: DNDi expenditure 2014: EUR 36.4 million, **Swiss contribution:** 2010-2016: CHF 12.9 million

Achievements: DNDi has launched one improved treatment for sleeping sickness, three for leishmaniasis, one for Chagas disease, and two new drugs for malaria. Eight treatments are in clinical development, including one for filariasis and two for paediatric HIV. DNDi has also launched the Neglected Tropical Disease Drug Discovery Booster experiment, a unique consortium with multiple partner pharmaceutical companies to search millions of unique compounds simultaneously, in the hunt for new treatment leads for leishmaniasis and Chagas disease.

Website: www.dndi.org

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND):

Mission: FIND is dedicated to turning complex diagnostic challenges into simple solutions to overcome diseases of poverty and transform lives.

Location: Geneva, with regional offices in India, Kenya, South Africa, Uganda, Vietnam

Target diseases: Tuberculosis (TB), acute febrile respiratory diseases, malaria, sleeping sickness, HIV, hepatitis C, Chagas disease, leishmaniasis, Buruli ulcer.

Foundation: FIND started with a grant from the Bill & Melinda Gates Foundation in 2003, initially focusing on TB. The scope later expanded to other diseases of poverty.

Financials: FIND's expenditures in 2014: USD 31.1 million

Swiss contribution: 2013-2016: CHF 3.2 million (plus CHF 1 million to WHO-FIND Ebola Collaboration)

Achievements: FIND has led the delivery of eleven tests, including 6 for TB which are estimated to save 300,000 lives per year. One of the TB test reduces time for detection of the disease from 120 days to 90 minutes. An improved blood transfer device that allows for safe collection and transfer of blood from a finger-prick for malaria rapid tests reached over 100 million patients in 2013. By building capacity in over 360 laboratories and testing sites in 39 countries, FIND is accelerating access to new tools and enabling speedy diag-

nosis of TB and its multidrug-resistant form. The first ever rapid diagnostic test for screening sleeping sickness, used in ten endemic countries in sub-Saharan Africa, supports efforts to eliminate the disease by 2020. FIND has partnered with WHO to rapid deployment of new Ebola diagnostic tools.

Website: www.finddiagnostics.org

INNOVATIVE VECTOR CONTROL CONSORTIUM (IVCC):

Mission: IVCC is dedicated to reducing the transmission of mosquito-borne pathogens through novel and improved insect vector control with innovative products. IVCC is the only product development partnership working in public health vector control.

Location: Headquarters in Liverpool, UK, but with employees in France and the US.

Target diseases: A strong emphasis on Malaria, but including insect vector borne diseases such as dengue, lymphatic filariasis, leishmaniasis, sleeping sickness, chagas disease and onchocerciasis.

Foundation: IVCC was established in 2005 with a grant from the Bill & Melinda Gates Foundation and was initially launched as a consortium hosted by the Liverpool School of Tropical Medicine. IVCC became an independent non-for-profit company and registered charity in November 2008.

Financials: IVCC expenditure 2014: USD 15 million, **Swiss contribution:** 2014-2017: CHF 3.2 million

Achievements: With its partners, IVCC has introduced a new long lasting insecticide formulation for indoor residual spraying (IRS), used in five countries and protecting over one million households. Additional high performance IRS products are in the pipeline. Two novel active ingredients entered the development phase in 2015, with a third in the development pipeline. Dual active ingredient bed nets to help manage insecticide resistance will be available in 2017. IVCC also supports field trial sites in Africa and an insecticide resistance testing facility in the UK.

Website: www.ivcc.com



THE FUTURE OF PDPs

Under the current constraints, PDPs remain crucial for developing new medical products for neglected diseases. But PDPs entirely depend on voluntary contributions from public and private donors, traditionally from OECD countries. It is problematic that many PDPs depend on a handful of donors, with a high level of dependence on philanthropic funding. The most critical challenge is financial sustainability. With new emerging diseases, potential expansion of tropical diseases and antimicrobial and insecticide resistances on the rise, health research and development needs are likely to substantially increase. The search for innovative new financing mechanisms is crucial.

PDPs have other disadvantages. While PDPs operate on a needs-driven basis, the selection of diseases is historical and know-how-driven rather than based on a global framework for priority-setting. In many cases, funding from public and philanthropic donors is earmarked for specific projects or programmes, further limiting the flexibility of PDPs in their priority-setting. Global critical voices increasingly demand a democratic, mul-

tilateral decision-making process for determining research and development priorities, provided they are evidence-based.

The different organisational cultures and backgrounds from which PDPs have emerged have led to a diversity of approaches and focuses. Although progress has been made in improving collaboration between PDPs, it is true that a certain level of competition remains. The current mushrooming of new funding initiatives adds to the complexity of PDP modalities. The diverse requests from different donors requires additional negotiations and reporting systems, further fragmenting approaches.

All these complexities and limitations do not call into question the work done by PDPs, but rather highlight the need for harmonisation and better orchestration of health research and development needs and responses. A global framework for research and development for and access to global health products for diseases disproportionately affecting people in low- and middle-income countries could enhance the efficiency and effectiveness of PDPs. The concept of delinking the costs of research and development from the price of health products, as proposed in the 2012 published Consultative Expert Working Group Report and later promoted by WHO in the follow-up process would be a powerful principle for enhancing the impact of funding.

The SDC considers PDPs to be an efficient and effective form of collaboration between the public and private sectors. It will continue to support PDPs that are actively engaged in research and development and access activities for neglected diseases, in line with the SDC global health strategic framework. In close collaboration with PDPs, the SDC is also deeply committed to advancing the global normative framework for research and development for and access to global health products for diseases disproportionately affecting people in low- and middle-income countries. Contributing to health research and development and access to products for reducing the burden of neglected diseases is a way of investing in global public goods and, ultimately, reducing poverty.



GLOBAL POLICY DISCUSSIONS TO OVERCOME MARKET FAILURE CONCERNING NEGLECTED DISEASES: SWITZERLAND'S POLITICAL ENGAGEMENT

How to overcome market failure for neglected diseases at a global level is an issue of lengthy policy discussions. Switzerland - with its broad global public health expertise and major pharmaceutical industry - has been actively engaged in negotiations to advance a global framework for research and development for and access to global health products for diseases disproportionately affecting people in low- and middle-income countries.

Global policy discussions on the market's failure to address neglected diseases have been ongoing since the late 1990s, triggered by legal action in South Africa. That country won its case against pharmaceutical companies, paving the way for parallel imports of AIDS medicines and bringing the inherent contradiction between patent protection and public health concerns to the forefront of public awareness.

The WHO Commission on Intellectual Property Rights, Innovation and Public Health - established in 2003, chaired by former Swiss President Ruth Dreifuss and financially supported by Switzerland - concluded in its report in 2006 that intellectual property rights are relevant incentives for developing new medical products. But they are an inefficient instrument when it comes to stimulating medical innovation in the absence of profitable markets. Subsequently, Switzerland was actively involved in negotiations that led to the adoption of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property by the WHO Member States at the World Health Assembly (WHA) in 2008.

In 2010, WHO established the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG), tasked with analyzing research and development gaps for medical products for diseases that disproportionately affect people in low- and middle-income countries. The CEWG recommended an international treaty that proposed mandatory financial contribution from WHO member states. This recommendation was not adopted by the World Health Assembly in 2012.



However, in recent years and despite a lengthy and difficult political process, substantial progress has been made towards a global framework for research and development financing and coordination for diseases that disproportionately affect the poor. WHO member states recently agreed to explore the establishment of a voluntary, sustainable research and development funding mechanism based on the principles put forward by the CEWG Report published in 2012. Most importantly, the funding mechanism is guided by the use of open knowledge innovation as well as by the concept of delinking - from the outset - the product delivery price from research and development costs, hence proposing alternative incentives to patent-driven research and development innovation. The idea is to build financial incentives into the research and development process itself so that developers do not have to be 'rewarded' through high prices later on.

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. In recent years, Switzerland has been actively involved in advancing the establishment of a fund hosted by the Special Programme for Re-

search and Training in Tropical Diseases (TDR). The SDC has granted a contribution to TDR for conceptualising and piloting this fund. In addition, as one of the first WHO member states, it has made substantial contributions to the demonstration projects currently selected for support through this voluntary funding mechanism. Moreover, Switzerland is also assisting WHO in promoting the voluntary funding mechanism by co-hosting stakeholder meetings. So far, Brazil, India and South Africa (i.e. three of the BRICS countries) as well as Norway have already contributed to the fund.

Product Development Partnerships (PDPs) - with their extensive experience in neglected diseases research and development and innovative financing - are informing a global framework by actively implementing projects based on 'open' innovation, and by delinking research and development 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 research and development and advancing the global policy discussion towards a global health research and development framework.

IMPRINT

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