



Funding neglected disease R&D

The next hurdle

An international campaign to enhance access to medicine in the developing world by discovering and developing new treatments for “neglected” diseases is beginning to pay off.

Almost a dozen products from different sources targeting afflictions ranging from malaria and sleeping sickness to cholera and Japanese encephalitis have reached the market in recent years. Moreover, several companies have more than 100 additional medicines, vaccines and diagnostics currently in preclinical development or undergoing clinical testing.

That burst of scientific productivity, however, has spurred new challenges. Sufficient funding isn’t currently available to sustain clinical development, win regulatory approval and bring those potential medicines and vaccines to patients.

Paul Herrling, Head of the Novartis Institutes for Developing World Medical Research, estimates that the neglected disease development portfolio has cost between USD 1 billion and USD 3 billion to date – but additional funding of at least USD 1 billion per year will be needed over the next decade for successful compounds and vaccines to be registered. The Global Plan to Stop Tuberculosis estimates that USD 9 billion is needed between 2006 and 2015 for research and development. Moreover, at least USD 750 million is needed every year through 2018 for development of new tools against malaria, according to the Global Malaria Action Plan.¹

“The most urgent and immediate priority is to make sure that this nascent, growing pipeline doesn’t stall because the largest part of funding is yet to come,” Dr. Herrling said. In addition to financial pressures, development teams must surmount formidable scientific, medical and technological hurdles in making medicines for the developing world. “The challenges are in no way easier than for medicines used in wealthy developed countries. In some ways they are even more difficult because of what medicines earmarked for developing countries must look like in terms of affordability, stability and so on,” he added.

Extending scientific advances to developing countries

The vision of a global research effort to tackle some of the world’s most neglected diseases dates from the early 1970s.² As researchers in biomedical science made giant leaps forward in genetics, molecular biology and other cutting-edge technologies and life

expectancy improved dramatically in industrialized nations, attention turned to the plight of those in the less-developed world where infectious diseases continued to cause suffering and death, slowing socio-economic development.

The adoption of the “[Millennium Declaration](#)” by 189 countries and subsequent mobilization of development agencies around the Millennium Development goals renewed focus on the resources required to advance healthcare in general, and research and development in particular. Public sources of funding are not adequate and it has become increasingly clear that the gap must be bridged from other sources.

Novartis has been in the front ranks of neglected disease research and development for decades – initially with programs against leprosy and development of the pioneering antimalarial drug *Coartem*. More recently, Novartis established research institutes in Singapore and Italy, focused on medicines and vaccines, respectively, which would be provided to patients in developing countries at affordable prices.

A vaccine against *Salmonella typhi*, the bacterium that causes typhoid fever, has begun clinical testing at the **Novartis Vaccines Institute for Global Health** (NVGH). A novel treatment for malaria discovered at the **Novartis Institute for Tropical Diseases** (NITD) could enter formal development later this year if ongoing toxicology studies are completed successfully.

Novartis isn’t alone in creating nonprofit research institutes: both GlaxoSmithKline and Eli Lilly & Co have similar operations. “But we need more pharmaceutical and biotechnology companies to do the same,” Dr. Herrling added.

Funding pool

Advancement of these initial neglected disease projects by Novartis has increased the urgency of securing funding for clinical development. Over the past three years, Dr. Herrling has been the driving force in design of a new financing mechanism – The Fund for R&D in Neglected Diseases, or FRIND – to support development of medicines and vaccines against neglected diseases. Funding would come primarily from a pool fed by donors ranging from industry and non-governmental organizations to private charities as well as governments, which increasingly are rechanneling existing funds already reserved for developing countries into research and development.

The **FRIND model** would apply principles of portfolio management refined by major pharmaceutical companies to the neglected disease portfolio. “It is crucial to allocate the money that is available to the most promising projects,” Dr. Herrling said. “In drug development, there are always more failures than successes and the largest single cost in developing a pipeline is the money invested in projects that never reach the market.”³

Another core principle of industrial portfolio management is to allocate funding on a stage-by-stage basis, rather than as a lump sum. When an experimental medicine or compound passes one of six key decision points during development, sufficient funds are released to pay for activities needed to reach the next decision point.

Importantly, the FRIND mechanism would function within the framework of the existing intellectual property system. Companies, academic groups or other applicants for funding would allocate to the fund exclusive licenses for the specific indication linked to a neglected disease. Intellectual property covering other indications with commercial potential would not be affected.

“In some cases, innovation consists of simply having a drug where there was none before. But we also need to get safer drugs in areas where existing treatments have serious side effects, or to replace drugs that have become ineffective because of resistance,” Dr. Herrling said. “What we are trying to do here is get this great pipeline to patients. The model is based on mechanisms that pharmaceutical companies have found to be successful in the past in other contexts – minus the profit.”

Exploring innovative financial models

Earlier this year, the FRIND proposal received a crucial endorsement from an Expert Working Group established by the [World Health Organization](#) to explore innovative models to finance neglected disease research and development. In its report to WHO Director-General Margaret Chan, the Expert Working Group acknowledged a persistent and growing concern that the benefits of advances in health technology are not reaching the poor who bear a double burden of poverty and disease. “There is a need for incentive structures to stimulate research and development when there is no market, or there is market failure in the production and diffusion of knowledge,” the group added.

A key factor in the WHO’s positive assessment is that the FRIND model builds on the foundation of so-called **Product Development Partnerships**, widely viewed as donors’ vehicle of choice to disburse neglected-disease funding. Product Development Partnerships are quasi venture capital funds that operate on a not-for-profit basis in the domain of developing world health. They raise funds from a wide range of public, private and philanthropic sources and usually play a central role in developing and managing a product portfolio in a given disease area.

Novartis works closely with some of the biggest Product Development partnerships including [Medicines for Malaria Venture](#) (MMV), the Global Alliance for TB development, Drugs for Neglected diseases Initiative and Institute for One World Health. Novartis and MMV, a nonprofit foundation based in Switzerland, jointly developed Coartem Dispersible, a new pediatric formulation of the pioneering antimalarial therapy Coartem, and are collaborating on development of other potential treatments against malaria.

“Product Development Partnerships are one of the business models that emerged from market failure in terms of producing new drugs and vaccines for diseases such as TB,” said Antony Mbewu, Executive Director of the Global Forum for Health Research. Today, Product Development Partnerships manage roughly 20% of funding for neglected disease research worldwide.

One flaw in the current Product Development Partnership model is the lack of a reliable, long-term revenue stream. “Most product development for the developing

world is underfunded and relies on short-term grants – very hand to mouth,” said Mary Moran, Director of Health Policy at the George Institute, a healthcare think tank based in Sydney, Australia. “Running a 10- to 15-year development program when you are funded year to year is a hopeless way to make products. A number of groups have been set up to examine how to do this better.”

Assisting donors

In addition to FRIND, the WHO’s Expert Working Group recommended further analysis of several proposed funding models. Product Development Partnerships were the focus of proposals from two other groups: the Product Development Partnership Financing Facility (PDPFF) and the Industry Research and Development Facilitation Fund (IRFF).

PDPFF is a proposal developed by the International AIDS Vaccine Initiative, the Aeras Global TB Foundation and the PATH Malaria Vaccine Initiative that proposes raising funds by selling bonds in private capital markets to support development of vaccines. Bond holders would be repaid from royalties on sales of the vaccines in high-and middle-income countries as well as donor-funded premiums on distribution of vaccines in developing countries. Borrowing by the fund would be backed with guarantees from governments and possibly donor foundations. IRFF is a funding vehicle designed to continuously reimburse a large proportion of money distributed through Product Development Partnerships. Most funding would go to product development partnerships that advanced their portfolios most efficiently.

The report of the WHO’s Expert Working Group observed that Product Development Partnerships provide “optimal funding allocation at all stages of research and development” and high health impact in developing countries, as well as operational efficiency. “However, a mechanism is needed to assist donors to fund across product development partnerships, in a simpler manner than is currently possible,” the Working Group added, and raised the possibility of combining the three proposals to provide reliable, long-term funding to accelerate global health R&D.

Defining core principles

In early April 2010, Dr. Herrling met with representatives of PDPFF and IRFF to explore possibilities of consolidating the best elements of each individual proposal within a single, joint mechanism to fund Product Development Partnerships. By mid-May, the talks had produced a preliminary agreement; core principles of the Product Development Partnership Plus (PDP-Plus) Fund were outlined for stakeholders during the WHO’s annual meeting in Geneva, Switzerland.

“There is no point in each of our three organizations pursuing this on its own,” Dr. Moran of the George Institute said. “This is a proposal that looks at existing Product Development Partnerships that are underfunded and have products about to fall off the cliff for want of the dollar. We need a mechanism that provides not only long-term funding but a lot more money than we had before – in a super risk-averse environment. So we need to reduce risk by pooling and address other

needs of organizations and governments that don't currently donate to neglected disease R&D.”

Many details – including diseases products and stages of R&D to be covered by the Fund – are yet to be finalized. While the PDP-Plus Fund would offer donors a single point of contact with Product Development Partnerships, portfolio management and resource allocation options remain under discussion.

The next step in evolution of the PDP-Plus Fund will be further consultations with stakeholders. “Clearly, we need to continue discussions with donors, representatives of Product Development Partnerships and other stakeholders in the global health and R&D worlds,” said Holly Wong, Vice President, Public Policy at the International AIDS Vaccine Initiative. “We have to figure out what our priorities and what trade-offs among our proposals might be possible. After getting these projects this far, it would be a tragedy for all of us if nothing more can be done to get these treatments to the patients who need them most.”

¹ Moran, M. et al, (2009), *Neglected Disease Research & Development: New Times, New Trends*, The George Institute for International Health, p. 75

² World Health Organization, (2007), *Making a Difference – 30 years of Research and Capacity Building in Tropical Diseases*, WHO, Geneva, (Introduction)

³ *Nature Reviews, Drug Discovery*, Volume 8, February 2009