
# The changing landscape of medical innovation: How have business models responded?

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## 1 minute read: key messages

- New economic challenges and unmet needs linked to the innovation and diffusion of technologies in medical research have encouraged new collaborative business models
- A range of incentives, both financial and non-financial, exist to stimulate innovation along the R&D pipeline
- New public- private partnership models are emerging to foster medical R&D and to facilitate access to medicines
- Public-private partnerships and product development partnerships can leverage the comparative advantages of partners to stimulate and finance medical innovation where gaps exist.

## A Global Challenge

The landscape for medical innovation has changed significantly in recent years as a result of new industry structures, emerging markets, changes in the global disease burden and increasingly complex market requirements. These changes have prompted the emergence of innovative models of medical research and development (R&D) and new ways of disseminating medical technologies. However, a distinctive feature of today's medical R&D landscape is greater collaboration between the public and private sectors.

Improving public health is a global issue that is near the top of the international policy agenda. The World Health Organization (WHO), the World Intellectual Property Organization (WIPO) and the World Trade Organization (WTO) have strengthened interagency collaboration to support policy-makers in this area. This has resulted in a series of technical symposia designed to promote the exchange of ideas and experiences in relation to various health-related topics. The third joint Symposium hosted by WIPO in 2013 focused on new innovation models for medical R&D.[1] The following addresses a number of the key issues arising from the discussions.

## Incentivizing Innovation

Both financial and nonfinancial incentives can be used to stimulate medical R&D in areas that are generally less attractive to commercial investors, for example Neglected Tropical Diseases (NTDs).

Nonfinancial incentives indirectly encourage innovation at various stages of product development, production and delivery. They typically identify and address specific obstacles to research, product development and market access. For example, open research databases host a wealth of information and can assist in the early stages of drug discovery, for example India's Open Source Drug Discovery (OSDD) project (www.osdd.net). A different example is the US Food and Drug Administration's priority review voucher, which encourages R&D into orphan and NTDs by reducing the time required for regulatory approval.[2] Such vouchers can be used for different drugs, are tradable and frequently attract values in excess

of US$100 million. As a significant proportion of the twenty year period of protection conferred by a patent can be eaten up by pre-market approval processes, such schemes can make orphan drug development a more financially viable option.

Financial incentives encourage innovation by offering direct financial rewards to the inventor. Such so-called "pull mechanisms" typically offer rewards for the final R&D outcome. Examples include milestone payments or end prizes, advance market or purchase commitments (AMCs or APCs), and patent buyouts. Large donors such as the Global Fund for AIDS, Tuberculosis and Malaria act as a "pull" mechanism by providing certainty to innovators that there will be a final market for their product.

"Push mechanisms", on the other hand, aim to stimulate innovation by providing upfront financing. Examples include grants and tax credits. The Innovation Fund, which arose from the collaboration between the International AIDS Vaccine Initiative (IAVI) and the Bill & Melinda Gates Foundation, is one example of a push mechanism that is discussed in more detail overleaf (see Box).

## Cooperative Innovation Models

Until recently, most pharmaceutical innovation took place in-house. Changes in the commercial, political and scientific environments, however, have led R&D entities to explore new forms of collaboration across the private and public sectors, making it possible to access new skills, sources of finance, specialized R&D infrastructure, and product pipelines. Such public-private partnerships (PPPs), or product development partnerships (PDPs), for example the Drugs for Neglected Diseases initiative (DNDi), the International AIDS Vaccine Initiative (IAVI) and the Medicines for Malaria Venture (MMV) are demonstrating that complementary partnerships can significantly boost innovation (see Box). PDPs typically use public or philanthropic funds to undertake research and development work that might otherwise be impossible due to a lack of market incentives. PDPs usually lack the infrastructure to undertake research in-house, so instead leverage the capacities of partners to move promising targets along the R&D pipeline. In this way, PDPs act as important facilitators in the quest to develop new vaccines, drugs and diagnostics for diseases disproportionately affecting the developing world.

## AMCs as Effective Financial Incentives

Advance Market Commitments (AMCs) guarantee a market for a drug if a successful product is developed. A procuring entity (usually a government or other funding organization) agrees on a specific supply contract with a prospective producer and guarantees the purchase of a certain quantity and price. This mechanism encourages innovation and investments in areas where there are no viable markets.

The Global Alliance for Vaccines and Immunization (GAVI) demonstrated the effectiveness of AMCs in facilitating access to new medicines when it oversaw the speedy introduction of innovative pneumococcal vaccines in low-income countries (LICs). Traditionally, new vaccines would not reach LICs until 10-15 years after their entry in industrialized countries. However, the pneumococcal AMC enabled children in over 25 GAVI-eligible countries to be immunized and protected against pneumonia within a few years (following regulatory approval in recipient countries) of the vaccine's introduction in developed countries.

GAVI, through negotiation and effective supply-chain management, obtains medicines at steeply discounted prices for specific diseases in specific geographical areas. The financial incentives it employs have helped increase the number of drugs for neglected diseases in the R&D pipeline. This has fostered the development of a market for vaccines in many developing countries. At the same time, GAVI is ensuring that the contributions of donors reach as many as possible through the guarantee of lower vaccine price from producers. The push and pull mechanisms it employs sustain the type of competition needed to drive prices lower, sustain supply and expand innovation.

## Catalyzing R&D Partnerships

Whereas larger PDPs have relatively easy access to private-sector partners, there is a plethora of less well-connected research organizations interested in licensing intellectual property (IP), and gaining access to compounds for further development unpublished scientific information, regulatory documentation and other forms of know-how. *WIPO Re:Search* (www.wipoReSearch.org) offers these organizations a solution. Launched in October 2011, *WIPO Re:Search* is an open innovation consortium that brings together a range of public and private entities from academia, industry, non-governmental organizations (NGOs) and PDPs. Members of the consortium agree to share their IP and expertise with others in the research community. They make their IP assets available on a royalty-free basis to researchers of NTDs, malaria and tuberculosis. Members also agree that any products arising from the research collaborations facilitated by *WIPO Re:Search* are to be sold royalty-free in all least developed countries (LDCs).

The *WIPO Re:Search* platform comprises a database of available IP assets to enable researchers to identify licensable compounds, enabling technology, know-how, information on hits, leads, drug candidates, and other forms of IP. It also features a Partnership Hub, administered by BIO Ventures for Global Health (BVGH) which connects members in line with their research needs. For example, Merck & Co., Inc. is sharing its expertise in purifying membrane-bound proteins with researchers at Emory University working on new treatments for tuberculosis.

## Experiences Shared from the Field

The **Drugs for Neglected Diseases initiative (DNDi** – www.dndi.org) is a collaborative non-profit R&D organization that works on the development of treatments for neglected diseases. The organization seeks to bridge existing R&D gaps through alternative development models and aims to provide equitable access to new medicines. DNDi's activities cover all stages of the pipeline via R&D networks built around South-South and North-South collaborations. This model aims to maximize the resources and efforts of each entity.

DNDi's collaborative approach is proving fruitful. DNDi's partnership with Sanofi, for example, has led to the development of the innovative anti-malarial fixed-dose combination (FDC) pill, ASAQ Winthrop. This drug enables better treatment adherence and reduces the risk of drug resistance. To date, over 200 million treatments have been distributed in 33 countries. In 2011, the drug was included to the WHO Essential Medicines List and boasts the longest shelf-life (3 years) of any pre-qualified FDC artemisinin-based treatment for malaria. The technology to produce the treatment has since been transferred to the United Republic of Tanzania to increase output and distribution.

The **International AIDS Vaccine Initiative** (**IAVI** – www.iavi.org), contributes to the early stage design and development of AIDS vaccine candidates. It seeks to accelerate the development of safe, effective, and accessible vaccines to prevent the spread of HIV/AIDS in developing countries. IAVI's approach to product development partnerships has enabled it to close gaps at different stages of the R&D process, from applied research to advanced clinical trials of vaccine candidates. Strong in-country partnerships have helped IAVI build a network of clinical research centers and laboratories to enable testing of vaccine candidates and ensure they are adapted to the locations in which they will ultimately be used.

Collaboration between the Bill & Melinda Gates Foundation and IAVI created the Innovation Fund in 2008 to support early-stage technologies with the potential to advance AIDS vaccine development. The Fund has enabled the testing of short-term, high risk, proof-of-concept innovations and has expanded the AIDS vaccine pipeline by encouraging experimentation with new ideas. In some cases, it has enabled start-ups to gain critical financial backing and leveraged PDPs to introduce new innovations to the market. The Fund's partnership with Theraclone Sciences led to the isolation of over 20 new broadly neutralizing antibodies for HIV, and facilitated the formation of joint ventures with Pfizer and Japanese pharmaceutical company Zenyaku Kogyo.

The **Medicines for Malaria Venture** (**MMV** – www.mmv.org) is a not-for-profit PDP targeting more effective treatments for malaria. Through its collaboration with industry and academia, MMV has helped bridge an important R&D gap in the development and delivery of new, effective and affordable anti-malarial drugs. In 2009, in collaboration with Novartis, MMV commercialized Coartem® Dispersible, introducing it into Africa. The drug is the first artemisinin-based combination therapy for children (with a cure rate of 97% for uncomplicated childhood malaria). In 2011, an alliance between MMV, Sigma-Tau Industrie Farmaceutiche Riunite SpA and others led to the development of "Eurartesim", a fixed-dose combination treatment for uncomplicated malaria. The drug is easy to administer and protects patients from repeat malarial infection. The drug is of particular relevance in countries with high rates of drug resistance.

One of *WIPO Re:Search*'s objectives is to repurpose data. As it sits at the center of an expanding network of public and private sector research institutions, WIPO Re:Search is well placed to identify complementary and collaborative research opportunities. For example, thanks to *WIPO Re:Search*, researchers at the National Institute of Immunology (NII) in New Delhi, India, were able to obtain kinase inhibitors from GlaxoSmithKline (GSK) to advance their studies into the molecular signaling pathways of malaria parasites. To date, BVGH has facilitated over 60 collaborations. The first such collaboration linked up the Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR) in Ghana with Stanford University to develop and test a diagnostic tool for helminthes parasitic worms. An agreement between GSK and the Center for World Health and Medicine (CWHM) which involved the sharing of information and data on the development of MetAp-1 inhibitors for tuberculosis saved CWHM around US$50,000 and three months of employee time.

## Key Implications & Considerations for Policy & Policymakers

The following implications and considerations for policy and policymakers are intended as starting points for reflection, to be adapted to specific needs and circumstances.

1. Cooperation and partnerships underpinned by creative thinking and pragmatism help foster innovation and improve access to medicines for poorer populations.
2. Results-oriented government policies, such as priority review vouchers, can serve as strong incentives for industry to address unmet health needs.
3. Product development partnerships leverage the specific strengths of each partner and can be effective in stimulating and financing new medical innovation.
4. Open innovation consortiums such as *WIPO Re:Search* can complement traditional PDPs by allowing smaller research institutions to partner and share IP with larger organizations.
5. Both financial and nonfinancial incentives play a critical role in supporting R&D investment in fields that are not commercially attractive. Government policies, such as fiscal and IP policies, can have a positive impact on medical innovation.
6. Achieving the right policy mix is essential. Considerations for policymakers include:
   - How to identify specific R&D needs and how can government address these needs?
   - What are the most effective ways to support public-private research collaborations?
   - How is success measured?

## New Models, New Directions in Innovation

In meeting global public health goals, the challenges are to develop collaborative models that stimulate research and innovation while also ensuring that the resulting products are accessible to those that need them. Collaborative R&D models combined with appropriate funding mechanisms and effective policy frameworks are helping meet these challenges. Connecting with complementary actors is critical to the success of new models of medical research and drug development and delivery. Such partnerships are proving to be an effective means of catalyzing and accelerating R&D into NTDs, malaria and TB. We need to build on these successes if we are to succeed in effectively tackling the major health challenges of the 21st century.

## Further Reading


World Economic Forum, 2013. *Global Agenda Council on Genetics: Intellectual Property Law, Genetics and Ethics: Facts, Challenges and Opportunities.* Available at: ow.ly/wP22l

*WIPO Re:Search*, 2014. *Collaboration Agreements.* Available at: ow.ly/upHQb

International Policy Network, 2005. *Incentivising research and development for the diseases of poverty.* Available at: ow.ly/upHSX


References


1 "*Medical Innovation – Changing Business Models*". A WHO-WIPO-WTO Symposium held at WIPO headquarters, Geneva, July 5, 2013. Presentations from the symposium are available at ow.ly/wMWWk

2 "*Priority Review to Encourage Treatments for Tropical Diseases,*" Title 21, U.S. Code, Pts. 360n, 2007 ed. Available at: ow.ly/wP2iN



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