Assembling the pharmaceutical R&D puzzle for needs in the developing world – Excerpt

An assessment of new and proposed delinking initiatives aimed at encouraging R&D into neglected and tropical diseases and specific Type II diseases

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Introduction & background

This report was commissioned by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

The report examines and evaluates the opportunities and challenges associated with existing and proposed initiatives aimed at stimulating research and development (R&D) of drugs and other treatments targeting neglected and tropical diseases (NTDs) and specific Type II diseases.[1]

The concept of delinking, which is described in detail in this report, refers to all efforts which seek to mitigate the risk and cost associated with developing new drugs and treatments aimed at these diseases, while at the same time ensuring that populations which need these treatments the most are able to access them.

This report notes that the existing biopharmaceutical R&D model is undergoing a process of evolution to fit new conditions, demands and capabilities – economic, social, scientific and structural. Still, even in light of these changes, the underlying principles behind the biopharmaceutical R&D model remain sound. These elements include: robust scientific and technological life science capabilities and infrastructure, facilitative regulatory and clinical environments, effective exclusivity periods derived from intellectual property rights (IPRs) and market incentives for the launch of both innovative and generic products.

Nevertheless, there are several systemic gaps in the R&D model for NTDs and specific Type II diseases that should be further addressed in order to create an effective forward pathway. They include: insufficient dedication to basic research efforts aimed at these diseases; inadequate financial and commercial incentives for further investment in these diseases during the applied research and development stages; and the possibility that even if developed, these drugs may still be too costly for populations in developing countries.

In order to promote R&D into NTDs and specific Type II diseases, various push and pull mechanisms which delink the cost of R&D from the price of medicines have been developed and proposed. These models operate at different points in the pharmaceutical innovation process, including at the stages of research & discovery, preclinical & clinical research and development, and postmarketing & delivery. The report provides an overview of the following key delinking models:[2]

[1] See the Appendix for a full definition of the diseases which are collectively referred to "Type II and III diseases" throughout the report.
[2] See the Appendix for a sample of empirical evidence provided in the full report on these models.

- **Open databases or compound libraries** – Provision of access to proprietary databases of technologies and know-how to other R&D actors in order to facilitate drug discovery
- **R&D grants** – Additional funding in advance of R&D aimed at specific research outcomes
- **R&D prizes** – Payments to R&D entities in lieu of sales; conditional on achieving a particular outcome
- **Targeted R&D tax credits** – A direct contribution to research entities in order to promote R&D in specific research areas by increasing returns to R&D in these areas
- **Orphan drug-like schemes** – A combination of additional market exclusivity, tax credits, accelerated market authorisation and other funding support to incentivise product development and marketing
- **Patent pools** – Platforms for the cross-licensing of intellectual property for use in R&D
- **Product development partnerships** – Public private partnerships involving a combination of grant funding and R&D partnerships focused on product development
- **Advanced market commitments** – Agreements to develop and supply a product in exchange for a temporary purchase guarantee
- **R&D treaty** – International agreement to increase funding commitments targeted towards open innovation and delinking mechanisms for R&D into NTDs and specific Type II diseases

Analysis

The report sets out a new model for measuring and assessing these mechanisms. It should be noted that since many of these mechanisms are in the early development stages and that the biopharmaceutical R&D process is long-term in nature, it is difficult to fully assess their effectiveness and what we can expect them to achieve. More time and further development of the mechanisms is necessary for a clear picture of the most effective manner for incentivising the needed levels of research and development of affordable treatments.

Still, it is nonetheless important to be able to concretely assess these and other mechanisms as much as possible. This paper provides a set of factors for success, against which the wide range of push and pull mechanisms under discussion in international fora may be benchmarked. The criteria proposed here represent a concise and measureable framework for evaluating whether a delinking model can be expected to be effective or not. They capture the topline elements that should be present in such mechanisms, including a concrete objective, targeted problem or problems within the R&D process (including access to new medicines), effectiveness and sustainability. The first five success factors relate to the three pillar cycle of research, development and access discussed in Section 4. The final criterion, which is independent of the above factors, provides an assessment of the extent to which different mechanisms can function together and be integrated successfully.

The following table provides a proposed blueprint of these success factors and their key components.

Blueprint for Success – A model for evaluating mechanisms incentivising R&D into NTDs and specific Type II diseases

Success factors	Key components
Accurate identification and definition of systemic gaps in the R&D process	Relevant gaps include: • Scientific gaps (a given stage or stages of R&D, including basic research, compound discovery, preclinical research and translational and clinical development) • Financial gaps (ability and willingness of actors at different stages in the R&D process to invest in R&D activities) • Logistical gaps (manufacturing, availability and distribution of new products)
Mitigation of cost and risk of relevant R&D	• Accurately identifies incentives of various R&D actors (based on the type of R&D inputs provided and the environment in which each operates) • Creates and targets rewards accordingly
Leveraging of capabilities of partners to translate research into clinical outcomes	Successfully leads to creation of an end-product, milestone in the R&D process, or supporting technology
Sustainability of R&D funding for specific disease areas	Enjoys sustained funding over the long-term for achieving R&D commitments
Effective access to end product	Including through: • Affordable prices • Necessary administrative and logistical arrangements for delivery • Coordination with local health care authorities to develop regime for patient compliance and disease prevention
Compatibility with other mechanisms	• Able to function in tandem with other push and pull mechanisms targeting different aspects of the R&D process • Does not erode the effectiveness of these other mechanisms

Source: Pugatch Consilium (2012)

Findings

Based on these factors, it is possible to assess the potential for success among the delinking mechanisms analysed in this report. What follows is an assessment of each mechanism using the six success factors, as well a brief explanation for each category. It is worth noting that there are several cases in which a mechanism partially meets or fails to meet a given success factor.

Open databases

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; open databases target scientific gaps, including basic research and preclinical and translational R&D, as well as associated financial gaps.
- **Mitigation of cost and risk of relevant R&D:** Yes; open databases reduce the cost of discovering essential compounds and technologies.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Yes, although open databases are still in the early stages; thus far, there has been some success in increasing research collaboration that may lead to translation of research into clinical outcomes.
- **Sustainability of R&D funding for specific disease areas:** Not applicable; funding is not an essential component of the success open databases.
- **Effective access to end product:** Yes; licenses involving R&D or product supply to least developed countries must take place on a royalty-free basis.
- **Compatibility with other mechanisms:** Yes; open databases complement other mechanisms targeting the research stage, as well as the development and access stages.

R&D grants

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; R&D grants fill various scientific gaps, including basic research (for example, NIH grants for university research) and clinical development (for example, from government development agencies and philanthropic foundations) by providing the financial capability to conduct these types of R&D.
- **Mitigation of cost and risk of relevant R&D:** Yes; R&D grants mitigate the cost and risk of conducting R&D at a given stage. However, there are important exceptions; additional funding support may be necessary to fully fund certain R&D activities, particularly clinical development, manufacturing and market authorisation.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Yes; R&D grants have been one of the most successful models for basic R&D activities, and are the predominant funding model used by successful PDPs.
- **Sustainability of R&D funding for specific disease areas:** No; the frequency and amount of R&D grants depend on the financial capability and political will of public and philanthropic donors.

- **Effective access to end product:** No, although there are important exceptions. For grants aimed at product development, many donors require the affordable delivery of such products to low and middle income countries; however, such a requirement is not explicitly part of the grant model.
- **Compatibility with other mechanisms:** Generally, yes; however, there are important exceptions, including grants with conditions on the delivery of end products which may not be compatible with certain mechanisms aimed at access, such as AMCs and manufacturer pricing programmes.

R&D prizes

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; R&D prizes target various scientific gaps, including basic research and the development of preclinical compounds, which exist due to gaps in financial support for these types of R&D.
- **Mitigation of cost and risk of relevant R&D:** Overall, no; this is because for the majority of the prize models aimed at Type II and III diseases, proposed or in existence, financial support is only afforded to 'winners'; those who are not awarded are not afforded any mitigation of the costs of R&D, and therefore bear all of the risk of engaging in that R&D. In addition, the amount awarded through a prize is not necessarily sufficient to cover all of the R&D costs.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Generally no; at this point, there have been very few tangible outcomes aimed at Type II and III diseases.
- **Sustainability of R&D funding for specific disease areas:** No; as with grants, the frequency and amount of R&D prizes depend on the financial ability and political will of public, philanthropic and private donors.
- **Effective access to end product:** Generally speaking, no; thus far, the prize model has only led to milestones in the R&D process or supporting technologies. Prize models aimed at the development of end-products are expected to involve commitments to delivering an affordable product to low and middle income countries, however no such prize is in use at this time.
- **Compatibility with other mechanisms:** Generally, no. Prizes entail the possibility of operating in tandem with other mechanisms aimed at the research and development stages, but whether they actually do or not depends on implementation (which is so far limited). However, prizes which fully separate the price of products from the cost of R&D may erode mechanisms aimed at access, such as AMCs and manufacturer pricing programmes.

R&D tax credits

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; R&D tax credits target general financial incentives to invest in any stage of the R&D process.
- **Mitigation of cost and risk of relevant R&D:** Generally speaking, no; tax credits are only available to profit-making entities, and are predicated on the existence of a large paying market, which for the most part does not exist for R&D into Type II and III diseases.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Overall, no; tax credits for R&D into Type II and III diseases have only had a limited application so far, and where they have been introduced, such as in the UK, they have not been shown to be successful. A programme in the US is in the initial stages; therefore it is difficult to judge its success at this time.
- **Sustainability of R&D funding for specific disease areas:** No; the availability of public funding for tax credits depends on political will and the government budget.
- **Effective access to end product:** Not applicable; R&D tax credits specific to Type II and III diseases are thus far not linked to the delivery of the medicines to low and middle income countries.
- **Compatibility with other mechanisms:** Yes; R&D tax credits have the ability to complement other mechanisms targeting the research stage, as well as the development and access stages.

Orphan drug-like schemes (including additional exclusivity and priority review vouchers)

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; orphan drug-like schemes target general financial incentives to conduct R&D at any stage of the process. They also reduce the burden of market authorisation and preparing the approval dossier, and as such partially fill gaps in the clinical development stage.
- **Mitigation of cost and risk of relevant R&D:** Generally speaking, no. This is because orphan drug-like schemes only target profit-making entities, and the headline component of such schemes, additional exclusivity, is predicated on the existence of a large paying market, which for the most part does not exist for R&D into Type II and III diseases.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Not applicable; although such schemes have largely been successful in producing medicines and R&D into rare diseases, at this point their usefulness in stimulating R&D into Type II and III diseases is unproven.
- **Sustainability of R&D funding for specific disease areas:** Yes; this is because generally speaking no additional funding is required to operate such schemes.
- **Effective access to end product:** No; thus far, no such schemes are in existence.

- **Compatibility with other mechanisms:** Yes; orphan drug-like schemes would be able to complement other mechanisms targeting the research and development stages, as well as those aimed at access.

Patent pools

- **Accurate identification and definition of systemic gaps in the R&D process:** Generally speaking, no. Patent pools are aimed at the sharing and licensing of essential patents; however, there do not seem to be a great deal of demand for such patents, at least at this point in time. Nevertheless, there may be important exceptions, including for incremental modifications to existing products as well as in the field of vaccines, although there areas are relatively untested.
- **Mitigation of cost and risk of relevant R&D:** Overall, no. So far, patent pools only serve to mitigate the cost of manufacturing generic drugs. However, if there were to be demand for essential patents, patent pools would reduce the cost of drug discovery and translation to an actual product.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Thus far, no. Patent pools are still in the very early stages; however thus far, they have not produced any tangible clinical outcomes with regards to new or improved products treating Type II and III diseases.
- **Sustainability of R&D funding for specific disease areas:** Not applicable; funding is not an essential component for the success of patent pools.
- **Effective access to end product:** Not applicable; at this point, there is no evidence to suggest that collaboration in the scope of patent pools involves special arrangements for pricing and delivery of end products resulting from the pool.
- **Compatibility with other mechanisms:** No, not in their current use to promote the manufacturing of generic drugs, since this overrides the development stage and hence, also overrides other mechanisms aimed at development as well as those supporting access.

Product development partnerships (PDPs)

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; PDPs fill various scientific gaps, particularly translation of research into actual products and their clinical development, by providing the financial capability and collaboration to carry out these types of R&D.
- **Mitigation of cost and risk of relevant R&D:** Yes; PDPs mitigate the cost and risk of product development. However, there are also important exceptions; as with grants, additional funding and other types of support may be necessary to fully fund clinical development, manufacturing and market authorisation.
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Yes; PDPs have been very successful in the last ten years in leading clinical

development, and in many cases production and delivery, of new products targeting Type II and III diseases.

- **Sustainability of R&D funding for specific disease areas:** No. This is because most PDPs rely heavily on grants from public and philanthropic donors, as well as on contributions by industry, all of which are affected by financial capabilities and political will (to varying degrees). The most recent data shows that funding to PDPs is somewhat volatile, particularly from government development agencies and philanthropic donors such as the Gates Foundation.
- **Effective access to end product:** Yes; PDPs generally involve affordable pricing of end products as well as delivery arrangements.
- **Compatibility with other mechanisms:** Generally, yes; however, there are important exceptions, including PDPs or funding with conditions on the delivery of end products which may not be compatible with certain mechanisms aimed at access, such as AMCs.

Advanced market commitments (AMCs)

- **Accurate identification and definition of systemic gaps in the R&D process:** Yes; AMCs target the financial incentives of R&D entities, mainly biopharmaceutical companies, to fully develop, manufacture, market and deliver a new product to low and middle income countries.
- **Mitigation of cost and risk of relevant R&D:** Yes; although they have had limited application thus far, they have been successful in replicating market incentives (i.e. providing a profit to sponsors of a new product for a certain period of time).
- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Yes; although the use of AMCs is still in the early stages, thus far they have successfully enabled end-stage development, production and marketing of two vaccines.
- **Sustainability of R&D funding for specific disease areas:** Yes; although the frequency and amount of funding available to AMCs depend in part on the financial capability and political will of government and philanthropic donors, AMCs are also heavily reliant on other entities dedicated to the express purpose of providing funding to them (e.g. the GAVI Alliance).
- **Effective access to end product:** Yes; AMCs enable the production and generally, the supply and distribution, of affordable end products to low and middle income countries.
- **Compatibility with other mechanisms:** Yes; AMCs complement other mechanisms targeting the development stage, as well as those aimed at research.

R&D treaty

- **Accurate identification and definition of systemic gaps in the R&D process:** Not applicable at this time; the treaty is still in the proposal stage and therefore there is no evidence to suggest that it will accurately target systemic gaps.
- **Mitigation of cost and risk of relevant R&D:** Not applicable at this time, given that the treaty is still in the proposal stage.

- **Leveraging of capabilities of partners to translate research into clinical outcomes:** Not applicable at this time, given that the treaty is still in the proposal stage.
- **Sustainability of R&D funding for specific disease areas:** No. The treaty relies on a commitment by countries to raise funding, including through taxation, in order to meet obligations under the treaty; developments on this point are subject to the political will to agree to this level of commitment as well as be able to meet funding obligations over the long-term.
- **Effective access to end product:** Generally, yes. The affordable access and delivery of end products to low and middle income countries is a key principle of the treaty; however, it remains to be seen how this will occur in practice (it will depend on the type of delinking mechanisms which are implemented as part of the treaty).
- **Compatibility with other mechanisms:** Generally, no. It depends on the push and pull mechanisms that would be promoted as a result of the treaty; however, if it promotes delinking mechanisms which fully separate the price of products from the cost of R&D, it may erode mechanisms aimed at access, such as AMCs and manufacturer pricing programmes.

The matrix in the table on the following page provides a concise representation of the above assessment.

An assessment of push and pull delinking mechanisms using the Blueprint for success

R&D stage	Research	Development	Access			
Success factor	**Accurate identification and definition of systemic gaps in the R&D process**	**Mitigation of cost and risk of relevant R&D**	**Leveraging of capabilities of partners to translate research into clinical outcomes**	**Sustainability of R&D funding for specific disease areas**	**Effective access to end product**	**Compatibility with other mechanisms**
Open databases	✓	✓	✓	NA	✓	✓
R&D grants	✓	✓	✓	✗	✗	✓
R&D prizes	✓	✗	✗	✗	✗	✗
R&D tax credits	✓	✗	✗	✗	NA	✓
Orphan drug-like schemes, including additional exclusivity & priority review vouchers	✓	✗	NA	✓	✗	✓
Patent pools	✗	✗	✗	NA	NA	✗
Product development partnerships (PDPs)	✓	✓	✓	✗	✓	✓
Advanced market commitments (AMCs)	✓	✓	✓	✓	✓	✓
R&D treaty	NA	NA	NA	✗	✓	✗

Source: Pugatch Consilium (2012)

✓ = success factor exists; ✗ = success factor does not exist; NA = success factor is not relevant or is unknown at this point

This assessment here draws on empirical evidence and a pragmatic analysis of the R&D process. It is important to keep in mind that the objective of the mechanisms discussed here is not only to stimulate R&D but to fully develop and supply new products aimed at Type II and III diseases. In order to create a complete cycle of R&D, i.e. from drug discovery all the way to access, effective mechanisms need to be applied at each stage in the process. The following figure

provides an illustration of how a full R&D cycle could be incentivised using a mix of push and pull mechanisms.

Integration of delinking mechanisms in a full cycle of biopharmaceutical innovation

Source: Pugatch Consilium (2012)

Conclusions & recommendations

The above assessment and the existing evidence on delinking mechanisms suggest that certain mechanisms, most notably prizes and patent pools, may not be as effective as suggested, particularly compared to other mechanisms analysed in the report. Specifically, open compound databases, R&D grants, product development partnerships and advanced market commitments have demonstrated a success in stimulating significant R&D activities in various stages.

Furthermore, delinking models today are constantly evolving, as new approaches and mechanisms for stimulating R&D into these diseases are discussed and introduced.
In conclusion, the way forward is to apply highly targeted, yet complementary, push and pull delinking mechanisms in the key stages of the biopharmaceutical R&D process. The key objective should be to identify effective mechanisms which may be integrated and together drive a complete cycle of research, development and access to new medicines.

Implementing a high-level, yet pragmatic method for identifying the most appropriate mechanisms, such as the matrix proposed in this report, should help provide a more coherent and practical framework for evaluating and scaling up efforts in the future.

Appendix

Defining neglected diseases

There are no set or agreed definitions for what constitute neglected diseases or those which disproportionately affect developing countries. The WHO Expert Working Group (EWG) on Public Health, Innovation and Intellectual Property distinguishes between Type I, II and III diseases:

> *Type I diseases are incident in both rich and poor countries, with large numbers of vulnerable populations in each. Type II diseases are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries. Type III diseases are those that are overwhelmingly or exclusively incident in developing countries.*[3]

Examples of Type I diseases include communicable diseases such as measles and hepatitis B and non-communicable diseases such as diabetes and cardiovascular disease.[4] Type II diseases include HIV/AIDS, TB and malaria; more than 90% of cases occur in poor countries.[5] Finally, Type III diseases typically comprise a range of tropical diseases (which the WHO refers to as "neglected and tropical diseases", or NTDs), including Buruli ulcer, Chagas disease and dengue.[6]

Among these diseases, the WHO identifies the following as diseases which have not been adequately addressed:

> *...[D]iseases or conditions of significant public health importance in developing countries for which an adequate treatment does not exist for use in resource poor settings – either because no treatment exists whatsoever, or because, where treatments exist, they are inappropriate for use in countries with poor delivery systems, or unaffordable.*[7]

Furthermore, Policy Cures and the Bill and Melinda Gates Foundation in the G-FINDER survey use the term 'neglected diseases' to refer to developing country diseases that have a low incidence in developed countries or have different disease profiles when occurring in developing countries; and as such have seen a lack of R&D investment in developing country-specific product development.[8] These diseases include:[9]

- HIV/AIDS (mainly limited to vaccines, diagnostics and microbicides)

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[3] Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) (2006), *Public health, innovation and intellectual property rights*, WHO, Geneva, p.13
[4] Ibid.
[5] Ibid.
[6] WHO, "Diseases covered by NTD Department", http://www.who.int/neglected_diseases/diseases/en/ (Accessed February 2012)
[7] CIPIH (2006), pp.13-14
[8] Global Funding for Innovation for Neglected Diseases (G-FINDER), "Definitions for terms used in G-FINDER", http://g-finder.policycures.org/gfinder_report/registered/docs/glossary.jsp (Accessed February 2012)
[9] G-FINDER, "G-FINDER Diseases, Products and Technologies", https://g-finder.policycures.org/g-finder/registered/docs/G-FINDER-disease-product-matrix.pdf (Accessed February 2012)

- Malaria (including *P. falciparum* and *P. vivax* strains)
- Tuberculosis
- Kinetoplastids, including Chagas disease, Leishmaniasis and Sleeping Sickness
- Diarrhoeal diseases, including Rotavirus, Enterotoxigenic E. coli, Cholera, Shigella, Cryptosporidium, Enteroaggregative E.coli and Giardia
- Salmonella infections, including non-typhoidal Salmonella enterica, Typhoid and Paratyphoid fever
- Dengue
- Helminths, including Roundworm (Ascariasis), Hookworm (Ancylostomiasis & Necatoriasis), Whipworm (Trichuriasis), Strongyloidiasis and other intestinal roundworms, Lymphatic Filariasis (Elephantiasis), Onchocerciasis (River Blindness), Schistosomiasis (Bilharziasis) and Tapeworm (Cysticercosis/Taeniasis)
- Bacterial Pneumonia and Meningitis (*S. pneumoni*a, *N. meningitides*)
- Leprosy
- Buruli Ulcer
- Trachoma
- Rheumatic Fever

This report amalgamates these terms and refers to the above diseases collectively as ‘Type II and III diseases’.

A sample of empirical data on selected delinking mechanisms from the full report

General

Industry R&D into Type II and III diseases (as of November 2011)

Diseases	Ongoing medicines R&D projects	Ongoing vaccines R&D projects
Tuberculosis	28	3
Malaria	29	5
Other tropical diseases	25	3
Total	82	11

Source: IFPMA (2011)[10]

Open databases

Type and number of WIPO Re:Search contributions

Type of contributions									
Screening, Hits Data	**Hits-to-Lead**	**Lead Series**	**Pre-Clinical Candidate**	**Marketed Product**	**Enabling Technology (Platform)**	**IP (Patents)**	**Vaccine Technology**	**Other Data, Know-How, Services, Resources**	**Total**
7	4	9	36	6	4	91	1	9	167

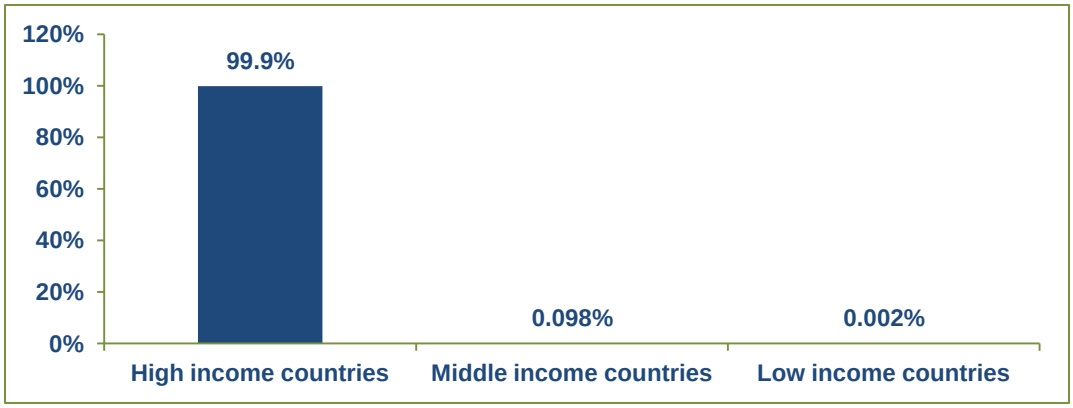
Pugatch Consilium calculations based on the WIPO Re:Search database[11]

[10] Adapted from IFPMA (2011), *Status Report – Pharmaceutical Industry R&D for Diseases of the Developing World*, November 2011

[11] Data drawn from the WIPO Re:Search website, http://www.wipo.int/research/en/search/ (Accessed February 2012)

Product development partnerships (PDPs)

Funding by country groups as a % of total PDP funding (2007-2009)[12]



Pugatch Consilium calculations based on GFINDER data[13]

Top funders of PDPs (2007-2009)

No.	Top funders	Amount (US$)	% of total PDP funding
1	Bill & Melinda Gates Foundation	871,352,698	55%
2	UK Department for International Development (DFID)	139,016,385	9%
3	United States Agency for International Development (USAID)	118,559,718	8%
4	Dutch Ministry of Foreign Affairs - Directorate General of Development Cooperation (DGIS)	71,431,531	5%
5	Royal Norwegian Ministry of Foreign Affairs/Norwegian Agency for Development Cooperation (NORAD)	37,329,040	2%
6	Irish Aid	35,634,268	2%
7	Canadian International Development Agency (CIDA)	32,385,221	2%
8	Spanish Ministry of Foreign Affairs and Cooperation for Development (MAEC)/Agency of International Cooperation for Development (AECID)	30,865,719	2%
9	Swedish International Development Agency (SIDA)	29,647,028	2%
10	Global Alliance for Vaccines and Immunizations (GAVI)	24,896,295	2%
Total (top 10 funders)		1,391,117,903	88%
Total (all funders)		1,579,526,151	100%

Pugatch Consilium calculations based on GFINDER data

[12] High income countries refer to those with a 2008 GNI per capita of $11,906 or more; middle-income to those with a 2008 GNI per capita of $976 – $11,905; and low income to those with a 2008 GNI per capita of $975 or less. For further information, see World Bank, "Country and Lending Groups", http://data.worldbank.org/about/country-classifications/country-and-lending-groups#High_income (Accessed February 2012)

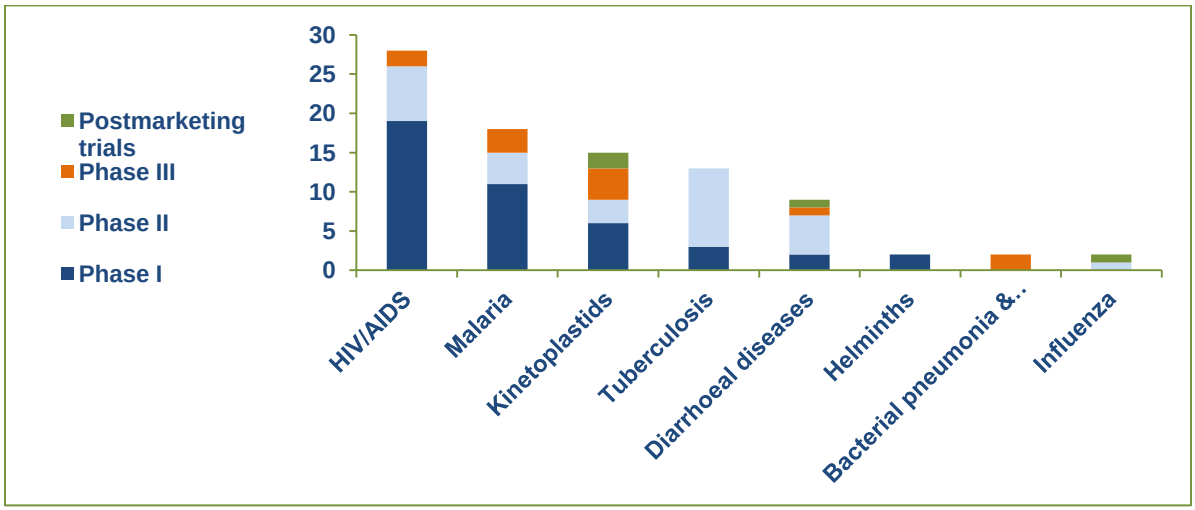
[13] Data drawn from G-FINDER Survey Data, 2007-2009, http://g-finder.policycures.org/gfinder_report/search.jsp (Accessed February 2012)

Type of funder as a % of total PDP funding by recipient (2007-2009)

Recipient PDP Name	Philanthropic	Public Sector
Program for Appropriate Technology in Health (PATH)	94%	6%
International AIDS Vaccine Initiative (IAVI)	9%	89%
Medicines for Malaria Venture (MMV)	75%	25%
Aeras	84%	16%
International Partnership for Microbicides (IPM)	28%	70%
Global Alliance for TB Drug Development (TB Alliance)	66%	34%
World Health Organization (WHO/TDR)	8%	88%
Drugs for Neglected Diseases initiative (DNDi)	49%	49%
Foundation for Innovative New Diagnostics (FIND)	82%	18%
OneWorld Health (OWH)	95%	5%
International Vaccine Institute (IVI)	93%	7%
Infectious Disease Research Institute (IDRI)	72%	19%
Sabin Vaccine Institute	100%	0%
Innovative Vector Control Consortium (IVCC)	100%	0%
European Vaccine Initiative (EVI)	0%	100%
Tuberculosis Vaccine Initiative (TBVI)	100%	0%
All PDPs	60%	39%

Pugatch Consilium calculations based on GFINDER data

Clinical activity by disease (with PDPs as lead sponsors, 2007-2012)



Pugatch Consilium calculations based on Clinicaltrials.gov data[14]

[14] Data drawn from ClinicalTrials.gov; includes all clinical trials with the PDP as lead sponsor initiated or in progress during the period 01/2007-02/2012.