RE:ROUTE

A map of the alternative
biomedical R&D landscape

ACKNOWLEDGEMENTS

We would like to acknowledge all the engaged and active student leaders in UAEM who have supported, participated and activated around the critical global health issue of alternative biomedical R&D, the role of universities and ensuring access to medicines for all. Thanks as well as to the staff and board of UAEM. Special thanks to Els Torreele PhD, Director of the Open Society Public Health Program's Access to Essential Medicines Initiative, for her advice, support and encouragement.

And thanks to the team at signals.ca for providing us with their design talent and enthusiastically agreeing to complete this project in record time!

AUTHOR BIOGRAPHIES

Rachel Kiddell-Monroe LL.M is a humanitarian, a lawyer and an activist. She is Special Adviser to Universities Allied for Essential Medicines (UAEM) and served 6 years as President of the UAEM board of directors. She is also a member of the International Board of directors for Médecins Sans Frontières/Doctors Without Borders (MSF). She lives in Montreal and has worked in south east Asia with human rights and environmental grassroots activists as well as with MSF in Djibouti, Rwanda, the Democratic Republic of Congo and throughout Latin America. Rachel has also served as the Canadian director of MSF's Access to Medicines Campaign. Rachel sits on the board of UAEM Europe, on the Advisory Council of UAEM Brazil and the board of the Young Professionals for Chronic Disease Network. Rachel is a Professor of Practice at McGill University, lectures on international development and is part of the Adult Clinical Ethics Committee at McGill University Health Centres. She holds a Masters in Law and Bioethics from McGill.

Alexandra Greenberg is a second year candidate for a Masters in International Health at the Johns Hopkins Bloomberg School of Public Health and is living in Lima, Peru conducting qualitative research on asthma care and treatment adherence as well as dengue vaccine introduction. She has been on the North American student coordinating committee of UAEM since September 2013 and worked as UAEM's summer intern that same year. She led the North American Report Card project and was the researcher for UAEM's map of alternative R&D initiatives. She has been the chapter president of UAEM at Johns Hopkins since September 2014.

Merith Basey MSC has over a decade of experience in global public health, advocacy and project management. Following her postgraduate studies on Latin America, the UK native spent many years leading AYUDA, where she was responsible for fostering new partnerships, growing youth-led programs and strengthening local capacity in type 1 diabetes communities across Latin America and the Caribbean. After a Master's degree at the London School of Hygiene and Tropical Medicine, she worked with the World AIDS Campaign in Amsterdam and went on to co-found the 100 Campaign. She is based in Washington, DC.

TABLE OF CONTENTS

01

IMPORTANT USER NOTES

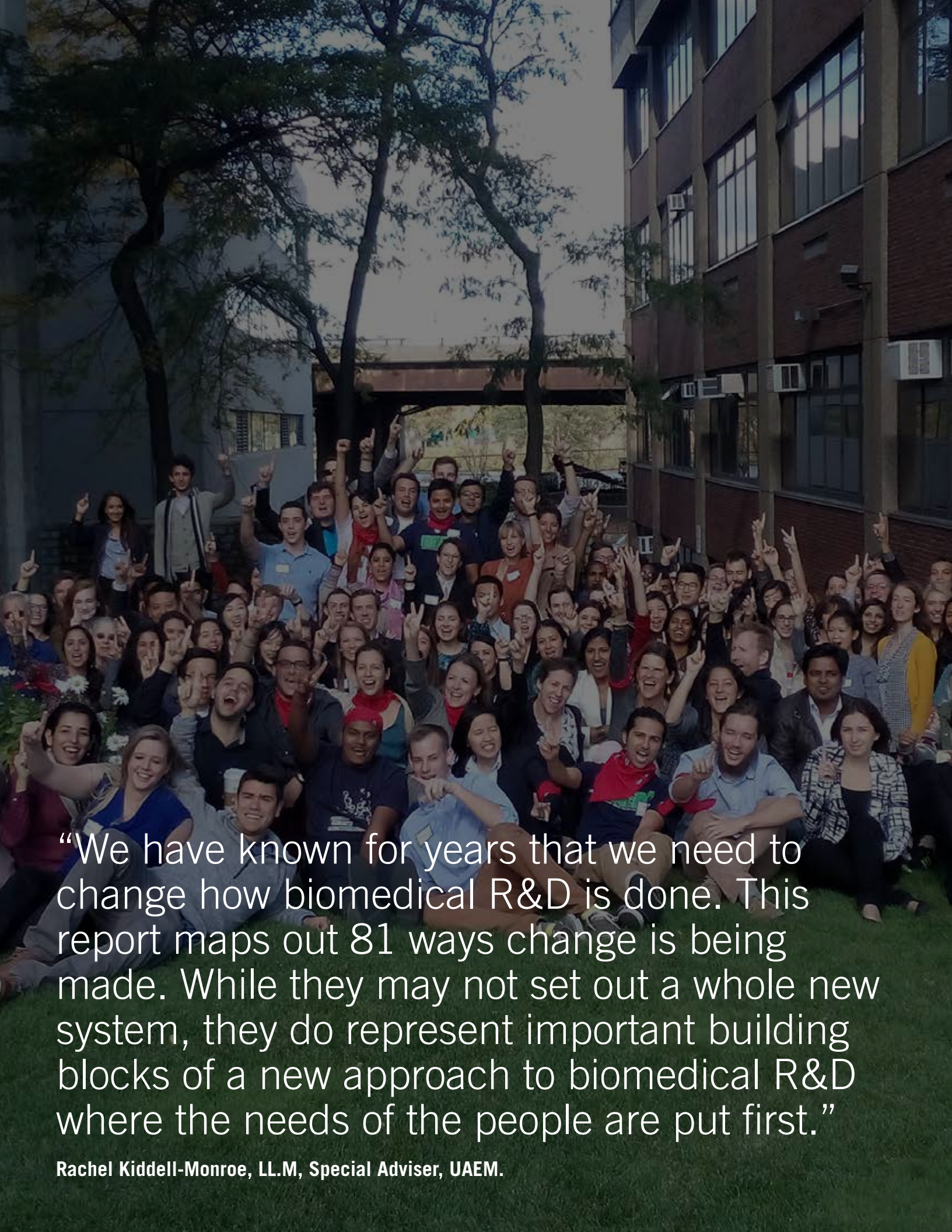
We have an historic opportunity to take the long-running debate on transforming biomedical R&D to a new level. Today, millions of people globally fall between the ever-widening cracks in access to medicines. At the same time, outrage in rich countries over drug prices charged by pharmaceutical companies grows and our publicly funded healthcare budgets balloon to bursting point. Therefore, despite the limits to this mapping, which we readily acknowledge, we have decided to launch it now because we believe this is needed to support and inform the public and civil society debates taking place worldwide.

Readers and users of this mapping should see this mapping as the start of a process and not the end. This mapping is not intended to be a comprehensive review nor does it seek to make judgments on the merits of initiatives included. Rather it is intended to give an overview of what is happening today in response to the gaps left by the current biomedical R&D model. In this sense the initiatives included are referred to as alternative since they respond to a need in a different way from the current biomedical R&D system and are based on different goals. This mapping provides a short description of each initiative's goals and principles. Beyond being a simple catalogue of initiatives, however, we have sought to provide a new way to think and talk about the different approaches aiming to promote and incentivize needs-driven R&D. We hope this mapping can provide a platform for discussion, collaboration and exchange to learn more about what each of these initiatives have achieved, the successes, the challenges and any lessons learnt.

In the spirit of openness, transparency and collaboration, users of the mapping are invited to take an active part in developing this document with us so that it can evolve over time and remain current. We see this project as a continuously evolving contribution to the important dynamic gaining traction in the alternative biomedical research and development (R&D) space.

We invite and welcome your comments and criticisms. As we launch this document, we accept that it is imperfect. Therefore, while maintaining our methodology and criteria, we are expecting to be challenged on the way we have categorized initiatives and for having missed information. We only ask that these challenges be based on information available in the public domain.

Any errors and/or misrepresentations are the sole responsibility of the authors.



“We have known for years that we need to change how biomedical R&D is done. This report maps out 81 ways change is being made. While they may not set out a whole new system, they do represent important building blocks of a new approach to biomedical R&D where the needs of the people are put first.”

Rachel Kiddell-Monroe, LL.M, Special Adviser, UAEM.

02

RATIONALE

The inertia of the current R&D system in the face of recent, ongoing, and emerging global health crises is all too evident.

The growing worldwide threat of antimicrobial resistance; the ongoing challenge of neglected diseases; and the tragic impacts of the 2014-2015 Ebola epidemic all highlight the urgent need to ensure that affordable and appropriate medicines are available for all. These public health emergencies demonstrate yet again that we need new and ethical ways to carry out biomedical research in a timely and proper way. We need a biomedical ecosystem that meets patient needs and benefits everyone who requires access to essential medical technologies.

In response to the systemic inequity in biomedical R&D processes, a broad range of initiatives exist or are proposed as offering 'alternatives' to the current biomedical R&D system. Yet when UAEM tried to get an idea of exactly what was going on in this space, we soon discovered that there was no single place to find the entire range of what was happening or was planned. Due to the fragmented nature of the landscape, we found no one shared understanding or application of access and innovation principles. On top of that, the landscape is changing so rapidly that the reports or articles that do exist are already out of date.

In order to address this gap in the literature, UAEM has created this mapping of alternative R&D initiatives with support from the Open Society Foundations. Based on a first review of over 130 initiatives, of which we considered 81 to be genuinely innovative on some level, we attempt to provide a one-stop place where users, readers, and researchers can obtain a clearer picture of the existing and planned initiatives that are truly unique in the way that they promote R&D for the public good.

The initiatives included are either already existing or are currently proposed. By including these initiatives we believe it provides a starting point for an open and ongoing collaborative process to support transformative biomedical R&D.

ONE IN FOUR

HIV/AIDS TREATMENTS WOULDN'T EXIST WITHOUT UNIVERSITY RESEARCH

03

METHODOLOGY

The initiatives included are either already existing or are currently proposed. By evaluating these initiatives we believe this mapping provides a starting point for an open and ongoing collaborative process to support transformative biomedical R&D.

Materials and Methods

In order to meet the objectives of this mapping, an initial list of existing and proposed initiatives were gathered from published literature. This list, detailed in Appendix 1, includes resources from UAEM, KEI, OSF, MSF, WHO, and WIPO, and was used as the initial baseline for the study. In this way, we sought to ensure the inclusion of many of the initiatives already identified as alternative through previous research to allow the mapping to build on an existing body of work.

In addition, grey literature was identified through Internet and website research on key initiatives and organizations that included a focus on alternative biomedical R&D models, both existing and proposed. This grey literature is referenced throughout the report and has been documented in detail in the bibliography. Key search terms came from specific models of biomedical R&D known to UAEM and allied organizations. The terms included delinkage; alternative health R&D; alternative biomedical R&D; neglected diseases R&D; alternative incentive models; alternative pharmaceutical models; alternative pharmaceutical financing; open biomedical R&D; innovative biomedical R&D; pharmaceutical innovation; biomedical innovation; neglected diseases innovation; push, pull, and pool; public-private partnerships; product development partnerships; alternative intellectual property for biomedical R&D; contests/prizes/ funds for (biomedical) innovation/ R&D; and more.

Once key search terms were identified and searched, a list of the initiatives discovered was laid out for further investigation. This list was updated as the mapping progressed based on further information found in the course of the research. Based on the initial list, the initiatives were organized alphabetically, and for each one we completed a Google search of the full name of the given initiative, and, if applicable, also the acronym (e.g. Drugs for Neglected Diseases DNDI). We reviewed all relevant web pages or links from the first five pages of results, beginning with the initiative's website, if applicable. During this review we focused on information relevant to (1) a summary of the initiative, (2) the main project(s), (3) the effectiveness, (4) questions/critiques, (5)

03

proposed changes/improvements, (6) organizations, stakeholders and partners, and (7) university involvement where appropriate. We kept track of all references and associated URLs (author/source, year of publication) as we progressed. During this review we also noted any reference to our key terms and/or criteria.

Once all sources had been reviewed for a model or mechanism, if insufficient information was found for a given section, the search was repeated adding in the key word for that section and looking at the first two pages of results (most frequently "model name" evaluation, "model name" effectiveness, or "model name" criticism/critique). While reviewing sources for a given model, if a new model was mentioned, it was added to the list and if information on another model already on the list was found then that source was noted for future reference. When the initial list of models was fully mapped, using information included in the summary and main projects section, we completed the general approach/methods applied section for each initiative. Based on the information retrieved from the review, we categorized each initiative according to the typology and determined whether any of the inclusion criteria were met and/or whether any specific exclusion criteria were applied. If no inclusion criteria were evaluated as being met and/or any exclusion criteria were met, the initiative was removed from the mapping.

Initiatives were then organized according to the typology assigned to them (see below). Aside from the authors of this project, three other experts reviewed the typology categorizations, the criteria listed as met, and additional research for each initiative in an attempt to minimize errors in classification and possibly point out gaps in the evaluation.

The search was limited to the English language. The last search of the literature was conducted on September 15th, 2015.

Typology

To provide more meaningful insights into the landscape of alternative R&D, we opted for a typology that first categorizes initiatives according to the stage of the biomedical R&D system they primarily seek to address and second identifies the key innovation and access principles they apply. This allowed us to first identify types of initiatives through mode of action within R&D and then further differentiate each initiative in terms of alternative approaches to financing and/or completing R&D that are regularly implemented. On the basis of this typology, we applied a set of inclusion and exclusion criteria.

Inclusion criteria

Initiatives were only deemed to be alternative, and therefore relevant to the mapping, if the publicly available information we reviewed indicated that they met one or more of a set of specific inclusion criteria. Various sets of inclusion criteria were tested before opting for a set of inclusion criteria based on the innovation and access methods, which are commonly deemed necessary for an effective, innovative and alternative R&D approach.

The inclusion criteria were:

(1) the initiative is driven by the needs of patients globally.

03

(2) the initiative is based on a clear and broad application or planned application of one or more of the following innovative principles:

a. providing a pull mechanism
b. providing a push mechanism
c. providing an IP pooling mechanism
d. allowing broad collaboration
e. adopting open approaches to R&D (open source, open data sharing, open innovation)

DEFINITIONS

Push Mechanism

Direct funding for R&D, often in the form of a grant, as well as indirect incentives, such as tax breaks and in-kind contributions, that help finance R&D upfront and thus mitigate the R&D investment required; they are given independently of the results of such research.

Pull Mechanism

Mechanisms to incentivize R&D activities through the promise of financial rewards once specified objectives or milestones have been met, creating viable market demand. It includes prizes, priority review vouchers (PRVs), advanced market commitments (AMCs), and cash payments.

Pooling Mechanism

Pooling of funds that are aggregated and managed jointly by an established entity, typically a board or committee, to be allocated based on priority setting in order to distribute risk and finance biomedical R&D. The goal of pooled funding is to address inefficient flow and volatility of funds as well as poor allocation of and lack of sufficient resources (Grace, 2011). Additionally, pooling of intellectual property (IP): typically via a patent pool, an agreement between two or more patent owners to pool their patent rights and license the rights to use these patents together to one another as well as third parties often with the requirement of royalties being paid. The goal of patent pools is typically to enable access to biomedical discoveries and encourage downstream competition by simplifying and improving voluntary and cooperative licensing negotiations (Bartels et al., 2013).

These two distinct types of pooling can occur independently or jointly.

Collaborative Initiative

An R&D initiative that involves a network, consortium, or partnership between two or more of any academic or research institutions, non-profit organizations, NGOs, governments, government entities, or members of the private sector including biotech and pharmaceutical companies. Exchange of information and data pooling is often regulated via Material Transfer Agreements and restricted to within the involved entities unless the initiative is also open.

Open Initiative

R&D initiatives that apply open source, open access, open data, or open knowledge principles. Interested parties are able to contribute knowledge or know-how, data, technology, etc. to be shared in the public domain and, in the case of open source, in coordination with patent-free research. Open initiatives provide literature and/or other information such as biomedical data, typically digital or online, often without any fee or cost and without any copyright and licensing restrictions such as royalties, in order to encourage further access to and reuse of this information and facilitate open collaboration and exchange in biomedical R&D (Creative Commons, 2011). Open access typically pertains to making publications freely available; open source typically pertains to making licenses or IP freely available; and open data typically refers to making data, methods, and/or tools freely available.

03

Application of Inclusion Criteria

We wanted to assess the application of inclusion criteria from an outsider perspective. In practice, this meant where existing initiatives claimed on their webpages or other sources to adopt the inclusion criteria, we verified this information against publicly available evaluations, progress and annual reports to see if the majority of their main projects were explicitly required to implement the inclusion criteria they claimed to espouse. It was not considered sufficient that an initiative simply states that it values one of the inclusion criteria or purports to apply that method without any evidence to support its claim. For example, we found several initiatives that claimed to be open (open source or open innovation) yet we were unable to find evidence of that open approach, such as licensing terms or details of financing or investments by collaborators, in the publicly available information.

Where initiatives did not specify one, some or all of our inclusion criteria, we also checked to see whether they were in fact incorporated in practice even if not explicitly stated on their website. Clearly, for potential projects, we can only rely on what inclusion criteria the initiatives claim they will apply.

We relied solely on publicly available information. We did not conduct interviews with any personnel from any initiatives nor use insider-only/anecdotal information about how or where the inclusion criteria were applied in practice. This strict parameter was necessary to keep the mapping as objective as possible as well as to respect one of the key inclusion criteria, that the initiative be open.

Exclusion criteria

If the initiative did not fulfill any of the inclusion criteria and/or if any exclusion criteria were applicable, then the initiative was removed from the mapping.

The exclusion criteria were:

(1) the claims by the initiative to be alternative, innovative, open, or otherwise were either not demonstrated in the publicly available information on projects and activities, or were only anecdotal, based on insider information, or on common knowledge;

(2) the initiative, through initial review, was found to primarily focus on activities outside of biomedical research and development, such as drug procurement, distribution or altogether non-biomedical work.

BETWEEN

1/4 AND 1/3

OF NEW MEDICINES ORIGINATE IN A UNIVERSITY LAB

04

LIMITATIONS OF THE MAPPING

This mapping is intended to be the beginning of an ongoing process to provide a landscape of alternative R&D initiatives, which exist or are proposed. Given the rapidly developing context and the lack of clarity around what is or is not alternative, this mapping unavoidably has to make assumptions, which can be considered a limitation.

The overarching limitation is based on an assumption of what should be considered key principles and methods to be adopted and implemented by an alternative R&D system. This set of principles and models is based on the commonly accepted wisdom of organizations involved directly in decades of access to medicines work globally as well as our own collective expertise and experience in this field. We also relied on key studies and literature related to this field.

Our goal is also an inherent limitation. We did not intend to provide a comprehensive map of all the initiatives and we did not intend to thoroughly evaluate or critique them. We consider our role as being to provide the platform, the basic structure and information which will allow the alternative R&D community to develop, improve and elaborate on its activities and overall strategy.

Aside from the limitations particular to our philosophical approach, there are the usual limitations, which should be noted. We completed this review and evaluation in less than three months on a limited budget and with limited research capacity.

Therefore, the list may have omitted existing or proposed R&D models or mechanisms that were not found through the search methods implemented, and/or were not included due to the inclusion criteria chosen, and/or were excluded due to a general lack of pertinent information available during the time of the search. Various detailed aspects of each model, mechanism, or main project may have been omitted due to difficulty in locating more specific information given the constraints of the project. Furthermore, the mapping was conducted based on the authors' and readers' familiarity with some but not all of the included initiatives. We acknowledge that this may have created an inherent bias in the classification of these initiatives. We are willing to be challenged on any perceived bias or misclassification.

05

EXECUTIVE SUMMARY

A. EXISTING INITIATIVES (49 IN TOTAL)

1. Drug discovery and data-sharing platforms (10 initiatives)

- **Dialogue for Reverse Engineering Assessment and Methods - DREAM (PULL + OPEN): Data sharing** and crowdsourcing open source platform.
- **InnoCentive (POOL + OPEN):** Open innovation network for crowdsourcing with a non-profit area focused on accepting commissions to research and address development problems including those related to neglected health needs.
- **Indian Open Source Drug Discovery Initiative - OSDD (OPEN):** Drug discovery platform that promotes collaboration and an open approach to IP through crowdsourcing and social networking as well as open access repositories.
- **Collaborative Drug Discovery - CDD (OPEN):** Collaborative "cloud-based" tool to enable neglected disease/other researchers from usually separate areas to collaborate and share compounds and drug discovery data via an online database.
- **Structural Genomics Consortium - SGC (Collaborative + OPEN):** Consortium providing an open access, collaborative network focused on less well-studied areas of the human genome as a means towards developing new medicines.
- **WIPO Re:Search (Collaborative + OPEN):** Multi-stakeholder coalition with an online, open access, collaborative database providing access to IP, including pharmaceutical compounds, technologies, know-how and data available for R&D for NTDs, TB, and malaria.
- **Cambia's Patent Lens and Initiative for Open Innovation - IOI (OPEN):** Non-profit international research organization that provides an open access and collaborative public resource for innovation via its Patent Lens and IOI initiatives to create a more equitable and inclusive capability to solve problems using science and technology.
- **TDR Targets (OPEN):** Collaborative knowledge sharing platform with an open access database to facilitate the identification and prioritization of drugs and drug targets in neglected disease pathogens.
- **The Synaptic Leap (OPEN):** Open and collaborative network of online research communities that connect and enable open source biomedical research and drug discovery via knowledge sharing.
- **Kaggle (OPEN):** Online collaborative platform for data-mining and predictive-modeling competitions via crowdsourcing.

2. Drug discovery incentives (18 initiatives)

a. Prizes

- **Longitude Prize Open (PULL):** Incentive provided via an ex-ante inducement prize awarded to the submission considered most impactful and feasible, currently for a competitive AMR innovation.
- **X-prize (PULL):** Milestone inducement prize contest to spur and accelerate innovation with a current competition to develop an improved TB diagnostic tool.
- **Prize4Life (PULL+OPEN):** Milestone Inducement prize contest with competitions to accelerate discovery of cures and treatments for amyotrophic lateral sclerosis (ALS) as well as crowdsourcing challenges and a data sharing platform.
- **EU Vaccine Prize (PULL):** End product inducement prize to be awarded for a vaccine cold chain innovation.

05

b. Tax subsidy/priority review incentives

- **U.K. Vaccines Research Relief (PULL):** Tax-based incentive to encourage companies to increase their investment in research and development into vaccines and treatments for these diseases.
- **U.S. Orphan Drug Program - ODA (PULL + PUSH):** Incentive supplied via additional marketing exclusivity and priority review and grants awarded for development of orphan drugs, tax credits, etc.
- **U.S. Patents for Humanity Awards for Medicine (PULL):** Incentive supplied via a "prize", typically patent review acceleration, which encourages development of drugs for neglected health needs by reducing the cost and time required to enter the market.
- **Pneumococcal Vaccine Advance Market Commitment - Pilot AMC (PULL):** Market-based incentive supplied via an advance market commitment (AMC) for a vaccine product, or creation of a guaranteed subsidized market funded by donors, in this case specifically for pneumococcal diseases.
- **USFDA Priority Review Voucher - PRV (PULL):** Incentive supplied via a "prize", the PRV, which encourages development of drugs for NTDs and RPDs by reducing the cost and time required to enter the market.

c. Innovation fund/platform

- **Global Health Innovative Technology Fund - GHIT (PUSH):** Non-profit public-private partnership (PPP) fund that provides grants to encourage collaborative research on NTDs.
- **European Developing Countries Clinical Trials Partnerships - EDCTP II (PUSH):** International partnership that provides grants and additional support for collaborative research to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against poverty-related and neglected infectious diseases in sub-Saharan Africa, with a focus on phase II and III clinical trials.
- **The Bridging Interventional Development Gaps Programme - BrIDGs (PUSH):** Program that provides in-kind resources to facilitate drug development for both common and rare diseases.
- **Sustainable Sciences Institute - SSI (PUSH):** Institute that provides grants and non-financial contributions, including trainings, to support R&D in-country and capacity building for various diseases including dengue fever.
- **Global Health Investment Fund - GHIF (PUSH):** Social impact investment fund that provides milestone payments and royalties to finance drug, vaccine, and diagnostic development and encourage global access agreements through 'mezzanine' debt funding.
- **Humanitarian Assistance for Neglected Diseases - HAND (PULL):** Initiative focused on collaborative, non-commercial drug discovery and development, working to identify, evaluate and manage scientific projects and partnerships focused on neglected diseases.

d. Venture philanthropy for drug discovery and development

- **CQDM (Collaborative + PUSH):** Pre-competitive research consortium with pharmaceutical companies and government members that funds the development of breakthrough tools and technologies to accelerate drug development and discovery.
- **Cystic Fibrosis Foundation Therapeutics - CFFT (Collaborative + PUSH):** Non-profit collaborative network for drug development for cystic fibrosis employing venture philanthropy.
- **Dementia Discovery Fund (POOL + PUSH):** Venture philanthropy capital fund to accelerate research on dementia drugs.

05

3. Drug Licensing: patent pools and related initiatives (2 initiatives)

- **Medicines Patent Pool - MPP (POOL):** Patent pool currently focused on HIV/AIDS treatment implementing voluntary licensing of critical intellectual property in order to make patents work for public good.
- **GSK Pool for Open Innovation - POINT (POOL):** Patent pool that makes technology that could be used to solve problems that arise in R&D available and that contributes know-how to the public domain that may assist in drug discovery or development, specifically for NTDs.

4. Drug Advancement: Larger PPPs or organizations that house multiple innovative R&D initiatives (8 initiatives)

- **European Vaccine Initiative - EVI (Collaborative + PUSH):** Non-profit PPP that works to bring vaccines to market, specifically focusing on fostering an environment in which potential vaccines can be brought to clinical trials and made accessible to low income populations. Houses **TRANSVAC**, a collaborative project to create a network for vaccine R&D.
- **Sabin Vaccine Institute (Collaborative):** Larger organization that houses a PDP focused on vaccine-preventable and NT diseases along with the Global Network for Neglected Tropical Diseases and other advocacy and fundraising entities.
- **International AIDS Vaccine Initiative - IAVI (Collaborative + PUSH + PULL):** Global non-profit organization working to ensure the development of AIDS vaccines for use throughout the world through research, development of consortia and partnerships, funding of external work, and product development services (houses a PDP and an innovation fund).
- **International Vaccine Initiative - IVI (Collaborative):** International non-profit housing PDPs focused on development of vaccines for cholera, typhoid, and dengue fever.
- **Program for Appropriate Technology in Health - PATH (Collaborative + PUSH):** Large organization known for partnering with the private sector to develop lifesaving health technologies with global impact through five large programs dedicated to product development including the Malaria Vaccine Initiative and the Meningitis Vaccine Project. Incorporated the **Institute for OneWorld Health**, a PDP focused on orphan drugs and NTDs, in 2011. Houses the PATH Global Health Innovation Hub, which directly supports innovators in India and South Africa and incorporates start-ups, impact equity investors, and the transfer of knowledge from local to global.
- **The Critical Path to Tuberculosis (TB) Drug Regimens - CPTDR (Collaborative + OPEN):** PPP with an open source and open innovation collaborative database and Drug Development Coalition to speed the development and impact of new and markedly improved drug regimens for tuberculosis.
- **African Network for Drugs and Diagnostics Innovation - ANDi (Collaborative + PUSH):** PPP working on formation of an R&D network and product innovation initiative in disease-endemic regions. Responsible for the proposal for the ANDi Health Technology Fund, which would be equipped with grant making and social venture arms to support ANDi to ensure development, implementation and commercialization of technologies emanating from African Centres of Excellence and other sources.
- **BioVentures for Global Health - BVGH (Collaborative + PULL):** Non-profit organization that provides incentives and fosters collaboration and partnerships in various areas of global health. Supports the GSK patent pool and WIPO Re:Search.

05

5. Drug Development (11 initiatives)

PDPs may demonstrate push, pull and pool mechanisms in some of their projects, but the driving mechanism is collaboration.

a. Product Development Partnerships working on one disease

- **Medicines for Malaria Venture - MMV (Collaborative):** PDP focused on drug development for malaria treatment.
- **International Partnership For Microbicides (Collaborative):** PDP focused on preventing HIV among women using products based on microbicides.
- **TB Alliance (Collaborative):** PDP focused on drug development for TB treatment.
- **Aeras Global TB Vaccine Foundation (Collaborative):** Biotech firm and PDP focused on TB vaccine development.
- **Tuberculosis Vaccine Initiative - TBVI (Collaborative):** PDP focused on development and delivery of a TB vaccine.

b. Product Development Partnerships working across diseases

- **Drugs for Neglected Diseases initiative - DNDi (Collaborative):** PDP focused on drug development for neglected diseases treatment, currently beginning a new initiative with four pharmaceutical companies known as the Drug Discovery Booster Consortium.
- **Fund for Innovative New Diagnostics - FIND (Collaborative):** PDP focused on development of diagnostic tools for poverty-related diseases.
- **Infectious Disease Research Institute - IDRI (Collaborative):** Biotech firm and PDP focused on drug development for infectious diseases, specifically tuberculosis, leishmaniasis, leprosy, malaria, and Chagas Disease.
- **Medicine Development for Global Health - MDGH (Collaborative):** PPP focused on drug development for infectious diseases such as onchocerciasis.
- **European Commission's Innovative Medicine Initiative - IMI (Collaborative):** PPP focused on drug development for neglected health needs in both LMICs and HICs and providing grants for research.
- **UCSF/UCSD Center for Discovery & Innovation in Parasitic Diseases (CDIPD) (Collaborative):** NTD-focused drug discovery and development research center.

B. PROPOSED INITIATIVES (32 INITIATIVES IN TOTAL)

1. Drug discovery and data sharing platforms

- **Exploiting the Pathogen Box:** an international open source collaboration to accelerate drug development in addressing diseases of poverty (Collaborative + OPEN): Collaborative and open source platform to provide start points for the discovery of new medicines.
- **Establishing a Drug Discovery Platform for Sourcing Novel Classes of Antibiotics as Public Goods (PULL + OPEN):** Creation of a Drug Discovery Platform for Antibiotics with milestone monetary prizes for early stage antibiotic developments, non-exclusive licensing for promising antibiotics, and an open source platform to share intellectual property and data.
- **Building a Diagnostic Innovation Platform to Address Antibiotic Resistance (POOL + PUSH + PULL):** Creation of a diagnostic innovation platform to address antibiotic resistance with pooling of resources and use of push and pull mechanisms to incentivize research.

05

2. Drug discovery incentives

a. Prizes

- **Medical Innovation Prize Fund and Prize Fund for HIV/AIDS (PULL):** Proposed patent buy-out end product prize fund to delink R&D costs from drug prices.
- **The Open Source Dividend Proposal (Bangladesh, Barbados, Bolivia and Suriname) (PULL):** Proposed open source dividend and milestone prizes given to reward openness and sharing of knowledge, materials and technologies as part of larger innovation inducement prize efforts. Includes:
  - **Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis**
  - **Prizes as a Reward Mechanism for New Cancer Treatments and Vaccines in Developing Countries**
  - **Chagas Disease Prize Fund (CDPF) for the Development of New Treatments, Diagnostics and Vaccines**
  - **Prize Fund to Support Innovation and Access for Donor Supported Markets**
  - **Priority Medicines and Vaccines Prize Fund (PMV/pf)**

b. Tax subsidy/PRV

- **The Neglected Diseases Tax Credit Proposal (PUSH):** Proposed tax incentives to subsidize and encourage R&D on neglected diseases, specifically applicable for large firms.
- **Options Market for Antibiotics - OMA (PULL):** Proposed market-based incentive supplied via OMA for any antibiotic-related innovation, or creation of a guaranteed subsidized market funded by donors and available at various stages of the development process.

c. Innovation fund/platform

- **Health Impact Fund (PULL):** Proposed pull model that would use the prize incentive as an alternative to patent protection in order to delink the price of a health product and the cost of R&D through "pay-for-performance mechanisms".
- **U.K. AMR Innovation Fund (PULL):** Proposed plan to address AMR in which companies that develop a successful drug to address AMR are either bought out completely by a global body (Option 1) or, under the 'hybrid' model (Option 2), companies would maintain control of marketing but receive lower pay-outs and be subject to conditions on pricing and distribution. Additionally, pharma would support a global innovation fund for R&D.
- **WHO Global Biomedical R&D Fund Proposal (POOL + PUSH):** Proposed global inter-governmental pooled fund to finance biomedical R&D with an emphasis on neglected health needs.
- **Global Vaccine Development Fund (POOL+PUSH):** Proposed global pooled fund to finance vaccine development targeting neglected diseases and other public health threats such as MERS.
- **The Fund for Research in Neglected Diseases - FRIND (POOL + PUSH):** Proposed pooled fund and patent pool managed as a portfolio and focused on R&D for NTDs with support from PDPs emphasized.
- **The Industry R&D Facilitation Fund - IRFF (POOL + PUSH):** Proposed pooled fund to provide secure and flexible funding to select PDPs for R&D in order to encourage industry involvement.
- **Product Development Partnership Financing Facility - PDP-FF (POOL + PUSH):** Proposed bond-financed pooled fund to provide funding to support long-term development of PDPs in R&D for NTDs.
- **PDP-Plus Fund - PDP+ (POOL + PUSH):** Proposed pooled fund to support PDPs based on integration of the FRIND, IRFF, and PDP-FF proposals.

05

- **Revolving Fund to Finance R&D for NTDs (POOL + PUSH):** Proposed revolving fund specific to NTD R&D, wherein the initial investment is reimbursed out of resources generated by the projects that were financed.
- **Pilot Pooled International Fund (POOL + PUSH):** Proposed pilot pooled international fund to finance selected demonstration projects, the first of which have been chosen from those listed below, for both neglected and commercial diseases.

3. Drug Licensing: patent pools and related initiatives

- **Essential Medicines Licensing Agency - EMILA (POOL):** Non-profit entity created to manage patent pools for medical inventions in order to enable generic competition.

4. Drug Development:

a. Disease-specific Product Development Partnerships challenging current R&D system

- **Development Of Class D Cpg Odn (D35) As An Adjunct To Chemotherapy For Cutaneous Leishmaniasis And Post Kala- Azar Dermal Leishmaniasis (Pkdl) (COLLABORATIVE + POOL+ PUSH):** Coordinated and collaborative approach via pooled funding to develop D35 for treatment of Leishmaniasis.
- **Chagas R&D Accelerator Initiative:** A Coordination Mechanism For Accelerating The Development Of New Health Tools For Chagas Disease (Collaborative + PULL): Creation of a coordinated and collaborative Chagas Disease R&D Initiative focused on new biomarkers for testing therapeutic efficacy, a biobank portal, and development of drug candidates.

b. Product Development Partnerships working across diseases

- **Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases (Collaborative):** Use of a high-throughput biomarker screening platform for diagnostic development focused on NTDs.
- **Multiplexed Point-of-Care test for acute febrile illness (mPOCT) (Collaborative + OPEN):** Creation of a consortium to develop a Multiplexed Point-of-Care test for acute febrile illness via an open platform.

5. Initiatives addressing 4 or more innovative R&D mechanisms

- **MSF 3P Project (Collaborative + PUSH + PULL + POOL + OPEN):** Open collaborative platform with pooling of IP and push and pull incentive-based mechanisms to foster development of new drug regimens for TB, and particularly MDR-TB, with an emphasis on delinkage. Although the 3P Project Proposal was not accepted by the CEWG it is being developed by MSF and is in the active planning stage with a business plan being finalized.
- **The Visceral Leishmaniasis (VL) Global R&D & Access Initiative (Collaborative + PUSH + PULL + POOL + OPEN):** Creation of a coordinated and collaborative Visceral Leishmaniasis Initiative focused on financing R&D with development of a diagnostic tool and chemotherapy tools as primary objectives.
- **The Open Source Multiplex POC Fever Diagnostic Project (Collaborative + PUSH + PULL + OPEN):** Creation of a new ecosystem for financing the development of an open source, multiplex, point of care (POC) diagnostic test via push and pull incentive-based mechanisms.

05

- **ANDI as the regional coordination mechanism for demonstration projects and product R&D in Africa (Collaboration + PUSH + POOL + OPEN):** Leveraging of the existing ANDI structure and creation of an innovation hub to pool funds and provide grants in order to develop and promote access to medicines, diagnostic tests, medical devices, and other technologies primarily for type II and III diseases.
- **Antibiotics Innovation Funding Mechanism (AIFM) (POOL + PUSH + PULL + OPEN):** Creation of an innovation fund to address antibiotic resistance along with economic incentives including inducement prizes and grants to encourage open data and knowledge sharing.
- **Combating Tuberculosis in the region by Development of Diagnostics and Drugs (Collaborative + PUSH + POOL):** Creation of a collaborative platform for development of TB diagnostics and drugs with pooling of resources and push and pull incentives implemented.

06 MAPPING EXISTING INITIATIVES

"This mapping provides timely and valuable insights on the types and nature of a wide range of existing and proposed 'alternative' R&D models, to be refined as more information is shared publicly, and to inform ongoing discussions. It also shows that very few if any such initiatives are directly addressing the fundamentally flawed design of the current system, and that, in order to realign R&D and health needs, more transformative changes are needed."

Els Torreele, PhD
Director of the Open Society Foundations Public Health Program's Access to Essential Medicines Initiative.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

DREAM CHALLENGES

General Approach/Methods Applied:

(PULL) Data sharing and crowdsourcing open source platform.

Summary:

Started in 2006, DREAM (Dialogue for Reverse Engineering Assessment and Methods) challenges are run by Sage Bionetworks through its online Synapse platform via crowdsourcing and what has been coined 'the challenge improvement loop.' Incentives for participation include partnerships with journal editors; challenge webinars for live interaction between participants and organizers; community forums where participants can learn from each other; leaderboards to motivate continuous participation; and the annual DREAM Conference to celebrate and discuss challenge outcomes. The competition is open source and requires code-sharing from its participants with the winning code needing to be reproducible (Kellen, 2014).

Main Project(s):

While DREAM challenges are focused on diverse topics within biomedical discovery and emphasize computing, the ALS Prize4Life Challenge is being run via DREAM.
A list of current DREAM challenges can be found here: **http://dreamchallenges.org/challenges/**

Effectiveness:

"More than 40 different countries and 100 institutions" participated in the most recent DREAM challenge for breast cancer (Kellen, 2014).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

Potential "next generation" challenges include partners such as "GBM-NBTS, Colon, CHDI, NCI (pan-cancer), BROAD, NIEHS, [and] Alzheimer's-NIA" (Kellen, 2014).

Organizations, Stakeholders, And/Or Partners:

Organizers:
Gustavo Stolovitzky, IBM Computational Biology Center; Andrea Califano, Columbia University; Robert Prill, IBM Computational Biology Center; and Julio Saez Rodriguez, Harvard/MIT

Sponsors:
Columbia University Center for Multiscale Analysis Genomic and Cellular Networks (MAGNet); NIH Roadmap Initiative; IBM Computational Biology Center; and The New York Academy of Sciences

University Involvement:

Columbia University; Harvard; and MIT

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

INNOCENTIVE

General Approach/Methods Applied:

(POOL + OPEN) Open innovation network for crowdsourcing with a non-profit area focused on accepting commissions to research and address development problems including those related to neglected health needs.

Summary:

InnoCentive (IC) is a crowdsourcing company started in 2001 by Eli Lilly & Co. that accepts (by commission) research and development problems, framed as "challenge problems," in various fields including life sciences and health. It gives cash awards for the best solutions to solvers who meet the challenge criteria (InnoCentive, 2015). Specifically, "in December 2006 . . . the company signed an agreement with the Rockefeller Foundation to add a non-profit area designed to generate science and technology solutions to pressing problems in the developing world" (RF Press Release, 2009).

Main Project(s):

IC has partnered with organizations including Prize4Life to solve problems related to rare diseases although its model is applied to all types of companies and ideas.
InnoCentive "Challenge Center":
https://www.innocentive.com/ar/challenge/browse

Effectiveness:

"Between 2006 and 2009, The Rockefeller Foundation posted 10 challenges on InnoCentive with an 80% success rate" (RF press release, 2009). Additionally, 33% of all challenges posted on InnoCentive were being solved within the specified timeframe as of 2008 (Lehrer, 2008).

Critiques/Questions Raised in the Literature:

Some critics argue that models like InnoCentive do not actually encourage collaboration but rather competition between individual participants (Woods, 2009).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

InnoCentive was started and funded by Eli Lilly & Co. However, IC was spun out of Eli Lilly in 2005 and is now an independent and privately held venture-backed company (InnoCentive, 2015). Many organizations and companies have posted challenges via InnoCentive.

Non-University Participants/Partners:
The Rockefeller Foundation; AstraZeneca; Cleveland Clinic; Lumina; NASA; Enel; DARPA; ChemAxon; Nosco; Strategos; Booz Allen Hamilton; Nature.com; Scientific American; The Economist, etc.

University Involvement:

None found.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

THE INDIAN OPEN SOURCE DRUG DISCOVERY (OSDD) INITIATIVE

General Approach/Methods Applied:

(OPEN) Drug discovery platform that promotes collaboration and an open approach to IP through crowdsourcing and social networking as well as open access repositories.

Summary:

OSDD, launched in 2008, is "an idea for open innovation designed by the Council of Scientific and Industrial Research [CSIR] Team India consortium with global partnerships" (So, 2014) working "to provide affordable healthcare to the developing world by providing a global platform where the best minds can collaborate & collectively endeavor to solve the complex problems associated with discovering novel therapies for neglected tropical diseases like Tuberculosis, Malaria, Leishmaniasis etc" (OSDD, 2015). "Through an online collaboration platform, [Sysborg 2.0], OSDD shares resources across a network of collaborators. Those joining this online community commit to a clickwrap license not to take from the research commons, nor to privatize the product of [its] work. With funding from the Indian government and a private foundation, OSDD shares the risks and rewards of these efforts" (So, 2014). OSDD emphasizes the importance of a translational approach to research, bringing together "the biological, genetic and chemical information available to scientists in order to use it to hasten the discovery of drugs" (OSDD, 2015). OSDD is funded by the Government of India, which has committed [US]$46 million towards the project, in addition to seeking funds from other private and philanthropic sources and bilateral scientific agreements (OSDD, 2015; OSDD WHO proposal). Submissions for challenges are open to anyone and subject to peer and expert review, with winning contributors receiving monetary awards on a case-by-case basis via a micro-attribution system (OSDD, 2015; OSDD WHO proposal). Additionally, OSDD allows contributors to share or even donate their IP if they hold exclusive rights and are willing to provide OSDD non-exclusive rights for use (OSDD, 2015).

Main Project(s):

While OSDD is primarily focused on TB and malaria (its research and development is described here: **http://www.osdd.net/research-development**), it has also begun to expand its work to additional neglected diseases (OSDD, 2015).

OSDDm, the malaria branch of the organization, has partnered with MMV, signing an MoU "for research towards the development of new and effective drugs for malaria and conducting the preclinical and clinical trials of potential drugs in India under the OSDD umbrella" (OSDD, 2015).

Current "computational resources integrated into OSDD" are:

1) TBrowse: Largest integrative genomic resource on Mtb H37Rv;
2) CRDD: Comprehensive resource for drug discovery;
3) OSDDChem: Database of molecules with anti-TB drug like properties;
4) MetaPred: Predict cytochrome P450 isoform responsible for drug metabolism;
5) KetoDrug: binding affinity prediction of ketoxazole derivatives against FAAH;
6) KiDoq: Docking energy score based prediction of antibacterials;
7) ccPDB: Compilation and creation of datasets from PDB; and
8) GiDoQ: QSAR and docking prediction of Mtb inhibitors (OSDD, 2015).

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

THE INDIAN OPEN SOURCE DRUG DISCOVERY (OSDD) INITIATIVE

Effectiveness:

"Currently more than 1500 registered participants are working on more than 100 projects posted online. These participants are from 31 countries. OSDD harnesses the competencies of private sector through public private partnerships in an open mode. All research results are published on the website"… "The new drug that is likely to come out of the drug discovery process will be made available as a 'generic' molecule, free of intellectual property (IP) constraints for the industry to manufacture and distribute anywhere in the world, thereby ensuring that the prices are affordable" (OSDD WHO proposal).
The "OSDD project created a data repository for genome-level information regarding the strain H37Rv, by recruiting volunteers to gather relevant research articles, extract the data and transcribe it into a standardized format. The aggregation of this process is TBrowse, a publicly-available integrative genomics map" (Ardal, 2012).

Critiques/Questions Raised in the Literature:

As of 2014, funds for OSDD had run out. It is unclear whether additional financing was procured (TOI OCDD, 2014). OSDD asserts ownership over all content published via its domain (Ardal, 2012). "OSDD encourages international collaboration, but its process facilitates contributions from mostly Indian researchers and students" (Ardal, 2012). On OSDD's newer online repository, Sysborg, "[n]o content may be viewed… without first logging on. When registering, the user must accept the terms and conditions of the CSIR OSDD license, a non-standard license written specifically for the project. The license affirms that CSIR OSDD owns all content posted to Sysborg. Therefore, content is not a part of the public domain" and "there is no stipulation in the license that CSIR OSDD must adopt non-exclusive licensing of the resulting products or any stipulations regarding the final price of these products" (Ardal 2012).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Non-University Partners:
AU-KBC; AstraZeneca; Cambia; HP; India 800 Foundation; Infosys; Jalaja Technologies; LeadInvent; Premas Biotech; SBI; Spicy IP; Sun Microsystems; TCG LifeSciences, etc.

University Involvement:

Acharya Narendra Dev College; Bangalore University; Bharathidasan University; Calicut University; Calcutta University; CDFD, Hyderabad; CUSAT; Ambedkar University; Guru Nanak Dev University; IIT Kharagpur; IIT, Madras; IIT Bombay; IIT Kanpur; IIT Technology Guwahati; IIT Delhi; Jawaharlal Nehru University; Kalyani University; Loyola College; Pune University; Malabar Christian College; Manipur University; MG University; Miranda House; Pondicherry University; Pune University; SASTRA University; Saurashtra University; University Of Delhi; University of North Bengal; University of Burdwan; University of Madras; University of Goa; University of Jammu; University of Hyderabad; University of Kerala; and Vidyasagar University.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

COLLABORATIVE DRUG DISCOVERY (CDD)

General Approach/Methods Applied:

(OPEN) Collaborative "cloud-based" tool to enable neglected disease/other researchers from usually separate areas to collaborate and share compounds and drug discovery data via an online database.

Summary:

Founded in 2004 as a spinout of Eli Lilly Co., Collaborative Drug Discovery (CDD) "is a hosted biological and chemical database that securely manages . . . private and external data" (CDD, 2015). "The broad goals of Collaborative Drug Discovery (CDD) are to enable a collaborative "cloud-based" tool to be used to bring together neglected disease researchers and other researchers from usually separate areas, to collaborate and to share compounds and drug discovery data in the research community, which will ultimately result in long-term improvements in the research enterprise and health care delivery" (Ekins, 2013). Many partners including DNDi, Johns Hopkins University, Pfizer, The Rockefeller University, Seattle BioMed, and University of Pennsylvania use the CDD Vault, its drug discovery data-sharing platform. CDD is "a tool for mining and sharing data with collaborators" (CDD, 2015). As a service to the community, CDD hosts Public Access Data relevant to drug discovery from leading research groups around the world" via CDD Public (CDD, 2015).

Main Project(s):

One project completed via CDD Vault is "[t]he FP7-funded Kinetoplastid Drug Development (KINDReD) consortium, [which] has been created to strengthen and advance the current drug development pipeline in neglected infectious diseases. The consortium's key objective is to bring promising anti-trypanosomatid drug discovery initiatives forward by combining the strengths of key experts in industry and academia to create a unique and powerful drug discovery platform with the common goal of advancing promising laboratory-driven discoveries into clinical utility. The KINDReD consortium integrates leading academic laboratories in Europe (Portugal, United Kingdom, France and Switzerland), the USA (California), India and South America (Brazil) with high throughput screening (HTS) facilities equally distributed between all three major kinetoplastid parasites. CDD Vault is the collaborative data management platform used across all consortium members" (CDD, 2015).

Additionally, as part of its work with the Gates Foundation on TB, funded via a US$1,896,923 grant from the Foundation, "CDD Vault is used by 250 researchers across 58 laboratories" and will be creating a CDD TB Database (CDD, 2015; CDD, 2008).

The International Anti-Malarial Collaboration "established to evaluate anti-malarial compounds for the growing challenge of chloroquine resistance" was run via CDD Vault, allowing for a great deal of time saved (CDD, 2015).

Effectiveness:

According to a 2013 article, "CDD has effectively lowered the "activation barrier" for data archival of low, medium, and even high throughput experiments" (CDD, 2013).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

CDD will be creating a CDD TB Database (CDD, 2015).

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

COLLABORATIVE DRUG DISCOVERY (CDD)

Organizations, Stakeholders, And/Or Partners:

Non-University Participants/Partners:
Accelrys; ADMEdata.com; Assay Depot; BMGF; ChemAxon; ChemSpider; Drug Discovery Alliances; Eli Lilly and Co.; EPFL; The Founders Fund; GlaxoSmithKline; InChi Trust; Microsoft; Omidyar Network; NIH; The Synaptic Leap; The Tropical Disease Initiative; DNDi (Drugs for Neglected Disease Initiative); MMV (Medicines for Malaria Venture); Sanofi Avenits; Wemberly Scientific, etc.

CDD Vault Users:
http://www.collaborativedrug.com/pages/who

University Involvement:

Vault users include UCSD; UPenn; Columbia University; Harvard; Johns Hopkins University; University of Sydney; Stanford, etc.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

THE STRUCTURAL GENOMICS CONSORTIUM (SGC)

General Approach/Methods Applied:

(COLLABORATIVE + OPEN) Consortium providing an open access, collaborative network focused on less well-studied areas of the human genome as a means towards developing new medicines.

Summary:

The Structural Genomics Consortium, SGC, formed in 2004, is "a public-private partnership that supports the discovery of new medicines through open access research" focused on "less well-studied areas of the human genome" (SGC, 2015), or "pre-competitive structural biology research" (RAND SGC, 2015). "The SGC accelerates research in these new areas by making all its research output available to the scientific community with no strings attached, and by creating an open collaborative network of scientists in hundreds of universities around the world and in nine global pharmaceutical companies" (SGC, 2015). SGC's Strategic Alliances and Communications team "is responsible for promoting, managing and fostering interaction with all external communities concerned with drug discovery, including scientists from correlated areas, patient groups, funders, government agencies and media" via "strategic grants, institutional collaborations, interaction with policy makers and governments, public engagement and outreach, and communications and media" (SGC, 2015). According to SGC, "for a donation of 8 Million US dollars, an organization gains the following rights: The right to nominate targets to the Target List; The right to nominate a member to the Scientific Committee and the Board of Directors; [and] The right to place scientists to work within the SGC laboratories, under a confidentiality agreement" (SGC, 2015). Structural information is only available to members prior to being released to the public by the Protein Data Bank (PBD) or SGC into the public domain (SGC, 2015).

According to a recent evaluation, "the [SGC] model is distinctive for three reasons. Firstly, all outputs produced by the SGC are made publicly available and intellectual property restriction on use is ruled out until later stages of clinical trials. Secondly, for a fixed annual sum, all SGC funders have the opportunity to determine the direction of SGC research, nominate someone to join the SGC board of directors and place scientists to work in SGC laboratories. Thirdly, the model represents a long-term, international, multiple-funder initiative which has the potential to provide stability to the sector" (Castle-Clarke, 2014).

Main Project(s):

SGC works primarily in epigenetics and also has a structural biology programme and technological science capacity via its Biotechnology and other affiliated groups (SGC, 2015).

Chemical Probes for Epigenetics: Since 2008 the SGC has "led an initiative to develop chemical probes that can selectively stimulate or block the activity of proteins involved in epigenetic control, complementing genetic knockouts and RNAi approaches to understand the cellular role of these proteins." SGC has also conducted research that led to "continual generation of high-quality, open access chemical probes for epigenetics proteins (in excess of 14 probes, as of July 2013)."

Target Characterization: In coordination with GSK, SGC "identified the potential of Brd4 as a drug discovery target"… "With the Frye laboratory, [SGC] found that methyl-lysine binding proteins can be targeted with small-molecules; possible relevance to reprogramming and regenerative medicine"…. SGK also "[h]elped GSK to identify the potential of histone demethylase JMJD3 as a drug discovery target in inflammation" and "[w]orked with scientists at Pfizer and at UBC to show that SETD7 is involved in the control of cell size" (SGC, 2015).

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

THE STRUCTURAL GENOMICS CONSORTIUM (SGC)

Structures: SGC "[d]eposited more than 1500 high-resolution structures of medically relevant human and parasite proteins into the public databases" and "[s]olved the structure of the first human ABC transporter: the mitochondrial ABC transporter ABCB10 (PDB ID 2YL4) and the first structure of human ZMPSTE24, a nuclear zinc metalloprotease involved in laminopathies, which includes progeria (PDB ID 4AW6, 2YPT)." SGC conducted [s]tructural and functional characterization of ERAP1 protease (PDB ID: 3QNF; Kochan et al, PNAS 2011) and TNIK (PDB ID: 2X7F, GWAS-linked targets for ankylosing spondylitis and schizophrenia respectively" and developed "3D structures of more than 75 novel human protein kinases (of which 63 were released for the first time in the public domain)" (SGC, 2015).

Recombinant Antibodies: SGC "[h]elped coordinate Renewable Protein Binding Working Group (incorporating more than 11 institutions worldwide) that produced hundreds of antibodies targeting 20 SH2 domain proteins" and "[l]aunched a project to develop technologies, libraries and recombinant antibodies to human epigenetic proteins. The project is carried out in partnership with several of the world leaders in the field (Sidhu, Kossiakoff, Dübel, Koide) and all output is to be made available without restriction on use." SGC also "[g]enerated single digit nM (nanomolar) recombinant antibody and antibody-like reagents to over 100 human proteins" (SGC, 2015).

Effectiveness:

"The SGC commissioned RAND Europe and the Institute on Governance in Canada to provide an evaluation of the SGC's unique, open-access model" (RAND SGC, 2015). The evaluation found "that the Structural Genomics Consortium is a viable model for drug discovery that appeals to investors, not least for advantages in efficiency over current models of public or commercial health research.

Specific findings included: "Research by SGC is viewed as reliable and highly reproducible, which is valued by investors; Many investors view the SGC as a way to "de-risk" novel areas of science; Many stakeholders cited the fact that the SGC enables rapid and efficient research processes as an incentive for investment; Open access facilitates extensive collaborations across public and private sectors and was welcomed by the clear majority of interviewees; [and] The mix of public and private investment in the SGC allows it to remain innovative and efficient, in terms of the structures it studies and the methods it develops" (RAND SGC, 2015).

RAND Report on SGC:
http://www.rand.org/pubs/research_reports/RR512.html

Critiques/Questions Raised in the Literature:

Questions raised about the SGC include "whether public sector funding in the consortium will continue in the long-term – a feature deemed by many to be essential to the maintenance of open access" (Castle-Clarke, 2014). Other criticism of the SGC model include that there are currently too many collaborators involved and that this is contributing to the dilution of the SGC mission (RAND SGC, 2014).

Organizations, Stakeholders, And/Or Partners:

Non-University Partners: Abbvie; Bayer; Boehringer Ingelheim; Canada Foundation for innovation; The Sao Paulo Research Foundation; Genome Canada; Janssen; Merck; Novartis; the Ontario Ministry of Research and Innovation; Pfizer; Takeda; The Wellcome Trust, etc.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

THE STRUCTURAL GENOMICS CONSORTIUM (SGC)

University Involvement:

UBC has collaborated with SGC; UToronto, Unicamp, and UOxford house SGC laboratories.

SGC Members: University of Oxford; University of Toronto; Universidade Estadual de Campinas; University of Karolinska; The University of North Carolina; and Goethe University Frankfurt

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

WIPO RE:SEARCH

General Approach/Methods Applied:

(COLLABORATIVE + OPEN) Multi-stakeholder coalition with an online, open access, collaborative database providing access to IP, including pharmaceutical compounds, technologies, know-how and data available for R&D for NTDs, TB, and malaria.

Summary:

Formed in 2011 by the World Intellectual Property Organization (WIPO), several leading pharmaceutical companies, and BIO Ventures for Global Health (BVGH), the multi-stakeholder coalition "WIPO Re:Search provides access to intellectual property, including pharmaceutical compounds, technologies, and . . . know-how and data available for research and development for neglected tropical diseases (NTDs), tuberculosis, and malaria. By providing a searchable, public database of available intellectual property assets and resources, WIPO Re:Search facilitates new partnerships to support organizations that conduct research" (WIPO, 2015). Members include providers who "contribute intellectual property know-how, expertise, materials, and other services," users, who "can search the public database and communicate their resource wants and needs to BVGH," and supporters who "provide meaningful support and guidance to ensure the long-term success of WIPO Re:Search. This category of membership allows interested parties, such as national patent offices, to support WIPO Re:Search's goals" (WIPO, 2015). "The Partnership Hub, led by BIO Ventures for Global Health, proactively identifies opportunities for collaboration and knowledge-sharing between members.

WIPO Re:Search, via its Database, Collaborations (via the Partnership Hub) and Supporting services such as R&D knowledge transfer, facilitates access to private-sector compounds and compound libraries, helping to repurpose drugs. It acts as a gateway to a range of development-related tools, including training in IP management" (WIPO, 2015). "WIPO Re:Search Guiding Principles seek to ensure that all products developed through WIPO Re:Search partnerships will be accessible, royalty-free in all least developed countries" (WIPO, 2015).

WIPO's Guiding principles: **http://www.wipo.int/export/sites/www/research/docs/guiding_principles.pdf**

Main Project(s):

WIPO Re:Search's "proactive partnering approach has proven to be highly successful, resulting in over 70 partnerships across 15 diseases" as of 2014 (Ramamoorthi, 2014).

"The WIPO Re:Search database provides information on the intellectual property assets available for licensing from WIPO Re:Search," available here: **http://www.wipo.int/research/en/search**

Effectiveness:

Effectiveness remains unclear although over 70 partnerships have been brokered via WIPO Re:Search (Ramamoorthi, 2014).

Critiques/Questions Raised in the Literature:

While larger pharmaceutical companies can screen products for smaller members of WIPO Re:Search, if something promising is found the problem of moving forward where more funding is needed arises since SMEs often do not have enough financial resources to carry out further research (New, 2015). Whether these candidates should be handed over to PDPs or developed in-house has yet to be answered, and what structure would be necessary for this next phase remains unclear (New, 2015). Currently, the project remains far from delivering actual drugs but has made immense progress in access to research (New, 2015). The project is supposed to promote patent-sharing partnerships but has yet to spur development

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

WIPO RE:SEARCH

of new drugs or therapies. Additional criticism includes the potential for limiting of sales for resulting products to the most unprofitable markets and the lack of a uniform license format for these products. “Without commitment of all the needed information, technical expertise, and funding and an orientation toward commercialization, [WIPO Re:Search] will be pretty useless in generating innovations for global health” according to critics (Dippel, 2013).

Proposed Changes/Improvements:

There is a possibility that WIPO Re:Search will expand its work into drug development (New, 2015). WIPO recently brought in Richard Mahoney as a consultant to assess its current status and make plans for the future including for the possibility of a product pipeline (New, 2015).

Organizations, Stakeholders, And/Or Partners:

WIPO Re:Search currently has 93 members from the private and public sector.

Non-University Partners:
Alnylam, Center for Infectious Disease Research; DNDi; Eisai; Eskitis; GSK; Infectious Disease Research Institute; International Vaccine Institute; Medical Research Council of South Africa; MMV; Merck; NIH; Novartis; PATH; Pfizer; Sanofi; Walter Reed Army Institute of research, etc.

University Involvement:

University of Bamako; University of British Columbia; University of Buea; University of California Berkeley; University of Dundee; University of Edinburgh; University of South Florida; University of Ibadan; University of Kansas; University of Washington; Stanford; LSTM; MIT; McGill; Northeastern; Caltech, etc.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

CAMBIA'S PATENT LENS AND INITIATIVE FOR OPEN INNOVATION (IOI)

General Approach/Methods Applied:

(OPEN) Non-profit international research organization that provides an open access and collaborative public resource for innovation via its Patent Lens and IOI initiatives to create a more equitable and inclusive capability to solve problems using science and technology.

Summary:

Founded in 1992, Cambia (The Centre for Applications of Molecular Biology in Agriculture) is a non-profit international research organization and social enterprise based in Australia, where it "is affiliated with and headquartered on the Gardens Point campus of Queensland University of Technology" (Cambia, 2015). Cambia's work is built around open science, biology, and intellectual property. As Cambia's website puts it, "Our mission is to democratize innovation: to create a more equitable and inclusive capability to solve problems using science and technology" (Cambia, 2015). Cambia's work, via BiOS (Biological Open Source), is focused on the Initiative for Open Innovation (IOI); and the Lens project, both of which work to provide an open and collaborative public resource for innovation (Cambia, 2015). "The BiOS initiative operates in two main areas: intellectual property informatics and analysis through the Patent Lens; and innovation-system structural reform through the BiOS licenses" (Cimoli, 2014). With ex post sharing of patented and patentable technologies, "those who join BiOS agree not to assert intellectual property rights against each others' use of the technology to conduct research, or in the development of products" (Cimoli, 2014).

Main Project(s):

Cambia's three main projects are the Patent Lens, BiOS, and CambiaLabs (Cambia, 2015).

Part of BiOS is the Initiative for Open Innovation (IOI), which launched in 2009, is endorsed by WIPO and funded by BMGF, and "is a new international facility to increase the effectiveness and equity of science- and technology-enabled innovation for public good. IOI fosters evidence-based navigation and operation within the complex intellectual property landscapes that surround innovation . . . With an initial focus on life science, IOI will create a comprehensive global cyberinfrastructure that is sector, discipline, jurisdiction and language agnostic. IOI will also, through 'embedded practice' explore the boundaries of open innovation to create, test, validate and support new modes of collaborative problem solving made possible with the heightened transparency of the system" (IOI, 2015). IOI is meant to make "the world's patent systems more transparent, inclusive, and navigable" (IOI, 2015).

"The major work product of the IOI is the Patent Lens – a worldwide, open-access, free full-text patent informatics resource. The Patent Lens can search and retrieve the full-text of nearly ten million patent documents from US, Europe, Australia and WIPO, their status and counterparts in up to 70 countries, and over 77 million DNA, RNA and protein sequences disclosed in patents" (IOI, 2015). The Lens project was started in 2000 but has been expanded and improved under IOI with the most recent Lens launched in 2013 (IOI, 2015). IOI, with its initial funding of AU$5 million, has worked to create "patent landscapes for malaria, tuberculosis, dengue and other critical infectious diseases of the developing world" (Smith, 2014).

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

CAMBIA'S PATENT LENS AND INITIATIVE FOR OPEN INNOVATION (IOI)

Cambia's BiOS initiative, launched in 2006, is "an effort to develop new innovation ecosystems for disadvantaged communities and neglected health priorities" via its '3-D' philosophy, "Democratize, Decentralize and Diversify" and "Design, Develop, and Disseminate" and is considered an open source licensing solution (BiOS, 2015). BiOS is meant to work to "foster decentralized, cooperative innovation in the application of biological technologies, through the merging of: intellectual property informatics and analysis; innovation system structural reform; [and] cooperative open access technology development activities" (BiOS, 2015).

BiOS Portfolio: **http://www.bios.net/daisy/bios/2029/version/default/part/AttachmentData/data/BiOS%20Initiative%20Phase%202006-2008.pdf**

Effectiveness:

BioForge, the collaborative platform under Cambia, was unsuccessful but Patent Lens has proven an effective open platform (Smith, 2014). BioForge, while successful immediately following its launch in 2005, accruing 2,000 registered users to the Web Portal-based active development community, stopped growing within a year. This may have been due to lack of motivation among scientists to collaborate online unless it helps solve immediate challenges and/or lack of standardization across biotech work (Spring, 2011). It appears that IOI, the follow-up platform to BioForge, may address some of these concerns.

"As of 2009, [Patent Lens] contained more than nine million patents, and over 68 million DNA and protein sequences disclosed in patents" (Spring, 2011). The success of Patent Lens has been attributed to the "low cost of entry for participants and subdivision of complex challenges into simpler sub-challenges among other things (Smith, 2014).

Critiques/Questions Raised in the Literature:

While the Patent Lens project has proven to be a success as "an open Web resource for patent search and analysis[,] the BiOS licensing infrastructure was met with enthusiasm by some organizations, but it had problems in becoming truly effective in its goals" (Smith, 2014), which is why Cambia has shifted its focus to IOI. One of the reasons why BiOS may not have had the desired impact of encouraging open projects is of course the price associated with biotechnology development, which makes Cambia's licensing scheme prohibitive for smaller organizations. Additionally, "in order to create a pool of components large enough to create new solutions, distinct methods may need to be licensed" (Spring, 2011).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Cambia receives funding from the Bill & Melinda Gates Foundation, the Lemelson Foundation, Horticulture Australia and the Queensland University of Technology as well as donations for project-specific work listed below.

Donors:
Rockefeller Foundation; Ministry of Foreign Affairs of the Government of Norway; Rural Industries Research and Development Corporation; Grains Research and Development Corporation; Australian Research Council; International Food Policy Research Institute; International Plant Genetics Resources Institute; NSW Agriculture; Charles Stuart University; Business ACT; Finkel Foundation

Non-University Partners:
International Rice Research Institute; Centro Internacional de Agricultura Tropical; International Maize and Wheat Improvement Center; International Food Policy Research Institute; Generation Challenge; HarvestPlus; Yale University Access to Knowledge (A2K), etc.

University Involvement:

Queensland Univ. of Technology. University of Melbourne on IOI (Singh, 2008). Yale University; Charles Stuart University, etc.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

TDR TARGETS

General Approach/Methods Applied:

(OPEN) Collaborative knowledge-sharing platform with an open access database to facilitate the identification and prioritization of drugs and drug targets in neglected disease pathogens.

Summary:

"TDR, the Special Programme for Research and Training in Tropical Diseases, is a global programme of scientific collaboration that helps facilitate, support and influence efforts to combat diseases of poverty. It is hosted at the World Health Organization (WHO), and is sponsored by the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the World Bank and WHO."
http://who.int/tdr/about/en/

"The TDR Targets project seeks to exploit the availability of diverse datasets to facilitate the identification and prioritization of drugs and drug targets in neglected disease pathogens. Th[e] database functions both as a website where researchers can look for information on targets of interest, and as a tool for prioritization of targets in whole genomes" (TDR Targets, 2015). The TDR Targets database is currently Version 5 of the project (TDR Targets, 2015). Updates in the past have included "the addition of new genomes (specifically helminths), and integration of chemical structure, property and bioactivity information for biological ligands, drugs and inhibitors and cheminformatic tools for querying and visualizing these chemical data. These changes greatly facilitate exploration of linkages (both known and predicted) between genes and small molecules, yielding insight into whether particular proteins may be druggable, effectively allowing the navigation of chemical space in a genomics context" (Magarinos, 2012).

Main Project(s):

TDR Targets includes information specific to Malaria, Tuberculosis, Leprosy, Toxoplasmosis, Filariasis, African Trypanosomiasis, Leishmaniasis, American Trypanosomiasis, and Schistosomiasis (TDR PPT, 2008).

List of TDR Targets: http://tdrtargets.org/search

Effectiveness:

No Information found.

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

"A number of key improvements are necessary to keep TDR Targets useful, up to date and relevant for the community of scientists working on tropical diseases. Development of web services and other computational tools to facilitate reuse of data is one area that will be a major focus in the future. Incorporating information on the commercial availability of compounds, and providing links to providers is another key aspect that will be incorporated in future releases. But more importantly perhaps, a sustained curation effort is also required to keep valuable target validation data and compound activity data up to date, and to identify valuable medicinal chemistry data for integration in TDR Targets' chemical database. As mentioned above, the focus of the TDR Targets curation effort has been largely put on the gathering of information on validating credentials for targets. However, now that a substantial investment has been made into the integration of compound data, curation should be extended to gather other supporting information, such as data on assays, and on the reported activities of compounds (in the form of IC50s, %inhibition, phenotypes, etc.)" (Margarinos, 2012).

Organizations, Stakeholders, And/Or Partners:

The TDR Drug Targets Network includes UNSAM, UPenn, UWash, Sanger, UniMelb, and WHO/TDR (TDR Targets, 2015).

University Involvement:

UPenn; UWashington; University of Melbourne.

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

THE SYNAPTIC LEAP (TSL)

General Approach/Methods Applied:

(OPEN) Open and collaborative network of online research communities that connect and enable open source biomedical research and drug discovery via knowledge sharing.

Summary:

The Synaptic Leap (TSL) website was launched as an open and collaborative research community in 2006 aiming "to provide a network of online research communities that connect and enable open source biomedical research" (Ardal, 2012). It began in 2005 as a partnership with the Tropical Disease Initiative, focused primarily on malaria, before it officially became its own entity (TSL RDI, 2015). "It was launched with four pilot disease research areas: malaria, schistosomiasis, toxoplasma and tuberculosis. Each area had a project leader with the responsibility of gathering and motivating international researchers to contribute to the Synaptic Leap community by sharing results, giving feedback and possibly undertaking new research tasks" (Ardal, 2012). Results shared via the website form a knowledge commons and are considered part of the public domain and "may be utilized by third parties without contracts or royalties" (Ardal, 2012).

Main Project(s):

The schistosomiasis project is the most active project; other projects include work on Malaria, Toxoplasma, and Tuberculosis (Kepler, 2006). One of the projects "at TSL concerns the synthesis of the active enantiomer of Praziquantel [,] the drug used in the treatment of schistosomiasis worldwide"… "The challenge for the community is to develop a method for its synthesis that competes with the current $US 0.07 per 600 mg pill of the racemate, namely $US 0.23 per enantiopure gram" (Kepler, 2006).

Effectiveness:

"Since launch, the malaria, toxoplasma and tuberculosis communities have been relatively silent. However, the schistosomiasis community has consistently utilized the website to share findings, discuss research results and identify new, necessary research tasks . . . The aim of the TSLS project was a well-defined drug development task – to generate the off-patent schistosomiasis drug, praziquantel, as a single enantiomer . . . This led to the funding of the TSLS project in 2008 by both WHO and the Australian government. The TSLS project completed this task in 2011" (Ardal, 2012).

Critiques/Questions Raised in the Literature:

"Intellectual property does not play a major role in this project since a version of praziquantel has been in the public domain for almost two decades." Praziquantel has been one of the main focuses of TSL (Ardal, 2012).

Proposed Changes/Improvements:

"TSL's website could also be improved. Postings are not necessarily in chronological order and there is no easy method to see all postings related to one disease area" (Ardal, 2012).

Organizations, Stakeholders, And/Or Partners:

The Synaptic Leap is an off-shoot of the Tropical Disease Initiative and is largely funded by the WHO and the Australian Government.

University Involvement:

Matthew Todd, University of Sydney, who focuses on schistosomiasis, is one of the biomedical research advisors as are Thomas Kepler from Duke University and Marc A. Marti-Renom from Prince Felipe Research Center and formerly UCSF. Stephen Maurer of UC Berkeley and Arti Rai of Duke University are the intellectual property and policy advisors (Gtaylor, 2006).

A1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

KAGGLE

General Approach/Methods Applied:

(OPEN) Online collaborative platform for data-mining and predictive-modeling competitions via crowdsourcing.

Summary:

Kaggle, founded in 2010 in Melbourne by Anthony Goldbloom, "is the world's largest community of data scientists. [Participants] compete with each other to solve complex data science problems, and the top competitors are invited to work on the most interesting and sensitive business problems from some of the world's biggest companies through Masters competitions" (Kaggle, 2015). Kaggle is a "two-sided marketplace that bridges the gap between data problems and data solutions. Kaggle is free to all data scientists; [the] fees are paid by the owner of the data problem" (Kaggle, 2015). Kaggle "began as a platform for hosting public data science challenges, in which sponsors posed their problem to the Kaggle platform" (Kaggle, 2015). According to the site, data scientists that are members of the Kaggle community use Kaggle for prize money and data as well as "to meet, learn, network and collaborate with experts from related fields" (Kaggle, 2015). Kaggle is essentially "an online platform for data-mining and predictive-modeling competitions" (Goetz, 2013).

Main Project(s):

Among its many projects, Kaggle hosts the Heritage Health Prize.

Ongoing competitions hosted by Kaggle:
https://www.kaggle.com/competitions

Effectiveness:

85,000 data scientists have entered Kaggle competitions (Goetz, 2013).

Critiques/Questions Raised in the Literature:

"One very valid criticism of Kaggle is that the competitions [it] hold focus on a very small subset of a data scientist's role: namely feature engineering and model validation" (Sornarajah, 2015). Additionally, in February 2015, Kaggle cut about a third of its staff as it was struggling to find new ways of creating money (McMillan, 2015).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Partners vary based on the given competition but have included Microsoft, Data Science London, the California Healthcare Foundation, Merck, and the Mayo Clinic (Kaggle, 2015).

University Involvement:

UC Berkeley, Columbia, Harvard, University of Oxford, Cornell, UToronto, and Stanford have all hosted competitions via Kaggle (Kaggle, 2015).

A2 DRUG DISCOVERY INCENTIVES
A. PRIZES

LONGITUDE PRIZE OPEN

General Approach/Methods Applied:

(PULL) Incentive provided via an ex-ante inducement prize awarded to the submission considered most impactful and feasible, currently for a competitive AMR innovation.

Summary:

The Longitude Prize (LP), which is a challenge with a prize fund of £10 million, was launched in 2014 and is being run by Nesta, the UK's innovation foundation. The public selected the focus for the competition from several of the most prominent current global issues. "It was launched by the Prime Minister at G8 . . . and is supported by the Technology Strategy Board, the UK's innovation agency, as funding partner" (LP Report, 2014). The prize will be awarded specifically for innovation in antibiotics, to a "competitor that can develop a point–of–care diagnostic test that will conserve antibiotics for future generations and revolutionise the delivery of global healthcare. The test must be accurate, rapid, affordable, easy–to–use and available to anyone, anywhere in the world. It will identify when antibiotics are needed and, if they are, which ones to use" (LP Report, 2014). According to the LP Report (2014), "diagnostics that can be used globally will have a greater potential impact than those that are only suitable for use in well-resourced medical systems."

The 'Impact Assessment' for submissions will be comprised of Stage 1 Access assessment criteria: 1. Level of healthcare resources required; 2. Need for diagnostic; 3. Time to result; 4. Cost per test, and Stage 2 assessment criteria: 5. Accuracy (independent lab verification); 6. Potential contribution to global surveillance of AMR; 7. Market analysis (LP Report, 2014). The prize criteria emphasize applicability across healthcare settings and 'value for money', or cost-effectiveness, as well as clear and measurable impact and an open review process is being applied in developing the assessment process.

Main Project(s):

The first challenge is ongoing and focused on AMR.

Effectiveness:

Unknown.

Critiques/Questions Raised in the Literature:

Critics argue that the LP focuses solely on science, ignoring the larger political and social factors that may very well impede adequate supply and distribution of any subsequent discovery (NRM, 2014).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Nesta (UK innovation foundation); Innovate UK (UK Technology Strategy Board); BBC; Science Museum; Amazon; National Maritime Museum; Sciencewise (UK national centre for public dialogue in policy-making involving science and tech issues); National Schools Partnership; Science Practice; Marks & Clerk IP Services; and Antibiotic Action.

University Involvement:

Imperial College London; Polish Academy of Sciences; Imperial College London; Erasmus Univ. Medical Centre; London School of Hygiene and Tropical Medicine; University of Reading; York University; Harvard University; University of Antwerp; UBC; University of Birmingham; Imperial College; University of Cambridge; University of Nottingham; and University of Edinburgh.

A2 DRUG DISCOVERY INCENTIVES
A. PRIZES

X-PRIZE FOUNDATION

General Approach/Methods Applied:

(PULL) *Milestone inducement prize* contest to spur and accelerate innovation with a current competition to develop an improved TB diagnostic tool.

Summary:

XPrize is an incentivized prize competition meant to spur and accelerate innovation. The Prize focuses on problems without current solutions, with objective and measurable goals defined as audacious but achievable, and targets market failures concerning capital being spent or lack thereof. Additionally, winning submissions must be achievable within a reasonable time frame. The prize is designed to be leveragable and drive investment, allowing and enabling innovators to attract capital, support and team members (XPrize, 2015).

Main Project(s):

While many of the prize competitions run by X-Prize are not specific to global health, the Foundation has recently partnered with the Bill & Melinda Gates Foundation to develop a prize for a better tuberculosis diagnostic tool.

Effectiveness:

In 2013, XPrize had to cancel its US$10 million Archon Genomics competition due to lack of interest and only a handful of submissions (Kaiser, 2013).

Critiques/Questions Raised in the Literature:

There is criticism concerning the topics selected for XPrize competition, which are often seen as not of social value and as “the domain of the rich” (OTC XPrize, 2007).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Westfield; Suncor Energy; Credit Suisse; Barclays; Cisco; Google; Heritage Provider Network, etc.

XPrize has numerous donors:
http://www.xprize.org/benefactors/vision-circle

University Involvement:

None found.

A2 DRUG DISCOVERY INCENTIVES
A. PRIZES

PRIZE4LIFE FOUNDATION

General Approach/Methods Applied:

(PULL + OPEN) *Milestone inducement prize* contest with competitions to accelerate discovery of cures and treatments for amyotrophic lateral sclerosis (ALS) as well as crowdsourcing challenges and a data sharing platform.

Summary:

Prize4Life (P4L), founded in 2006 by a group of Harvard Business School students, is a non-profit that holds prize competitions specifically geared towards accelerating the discovery of cures and treatments for amyotrophic lateral sclerosis (ALS) by using powerful incentives to attract new people and drive collaborative innovation (Prize4Life, 2015). Additionally, Prize4Life "proactively track[s] the current efforts of other ALS related organizations to avoid redundancies. With every dollar that [it] invest, [P4L] seek to encourage the investment of others, and amplify the impact of external investments to develop new treatments and a cure for ALS" (Prize4Life, 2015).

Main Project(s):

P4L awarded the US$1M ALS Biomarker Prize in February of 2011 to Dr. Seward Rutkove for "the development of electrical impedance myography (EIM) which allows for a much more sensitive measure of disease progression" (Prize4Life, 2015).

The $1M Avi Kremer ALS Treatment Prize, which was launched in 2012, "aims to fill the drug development pipeline with promising therapeutics by encouraging researchers to extend the lives of ALS mouse models by 25%" (Prize4Life, 2015).

Effectiveness:

"Prize4Life and DREAM have demonstrated the power of open Challenges to advance ALS disease research. The ALS Prediction Prize, conducted in 2012, had over 1,000 registrants from 63 countries, and the winning approaches"… "outperformed the predictions of more than 12 expert clinicians of ALS, and should make it possible to reduce the costs of future clinical trials by roughly [US]$6 million per trial in part by reducing patient enrollment by up to 20%" (Business Wire, 2015).

ALS Prediction Prize details:
http://www.innocentive.com/prize4life-announces-50000-als-prediction-prize-winners

"The Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database houses the largest ALS clinical trials dataset ever created. It is a powerful tool for biomedical researchers, statisticians, clinicians, or anyone else interested in "Big Data." PRO-ACT merges data from existing public and private clinical trials, generating an invaluable resource for the design of future ALS clinical trials" (Prize4Life, 2015).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

IBM Research; Neurological Clinical Research Institute at Massachusetts General Hospital; ALS Therapy Alliance; Northeast ALS Consortium (Prize4Life, 2015).

University Involvement:

The Icahn School of Medicine at Mount Sinai; Harvard Business School

A2 DRUG DISCOVERY INCENTIVES
A. PRIZES

EU VACCINE PRIZE

General Approach/Methods Applied:

(PULL) *End product inducement prize* to be awarded for a vaccine cold chain innovation.

Summary:

The EU (European Union) Vaccine Prize was developed by the European Commission. EUR 2 million is being offered for an innovation that can help solve the challenge of guaranteeing that life-saving vaccines are not damaged during transport and storage to those in tropical and developing countries. The prize is meant to spur a viable alternative to current cold-chain technology. Solutions can include changes in vaccine formulation, preservation, transportation, etc. (European Commission, 2014). The prize is only available to entities established in a Member State of the European Union or an associated country. The jury prefers proposals that demonstrate applicability to vaccines for a wide range of diseases and which demonstrate effectiveness under various field conditions. Safety and affordability are also key criteria.

Main Project(s):

The German biopharmaceutical company CureVac GmbH won the EU Vaccine Prize in 2014 after 12 entries out of the 49 registered competitors were assessed by the Vaccine Prize Jury (European Commission, 2014).

Effectiveness:

Following the award of the prize to CureVac GmbH for its thermostable vaccine technology, the Gates Foundation committed to invest EUR “46 million in CureVac to accelerate the development of its innovative vaccine technology and the production of numerous vaccines against infectious diseases” (European Commission, 2015b). This is a sign that the prize may be effective in attracting additional private investment research.

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Administered by the European Commission and decided by the ‘Jury’.

BMGF; PATH; EU CDC; WHO; Medacta, etc.

University Involvement:

University of Pennsylvania

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.K. VACCINES RESEARCH RELIEF

General Approach/Methods Applied:

(PULL) Tax-based incentive to encourage companies to increase their investment in research and development into vaccines and treatments for certain diseases.

Summary:

Introduced via a bill in 2003, Vaccines Research Relief (VRR), via a tax-driven incentive, aims "to encourage companies to increase their investment in research and development into vaccines and treatments for" diseases including TB, malaria, and HIV/AIDS. The incentive is intended to stimulate companies to increase overall spending on research and development of vaccines and drugs for the prevention and treatment of these diseases. According to the VRR Proposal (2003), "the vaccines research relief can take two forms, a tax relief, which any firms, irrespective of size, may qualify for, or for SMEs (small and medium-sized enterprises) only, a tax credit in the form of a lower level of cash payment up-front, in lieu of any tax relief available."

Main Project(s):

No information available.

Effectiveness:

"The UK authorities estimate[d] that the scheme will result in a real long-term increase in annual expenditure on research and development in this area of approximately £20m – £50m. This estimate [was] based on studies of other R&D tax credit schemes world-wide" (VRR Proposal, 2003).

Critiques/Questions Raised in the Literature:

"A restriction was announced in the Summer Budget 2015 that from 1 August 2015 universities and charities are prevented from claiming R&D expenditure credit on their own research or when working as a contractor" (RM VRR, 2015).

Proposed Changes/Improvements:

In 2008, the VRR was updated to "allow relief for clinical trial payments, extend the SME R&D scheme to mid-sized companies, and to increase the rate of SME R&D relief" (VRR Changes, 2008). Additionally, for large companies, a declaration must be submitted verifying that "availability of the relief claimed has resulted in an increase in the amount, scope or speed of the R&D undertaken by the company, or in the company's expenditure on R&D" (VRR Changes, 2008). As of 2012, VRR relief in addition to R&D relief is now only available to large companies.

Organizations, Stakeholders, And/Or Partners:

UK Government: HM Revenue and Customs and the Department for Business, Enterprise and Regulatory Reform (formerly the Department of Trade and Industry)

University Involvement:

None found.

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. ORPHAN DRUG PROGRAM (ODA)

General Approach/Methods Applied:

(PULL + PUSH) Incentive supplied via additional marketing exclusivity, priority review and grants awarded for development of orphan drugs, tax credits, etc.

Summary:

Under the U.S. Orphan Drug Act (ODA), passed in 1984, "companies are eligible for several extra years of marketing exclusivity, during which time FDA is not permitted to approve a generic, for getting a drug for a "rare" disease approved. This is meant to give companies an added incentive to produce drugs intended for rare diseases, as it allows the company extra time to recoup its development costs and likely turn a profit as well" (Gaffney, 2015). A combination of push and pull incentives offered include a 50% tax credit on clinical development expenses for the company that has developed an approved orphan drug as well as "development grants, counseling and guidance from the FDA, and a guaranteed seven year market exclusivity period" (Grabowski, 2003; Villa, 2008).

Main Project(s):

"Orphan Drug legislation has also been enacted in Japan (1993) and the European Union (1999)" (Grabowski, 2003) and, more recently, Australia (Villa, 2008).

All US FDA orphan drug designations and approvals: **http://www.accessdata.fda.gov/scripts/opdlisting/oopd/**

Effectiveness:

"The program has successfully enabled the development and marketing of more than 400 drugs and biologic products for rare diseases since 1983. In contrast, fewer than 10 such products supported by industry came to market between 1973 and 1983. The Orphan Grants Program has been used to bring more than 45 products to marketing approval. The Humanitarian Use Device Program has been the first step in approval of more than 50 Humanitarian Device Exemption approvals" (FDA, 2015). However, the program has only resulted in therapies for less than 10 percent of all 6,000+ rare diseases (IOM, 2009).

The ODA is also credited for inspiring other programs due to its success including "the Generating Antibiotic Incentives Now Act ("GAIN Act") (FDC Act 505E), and the Dormant Therapies Act provisions included in the draft 21st Century Cures Act" (Karst, 2015).

Critiques/Questions Raised in the Literature:

There is a great deal of concern that the Orphan Drug Grants Program is negatively contributing to exorbitant pricing of orphan drugs. Additionally, "as of July 2003, there [had] been only twelve orphan drug approvals in the United States targeted specifically to tropical diseases"… "This represents approximately five percent of the 238 market approvals for orphan designated indications. Moreover, the majority of the drugs are for conditions that either have some market in the developed countries or the travelers' market (TB, malaria and meningitis) or have other approved indications with a market in developed economies" (Grabowski, 2003). While neglected diseases are eligible under the ODA, the lack of market pull incentives in low- and middle-income countries (LMICs) "corresponding to the prevailing insurance

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. ORPHAN DRUG PROGRAM (ODA)

reimbursement available in developed economies" has counteracted encouragement of research on tropical diseases through the program. Additionally, a recent study found that for "just over two-thirds of all non-cancer orphan drugs approved between July 1, 2010, and June 30, 2014, FDA did not require the orphan drug applications to provide the conventional level of proof of effectiveness that is ordinarily expected for drugs for prevalent diseases" (Sasinowski, 2015).

Proposed Changes/Improvements:

Grabowski (2003) has various suggestions on how an ODA focused on NTDs could be designed involving transferable patent exclusivity rights, transferable priority review rights, or purchase guarantees.

Organizations, Stakeholders, And/Or Partners:

Run by the FDA's Office of Orphan Products Development.

University Involvement:

None found.

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. PATENTS FOR HUMANITY AWARDS FOR MEDICINE

General Approach/Methods Applied:

(PULL) Incentive supplied via an ex parte "prize", typically patent review acceleration, which encourages development of drugs for neglected health needs by reducing the cost and time required to enter the market.

Summary:

In 2012 the United States Patent and Trademark Office introduced the Patents for Humanity (PFH) pilot program, modeled after the PRV program, which similarly rewards "companies who bring life-saving technologies to underserved people" by accelerating approval for a patent (PHP, 2015). "Participating patent owners or licensees submit applications describing how they've used their patented technology or products to address humanitarian challenges for the less fortunate" and of particular relevance is submissions for medicine, which include "any medical-related technology such as medicines, vaccines, diagnostics, or medical devices." According to the website, applications are judged by one of two "sets of criteria, depending on how their technology benefits the less fortunate" (PHP, 2015).

"Humanitarian Use is for those applying eligible technologies to positively impact a humanitarian issue, focusing on demonstrable real-world improvements:

- Subject Matter – the applicant's technology, which is claimed in a U.S. utility patent in force at the time or a pending U.S. utility patent application, effectively addresses a recognized humanitarian issue;
- Target Population – the applicant's actions target an impoverished population affected by the humanitarian issue;
- Contribution – the applicant took meaningful actions to make the technology more available for humanitarian uses. This only includes actions taken by the applicant; [and]
- Impact – the applicant's contributions have significantly advanced deployment of the technology to benefit the target population. This includes downstream actions by third parties building on the applicant's contributions" (PHP, 2015).

"Humanitarian Research is to increase the availability of patented technologies to other researchers for conducting research with a humanitarian purpose, particularly areas lacking commercial application:

- Subject matter – the applicant's technology, which is claimed in a U.S. utility patent in force at the time or a pending U.S. utility patent application, effectively supports research by others, e.g., as a tool or input;
- Neglected Field – the research by others clearly targets a humanitarian issue in an area lacking significant commercial application;
- Contribution – the applicant took meaningful actions to make the technology more available for research by others in the neglected field. This only includes actions taken by the applicant; [and]
- Impact – the research by others has a high potential for significant impact on the neglected field. This includes downstream actions by third parties using the applicant's contributions" (PHP, 2015).

PFH Award recipients can accelerate "a patent application, ex parte reexam, or an ex parte appeal to the Patent Trial and Appeal Board" while Honorable Mention recipients "will receive accelerated examination of one patent application" (PHP, 2015).

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. PATENTS FOR HUMANITY AWARDS FOR MEDICINE

Main Project(s):

In 2013, winners included "Gilead Sciences for making HIV drugs available to the world's poor using a network of generics manufacturers in Asia and Africa [and] University of California, Berkeley for developing research and license agreements to provide a lower-cost, more reliable way to produce anti-malarial compounds" as well as "Becton Dickinson (BD) for creating a fast, accurate TB (Tuberculosis) diagnosis machine and placing 300 systems in 22 High Burden Countries" (PHP, 2015).

Honorable mentions included "Novartis for developing a new drug combination to treat malaria and distributing it with public sector partners in malaria-endemic countries [and] Anacor Pharmaceuticals for researching and licensing a new drug candidate for African sleeping sickness, a neglected tropical disease" as well as "Northwestern University for developing a quick, simple HIV test to screen newborns in Africa" (PHP, 2015).

In 2014, winners included "Sanofi for supplying large quantities of anti-malarial compounds on an at-cost basis for use in developing countries [and] Novartis AG for identifying new drug compounds for potentially treating drug-resistant tuberculosis and providing them to the non-profit TB Alliance for further development" and honorable mentions included "Case Western Reserve University for creating a novel, low-cost, accurate malaria detection device to improve treatment [and] InBios International for developing and distributing diagnostic assays for early detection of dengue fever, improving patient outcomes and aiding disease surveillance" (PHP, 2015).

Effectiveness:

The "pilot conducted in 2012-2013 gave ten awards and six honorable mentions to businesses, universities, and non-profits using patented technology to aid the less fortunate and reach underserved markets" and in 2014 the program was renewed by the Obama administration (PHP, 2015).

Critiques/Questions Raised in the Literature:

There is concern that the PFH program is not as significant as it is touted to be, with critics calling it a 'shadow solution'. "There is a gap between the grandiloquent claims made for the "Patents for Humanity" project, and the decidedly modest scale and nature of the programme. A patent fast-track seems a minor incentive. The "Patents for Humanity" project falls well short of implementing international agreements and declarations" (Rimmer, 2012). Additionally, "such mechanisms are vulnerable to gaming and strategic behaviour. Fast-tracking regulatory approval may also have an adverse impact upon the quality of granted patents. Vouchers could well be hoarded by intellectual property owners, and stacked on top of a variety of intellectual property rights, such as patent, trademark, and data exclusivity rights. It is of concern that the schemes are influenced by a larger ideology that strong intellectual property rights protection, coupled with other incentives, are the best means of promoting health-care and development" (Rimmer, 2012).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

In May 2015, Senators Patrick Leahy and Chuck Grassley introduced The Patents for Humanity Program Improvement Act (Leahy, 2015).

Recipients:
Gilead Sciences; Sanofi Pasteur; Becton Dickinson; Novartis; Anacor; InBios International.

University Involvement:

Case Western University, University of Berkeley and Northwestern have received honorable mentions but did not receive an award.

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

PNEUMOCOCCAL VACCINE ADVANCE MARKET COMMITMENT (PILOT AMC)

General Approach/Methods Applied:

(PULL) Market-based incentive supplied via an advance market commitment (AMC) for a vaccine product, or creation of a guaranteed subsidized market funded by donors, in this case specifically for pneumococcal diseases.

Summary:

A pull mechanism that ideally promotes needed vaccine R&D by guaranteeing a subsidized market, at a given price, for the resulting product if it meets certain specifications (target product profile) and is purchased by countries/donors (Wilson, 2010). The AMC calls for creating a US$3 billion market for diseases with high burdens, such as malaria, tuberculosis, and HIV/AIDS, wherein manufacturers sign legally binding Supply Offers. The pilot AMC is specifically focused on introduction of a pneumococcal vaccine and its objectives include: "accelerat[ing] the development of vaccines that meet developing country needs; bring[ing] forward the availability of effective pneumococcal vaccines – through scaling up of production capacity to meet developing country vaccine demand; accelerating vaccine uptake – through predictable vaccine pricing for countries and manufacturers; [and] test[ing] the AMC concept for potential future applications" (GAVI AMC, 2015). "In this pilot AMC, donors commit funds to guarantee the price of vaccines once they have been developed. These financial commitments provide vaccine manufacturers with the incentive they need to invest in vaccine research and development, and to expand manufacturing capacity. In exchange, companies sign a legally-binding commitment to provide the vaccines at a price affordable to developing countries in the long term" (GAVI AMC, 2015).

Main Project(s):

The pilot AMC for pneumococcal diseases.

Effectiveness:

While it is still in the early stages, the pilot AMC "is expected to prevent more than 500,000 child deaths over the 10-year contract period and over 5 million deaths by 2030" (CGDEV AMC, 2005). Ideally, AMCs could be used for both products in "an early stage of development (such as malaria, HIV/AIDS and tuberculosis vaccines) and for late stage products (such as vaccines against rotavirus, human papillomavirus, and pneumococcal disease)" (WHO AMC, 2006). "Incentives given to manufacturers using donors' pledges have helped reduce vaccine prices by 90% and accelerated the availability of these vaccines in developing countries. The long term market shaping impact has yet to be evaluated" (Porcher, 2011).

Critiques/Questions Raised in the Literature:

"The AMC launched by donors in 2009 to accelerate delivery of pneumococcal vaccines was aimed at two vaccines that were already in final stages of development and close to gaining marketing approval, thus rendering it more a procurement mechanism than an R&D incentive. It is possible that these vaccines could have been purchased as – or more – cheaply through conventional UNICEF tender procedures than with an AMC" (Wilson, 2010).

"While well-designed, AMCs could play a role in mid-stage development or for less complex vaccines – as a complement to public sector research funding, PDPs (product development partnerships), and other push mechanisms – they are unlikely

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

PNEUMOCOCCAL VACCINE ADVANCE MARKET COMMITMENT (PILOT AMC)

to be a practical way to drive R&D for challenging early-stage vaccines that face substantial scientific obstacles. The AMC has been criticized as too expensive and too complex, and is ultimately resulting in the procurement of a vaccine already in its final stages of development, in lieu of generating an innovative new product" (Wilson, 2010).

It is difficult to ensure that vaccines will be supplied "at affordable prices and in sufficient quantities once the commitment is exhausted, and [to] create an appropriate balance of incentives for manufacturers of first and second-generation products. A further challenge is the development of independent, transparent and accountable financial management and procurement systems" (WHO AMC, 2015). HAI has published a report delineating various concerns and criticisms of the current AMC program (Light, 2008). These include that the many uncertainties and contingencies of the AMC design may discourage engagement of many companies and because funding is only supplied once a new vaccine is developed the model is not appropriate for the many smaller companies because investment costs remain extremely high. Additionally, "its competitive design could undermine cooperative efforts and grant-based "push" funding. Thirdly, by favouring large companies with deep pockets over biotech companies and teams of researchers at universities or non-profit institutes that require intermediate funding, AMC could actually decelerate R&D, although alternative approaches could address these design problems. Finally, even the sharply discounted post-buyout prices would still not be affordable, and past experience with AIDS drugs shows that manufacturing in developing countries can supply medicines at much lower prices" (Light, 2008).

HAI argues that the current pilot AMC is more a procurement commitment than a market commitment (Light, 2008). According to HAI, "more flexible approaches are needed in the design that require sharing or licensing intellectual property and know-how, and that help developers of promising products to complete their trials. One needs to use different approaches for diseases with large affluent markets than for diseases with predominantly low-income markets" (Light, 2008).

Proposed Changes/Improvements:

See above critique.

Organizations, Stakeholders, And/Or Partners:

In 2007 donors committed US$1.5 billion towards the pneumococcal vaccine pilot (CGDEV AMC, 2005).

The Center for Global Development; GAVI/Vaccine Fund; Italy; UK; Canada; The Russian Federation; Norway; and the Bill and Melinda Gates Foundation.

University Involvement:

Harvard University; MIT; U Chicago; Emory U.

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. FDA PRIORITY REVIEW VOUCHER (PRV)

General Approach/Methods Applied:

(PULL) Incentive supplied via a "prize", the PRV, which encourages development of drugs for neglected tropical diseases (NTDs) and rare pediatric diseases (RPDs) by reducing the cost and time required to enter the market.

Summary:

According to the U.S. PRV program, created in 2007 and "launched in 2008, any organization that wins Food and Drug Administration (FDA) approval for a new drug or vaccine against a defined list of neglected diseases is eligible for a 'priority review voucher' (PRV) entitling the holder to expedited FDA review of another new drug application. The voucher is transferrable: it can be sold to and used by another organization" (Wilson, 2010). This facilitates the expediting of the review of any new drug by the entity that possesses the voucher, with priority review typically taking six instead of ten months (Gaffney, 2015).

Main Project(s):

In 2007, the Neglected Tropical Disease PRV was introduced and in 2012, the Rare Pediatric Disease PRV began. The NTD PRV covers drugs designated to treat Malaria, Blinding trachoma, Buruli Ulcer, Cholera, Dengue/Dengue haemorrhagic fever, Dracunculiasis (guinea-worm disease), Fascioliasis, Human African trypanosomiasis, Leishmaniasis, Leprosy, Lymphatic filariasis, Onchocerciasis, Schistosomiasis, Soil transmitted helminthiasis, Yaws, Tuberculosis and several additional infectious diseases later added to this list including Ebola and other filoviruses (Gaffney, 2015).

Effectiveness:

The effectiveness of the PRV program can't currently be determined because it can easily take a decade to develop a new drug so "any new development catalyzed by the creation of the voucher system may not be evident for several more years. One study recently published in the Public Library of Science estimated that FDA [would] issue between five and six new vouchers between 2016 and 2018" (Gaffney, 2015).

Only six PRVs have actually been awarded since the creation of the PRV: (2009) Tropical Disease PRV to Novartis which they unsuccessfully used to accelerate the review of the Biologics Licensing Application (BLA) for Ilaris (canakinumab), (2012) Tropical Disease PRV to Janssen which is unused, (2014) Rare Pediatric Disease PRV to BioMarin which was sold to Sanofi and Regeneron for US$67 million who intend to use the voucher to aid review of Alirocumab, (2014) Tropical Disease PRV to Knight Therapeutics which is unused but was sold to Gilead for US$125 million, (2015) Rare Pediatric Disease PRV to United Therapeutics which is unused, and (2015) Rare Pediatric Disease PRV to Asklepion Pharmaceuticals which was transferred to Retrophin under an existing agreement and sold to Sanofi for US$245 million in May 2015 (Gaffney, 2015).

Critiques/Questions Raised in the Literature:

The Rare Pediatric Disease PRV was designated to cover only three PRVs, all of which have been rewarded. Now it remains to be seen whether Congress will readdress this part of the PRV program before it formally ends on 17 March 2016 (Gaffney, 2015). In a recent article, Bernard Pécoul

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. FDA PRIORITY REVIEW VOUCHER (PRV)

and Manica Balasegaram critiqued the PRV program, arguing that it acts "as a giveaway to companies which would have developed the new products anyways" and in such does not incentivize needed R&D (research and development) (Gaffney, 2015). MSF has made similar claims and argues "that companies should be required to show they conducted the research necessary to obtain approval for the drug." (Gaffney, 2015). Additionally, critics such as the Drugs for Neglected Diseases initiative have noted that the voucher systems actually do not require a company to sell a drug. "In other cases, companies might seek regulatory approval for a tropical disease drug which is marketed outside the US in the hopes of obtaining a voucher" (Gaffney, 2015).

Furthermore, the PRV program has no requirements concerning affordability of drugs approved. "Another criticism, levied by Aaron Kesselheim in the New England Journal of Medicine in 2008, is that while the voucher program is intended to be used only for new drug ingredients, it ignores the potential utility of new innovations" and Kesselheim also pointed out "that the priority review process is improper to use for drugs lacking an urgent need" (Kesselheim, 2008 as cited in Gaffney, 2015). While the PRV encourages innovation it does not guarantee access to drugs for those with the greatest need.

If the 21st Century Cures Act passes, the RPD PRV program will be extended an additional three years and it is also possible that requirements of the PRV will become stricter. "Only rare pediatric diseases which are "serious or life-threatening" would qualify for the voucher, and companies could not obtain two vouchers (i.e. a tropical disease voucher and a pediatric voucher) for the same disease" (Gaffney, 2015). Although it has been proposed to extend the voucher program to the EU this has not yet occurred (Gaffney, 2015).

See also:
http://www.who.int/tdr/news/2014/prv-drug-develp/en/

Proposed Changes/Improvements:

MSF argues that the potential economic value needs to be increased "by making the voucher for neglected tropical diseases transferable indefinitely, instead of only being able to transfer a voucher just once. For rare pediatric diseases, a voucher can be transferred without any limit. Congress should extend this to neglected tropical diseases as well, because companies can keep trading a voucher and, theoretically, raising the economic value." MSF also states "there are several examples in which companies have received vouchers (from the federal government) that . . . have not deserved it. If you don't do innovation, you shouldn't get a voucher. Companies should demonstrate they have made a significant investment before receiving a voucher" (Silverman, 2014). "There [is] no guarantee these products will be accessible to patients anywhere in the world – the U.S. or globally. There is no mandate. Congress gives the reward, but there is no guarantee these [medicines] will be affordable. Paladin and Endo have exclusive rights globally and Knight has exclusive rights in the U.S. But the product has been in the market for many years and there is nothing to say it will be accessible" (Silverman, 2014). MSF proposes that companies could be rewarded only if they invest in R&D and they disclose their pricing strategy. "Ideally, this would make sure [a medicine] is affordable. And the companies should only be eligible for a voucher if they explain these two points" (Silverman, 2014).

Organizations, Stakeholders, And/Or Partners:

The PRV was first proposed by Duke University's David Ridley, Henry Grabowski and Jeffrey Moe via a 2006 paper published in Health Affairs, "Developing Drugs for Developing Countries" (Gaffney, 2015). Sen. Sam Brownback included

A2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW INCENTIVES

U.S. FDA PRIORITY REVIEW VOUCHER (PRV)

the NTD PRV as part of the Food and Drug Administration Amendments Act (FDAAA) of 2007 and then the RPD PRV was included as part of the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012 (Gaffney, 2015).

Recipients:
Novartis; Janssen; BioMarin; Knight; United Therapeutics; and Asklepion Pharmaceuticals.

University Involvement:

Duke University

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

GLOBAL HEALTH INNOVATIVE TECHNOLOGY FUND (GHIT)

General Approach/Methods Applied:

(PUSH) Non-profit public-private partnership (PPP) fund that provides grants to encourage collaborative research on NTDs.

Summary:

The Global Health Innovative Technology Fund (GHIT) is a non-profit public-private partnership based in Tokyo, Japan, funded by six leading Japanese pharmaceutical companies (Astellas Pharma, Inc.; Chugai Pharmaceutical Co., Ltd; Daiichi Sankyo Company, Limited; Eisai Co., Ltd.; Shionogi & Co., Ltd.; Takeda Pharmaceutical Company Limited), the Japanese Government and the Bill & Melinda Gates Foundation. Launched in April 2013 with an initial commitment of more than US$100 million, the organization taps Japanese research and development to fight neglected diseases by promoting the discovery and development of new health technologies. (GHIT website) "Where possible, capacity building and technology-transfer components will be integrated into these efforts" (Slingsby, 2013). "The GHIT Fund is the first public-private partnership fund to involve a national government, a UN agency, a consortium of pharmaceutical companies, and an international philanthropic foundation" (Slingsby, 2013).

GHIT, through its support of and collaboration with other international PDPs, provides access to Japanese pharmaceutical compound libraries in addition to providing financial resources (GHIT, 2015). "The Fund [has] invest[ed] in a new drug-discovery screening platform to assist the screening of compound libraries housed within Japanese companies and academic institutions. Japanese entities [have] provide[d] compounds to partners, with the Fund reimbursing screening costs and leveraging screening programmes of existing product-development partners" (Slingsby, 2013). The fund encourages affordability via pricing on a 'no gains, no losses' basis and sets milestones to encourage timely and realistic innovation. "The Fund [also] encourage[s] the equitable sharing of information and knowledge, and assignation of rights or licenses to third parties" (Slingsby, 2013).

Main Project(s):

GHIT focuses on malaria, TB, and the 17 WHO defined NTDs. It has "awarded grants totaling US$5.7 million to six global partnerships developing innovative drugs and vaccines against malaria, TB, and Chagas disease in the first round of requests for proposals (RFPs) in November 2013" and "awarded grants totalling US$12 million for TB and NTDs to four innovative projects in the second round of RFPs (requests for proposals) in March 2014" (BSR Healthcare Working Group, 2014).

US$766,000 given to PATH's Malaria Vaccine Initiative (MVI) and Ehime University to fast-track the research and manufacture of a novel malaria vaccine candidate (Pf75) that aims to block malaria parasite transmission from humans to mosquitoes.

US$3.83 million to Japan's National Institute of Biomedical Innovation (NIBIO), Aeras, and Create Vaccine Company, Ltd (CREATE) on the preclinical and clinical development of new mucosal TB vaccines based on NIBIO's human parainfluenza type-2 (rhPIV2) vector technology.

US$3.84 million, to Drugs for Neglected Diseases initiative (DNDi) and Eisai of Japan for a new combination therapy for Chagas disease consisting of benznidazole and an experimental triazole compound known as E1224 (listed on wikipedia page).

GHIT Fund Grant Portfolio:
https://www.ghitfund.org/impact/portfolio

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

GLOBAL HEALTH INNOVATIVE TECHNOLOGY FUND (GHIT)

Effectiveness:

As of May, 2015, the "GHIT Fund ha[d] financed the screening of over 250,000 compounds" (NM GHIT, 2015).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

As of May, 2015, GHIT expanded its investments into leishmaniasis and diagnostics for schistosomiasis and welcomed four additional companies into its Screening Platform, providing grants to TB Alliance and MMV to screen the libraries of these pharmaceutical companies (NM GHIT, 2015).

Organizations, Stakeholders, And/Or Partners:

Japanese Ministry of Foreign Affairs; Japanese Ministry of Health; Labour and Welfare; UNDP; Astellas Pharma, Inc.; Chugai Pharmaceutical Co.; Daiichi Sankyo Company; Eisai Co.; Shionogi & Co.; Sysmex Corporation; Takeda Pharmaceutical Company; BMGF; Wellcome Trust; All Nippon Airways Co.; Yahoo Japan Corporation; and Morrison & Foerster LLP.

University Involvement:

GHIT awarded Osaka University and Gulu University in Uganda a grant to improve the effectiveness of a proposed malaria vaccine.

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

EUROPEAN DEVELOPING COUNTRIES CLINICAL TRIALS PARTNERSHIPS (EDCTP)

General Approach/Methods Applied:

(PUSH) International partnership that provides grants and additional support for collaborative research to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against poverty-related and neglected infectious diseases in sub-Saharan Africa, with a focus on phase II and III clinical trials.

Summary:

The EDCTP, by funding collaborative research, "aims to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against HIV/AIDS, tuberculosis and malaria as well as other poverty-related and neglected infectious diseases in sub-Saharan Africa, with a focus on phase II and III clinical trials" (EDCTP, 2015). It falls under the purview of the European Framework for Research and Innovation, Horizon 2020, and is considered a public-public partnership between Europe, sub-Saharan Africa, and the EU. The EU has agreed to "provide a contribution of up to €683 million for the 10-year programme (2014-2024), provided this is matched by contributions from the European Participating States" (EDCTP, 2015). EDCTP promotes "development of effective, safe, accessible, suitable and affordable medical interventions for PRDs" (EDCTP, 2015).

The program has clear and specific objectives and time-bound goals (EDCTP, 2013). "EDCTP blends important aspects of partnership that includes ownership, sustainability and responds to demand-driven research" (Matee, 2009). EDCTP II (2014-2024) is a continuation of the original program, run from 2003-2015. In addition to supporting clinical trials and related research activities, EDCTP also supports capacity building and advanced testing and field evaluation and offers fellowships in order to facilitate career development of researchers (EDCTP, 2015). Grants offered by EDCTP are categorized as Research & Innovation Actions, Coordination & Support Actions, or Training & Mobility Actions.

EDCTP I Project Portfolio: **http://www.edctp.org/web/app/uploads/2015/01/EDCTP_project_portfolio.pdf**

Main Project(s):

The three calls currently open under the EDCTP include strategic projects with major co-funding, improved treatment and clinical management of poverty-related diseases, and research and capacity development in support of the EVD response (EDCTP, 2015). Independent experts external to EDCTP evaluate proposals.

List of EDCTP Calls for Proposals:
http://www.edctp.org/funding-opportunities/calls/

EDCTP Grants giving manual:
http://www.edctp.org/web/app/uploads/2015/05/EDCTP2_Grants_Manual_-_30_April_2015.pdf

Diseases researched under EDCTP "include HIV/AIDS, malaria, tuberculosis and the following neglected infectious diseases (NIDs): dengue; rabies; human African trypanosomiasis (sleeping sickness); Leishmaniases; cysticercosis/taeniasis; dracunculiasis (guinea-worm disease); echinococcosis; foodborne trematodiases; lymphatic filariasis; onchocerciasis (river blindness); schistosomiasis; soil-transmitted helminthiases; Buruli ulcer; leprosy (Hansen disease); trachoma; yaws; diarrhoeal infections; lower respiratory infections; as well as emerging infectious diseases of particular relevance for Africa, such as Ebola" (EDCTP, 2015).

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

EUROPEAN DEVELOPING COUNTRIES CLINICAL TRIALS PARTNERSHIPS (EDCTP)

Effectiveness:

During EDCTP I, 241 projects were funded in 30 different countries. "These included 88 clinical trials of which 31 were on HIV/AIDS, 25 on tuberculosis and 32 on malaria. The trials were on treatment drugs, vaccines, microbicides and diagnostics. This has led to the registration of one paediatric formulation of an antiretroviral product (Pedimune) in several African countries; informing national and international policies such as the World Health Organization (WHO) policy on the prevention of maternal to child transmission (PMTCT) of HIV3; and the coordination and integration of national research programmes in conducting these clinical trials" (EDCTP, 2013).

"During this first phase, EDCTP provided professional training to more than 400 African scientists and medical doctors (all schemes put together) including 55 Career and Senior Fellows who almost without exception have remained in their own countries to date as well as more than 320 Masters and PhD students" (EDCTP, 2013).

As of 2009, "the cumulative amount of funds spent on EDCTP projects ha[d] reached 150 million EUR" (Matee, 2009). EDCTP I was evaluated by the Technopolis Group, which was used to inform the development and implementation of the second phase of EDCTP and "the evaluation shows that the combination of support for clinical trials with capacity building and networking is rather unique and a best practice in funding clinical research activities in Africa" (Technopolis, 2015).

Technopolis Group EDCTP Report: **http://www.technopolis-group.com/?report=assessment-of-the-performance-and-impact-of-the-first-programme-of-the-european-developing-countries-clinical-trials-partnership-edctp**

Critiques/Questions Raised in the Literature:

As of 2009, "the EDCTP had not yet succeeded in its second major task, namely the integration of national clinical trials programmes. The "co-funding" arrangements constitute[d] a major source of difficulties and confusion. Only seven Member States had, until April 2008, shown substantial commitments (in cash or in kind) towards the EDCTP. The promised target of 200 million Euros co-funding ha[d] to be met before the end of 2010." (Velzen, 2009). It is unclear whether or not it was met.

Proposed Changes/Improvements:

Strategic Business Plan for EDCTP II, which is said to have an extended and more flexible mandate than the original program, exploring a wider range of mechanisms to integrate national activities: **http://www.edctp.org/web/app/uploads/2015/03/EDCTP_Strategic_Business_Plan_EDCTP2.pdf**; a second source is the 2009 five-year evaluation of EDCTP I: **http://www.academia.edu/4348238/Independent_external_evaluation_of_the_European_and_Developing_countries_clinical_trials_partnership**

Organizations, Stakeholders, And/Or Partners:

Participating countries: 14 European countries – Austria; Denmark; Finland; France; Germany; Ireland; Italy; Luxembourg; Netherlands; Norway; Portugal; Spain; Sweden; UK; and 13 African countries – Burkina Faso; Cameroon; Congo; The Gambia; Ghana; Mali; Mozambique; Niger; Senegal; South Africa; Tanzania; Uganda; and Zambia.

The program has a complex governance structure explained in further detail here, which includes representatives of various universities from participating countries: **http://www.edctp.org/get-know-us/governance/**

University Involvement:

None found.

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

BRIDGING INTERVENTIONAL DEVELOPMENT GAPS PROGRAMME (BRIDGS)

General Approach/Methods Applied:

(PUSH) Program that provides in-kind resources to facilitate drug development for both common and rare diseases.

Summary:

"The Bridging Interventional Development Gaps (BrIDGs) program makes available, on a competitive basis, certain critical resources needed for the development of new therapeutic agents for both common and rare diseases. Investigators do not receive grant funds through this program. Instead, successful applicants receive access to NIH experts and contractors who conduct pre-clinical studies at no cost to the investigator. In general, synthesis, formulation, pharmacokinetic and toxicology services in support of investigator-held IND applications to the Food and Drug Administration (FDA) are available. NIH contractors conduct pre-clinical studies on behalf of successful applicants. NCATS, along with any collaborating NIH Institutes and Centers, supports contract costs. Access to contracts is based on a peer-reviewed application process. The number of awards in any given cycle will depend on the number of applications received, their scientific merit and the availability of NIH funds" (BrIDGs, 2015).

A business is eligible for a BrIDGs award "if it meets the criteria for applying for an NIH Small Business Innovation Research (SBIR) or Small Business Technology Transfer (STTR) grant" (BrIDGs, 2015). "With most BrIDGs projects, intellectual property (IP) is retained by the applicant-owner, and no new IP is developed. This allows BrIDGs to operate as a non-dilutive investment into exciting pre-clinical drug development projects and to maximize the competitiveness of therapeutic agents for further private-sector funding" and "applications are accepted for the development of therapies for any disease or disorder. Studies may be proposed for a variety of therapeutic modalities, such as small molecules, peptides, oligonucleotides, gene vectors, recombinant proteins and monoclonal antibodies" (BrIDGs, 2015). Essentially, BrIDGs' contract[s] "access collaboration between DPI [the Division of Pre-Clinical Innovation] and extramural labs" and applications must be for an identified clinical candidate, any disease is eligible, and work has to be milestone driven (Portilla, 2012).

Main Project(s):

- A Pharmacological and Toxicological Evaluation of the Gene Transfer Vectors sc-rAAV2.5IL-1Ra (Rat) and scr-AAV2.5IL-1Ra (Human) in Rats
- Development of an ApoA1 Mimetic Peptide for Treatment of Atherosclerosis
- Development of Bone Morphogenetic Protein Inhibitors to Treat Blood and Bone Disorders
- Development of Exendin-(9-39) for the Treatment of Congenital Hyperinsulinism
- Development of Minihepcidins for the Treatment of Beta Thalassemia
- Development of Neurosteroids for Lysosomal Storage Disorders
- Development of Nogo Receptor Decoy for the Treatment of Spinal Cord Injury
- Evaluation of ACT1 to Treat Diabetic Keratopathy
- HBN-1 Regulated Hypothermia Formulation and Evaluation of Toxicity
- IND-Enabling Pre-Clinical Studies of 2DG for Treatment of Epilepsy
- Long-Acting Parathyroid Hormone Analog for Treatment of Hypoparathyroidism
- Manufacture of RLIP76-LyoPL for Acute Radiation Syndrome
- Novel Pre-Hospital Therapy of Myocardial Infarction
- Peripheral CB1 Receptor Antagonist for Therapeutic Use in Metabolic Syndrome
- Pre-Clinical Development of EDN-OL1 for Alzheimer's Disease
- Short Stabilized EPO-Peptide as Therapeutic Agents for Multiple Sclerosis and Acute Brain Trauma
- Studies of Tumor-Penetrating Microparticles for Pancreatic Cancer
- Toxicity Studies of Nebulized Propofol Hemisuccinate

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

BRIDGING INTERVENTIONAL DEVELOPMENT GAPS PROGRAMME (BRIDGS)

Effectiveness:

"As of fall 2014, BrIDGs ha[d] generated data to support 15 INDs that have been cleared by the FDA and one clinical trial application cleared by Health Canada. A total of 14 projects have been evaluated in clinical trials. Five BrIDGs-supported agents have gone as far as phase II human clinical trials, in which researchers give an experimental therapy to a group of patients to evaluate the effectiveness and safety of a treatment. Third-party investors have licensed seven agents during or after their development by BrIDGs" (BrIDGs, 2015).

Critiques/Questions Raised in the Literature:

Applicants can out-license their compound and still continue to receive BrIDGs support (BrIDGs, 2015).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Supported and administered by the National Center for Advancing Translational Sciences (NCATS) (BrIDGs, 2015).

Beth Israel Deaconess Medical Center; KineMed, Inc.; Massachusetts General Hospital; Children's Hospital of Philadelphia; Merganser Biotech LLc; Axerion Therapeutics, Inc.; FirstString Research; NIH, etc.

University Involvement:

University of Pittsburgh; UNC, Chapel Hill; University of Florida; University of Pennsylvania; UCSF; University of Wisconsin; The Rockefeller University; Regents of the University of California, etc.

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

SUSTAINABLE SCIENCES INSTITUTE (SSI)

General Approach/Methods Applied:

(PUSH) SSI provides grants and non-financial contributions, including trainings, to support R&D in-country and capacity building for various diseases including dengue fever.

Summary:

The Sustainable Sciences Institute, "SSI was founded in September 1998 in San Francisco, CA. In 2004, SSI incorporated in Managua, Nicaragua and in 2011 in Cairo, Egypt, though it apparently really began in 1988, when the Applied Molecular Biology/ Appropriate Technology Transfer Program (AMB/ ATT) was first conceived"… "The mission of SSI is to support scientific and public health communities in resource-poor settings to develop sustainable local research and public health systems"… "SSI works with local partners to better meet the public health needs of their own communities by: Informing and promoting action-led research (= research in response to locally identified problems); Identifying and adapting innovative technologies to local conditions; Developing a global network of colleagues and mentors; [and] Training and supporting professional development including scientific grant writing and manuscript writing"… "Through education, training, and support of locally relevant scientific projects, SSI seeks to "leverage the resources of the developed world to enhance the capacity and encourage the ingenuity of researchers in the developing world. By building local health research capacity, developing country researchers are empowered to reduce the burden of poverty and disease in their communities" (SSI, 2015). "The center emphasizes collaboration through participation in clinical studies with local health practitioners, investing in information and communication technology, research grants, scholarship funding, scientific workshops and funding for scientific equipment" (RDI SSI, 2015).

Main Project(s):

SSI conducts "a wide range of research in 3 major areas: Neglected Infectious Diseases (dengue, influenza, Chikungunya, Hep C); Information and Communication Technologies (ICTs) for Health; [and] Community based participatory disease prevention approaches" (SSI, 2015).

SSI's "FIRST program, funded jointly by the Bill & Melinda Gates Foundation and the Carlos Slim Health Institute, aims to speed the development of new tools and technologies that will address three diseases that place a huge health and economic burden on neglected populations in Central and South America: Chagas' disease, dengue and onchocerciasis. Led by scientists at UCSF Global Health Sciences, UC Berkeley and partner institutions including SSI, the two-year program focuses in Mesoamerica, which comprises the Southern states of Mexico and Central America from Guatemala to Panama. By developing and testing a set of affordable new tools, drugs, and prevention campaigns, the FIRST program will not only contribute to preventing, diagnosing and treating tropical diseases, but can also serve as a model for other regions of the world affected by the same ailments" (SSI, 2015).

Effectiveness:

"SSI has generally been involved in transferring existing technologies to the developing world"… "SSI is funding a collaboration between Harris and engineers at UC Berkeley to develop an inexpensive handheld diagnostic device that can be used for identifying dengue virus and other infectious diseases. Harris and SSI wanted to ensure that this technology could be made available in the developing world at the lowest cost possible, which requires protecting the intellectual property rights

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

SUSTAINABLE SCIENCES INSTITUTE (SSI)

on the technology so that it will not be patented and sold for profit by someone else"… "As a result, SSI worked with UC Berkeley to develop new licensing language in which products based on a technology can be developed 'for profit' in the developed world, but must be made available at low cost in developing countries. This effort by SSI to obtain a 'royalty-free' license has had an unexpected ripple effect in the United States" (Kotz, 2007).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

"SSI is now embarking on a new initiative in health information technologies (HITs). Building on the Nicaragua experience and the current mandate to improve vaccination efficiency and prenatal care in Managua, SSI is working to identify, test, and implement low-cost, open-source ICT solutions that facilitate infectious disease research, control, and prevention in limited-resource settings. It is also evaluating the potential impacts of ICT solutions (such as electronic medical records [eHealth], mobile phone applications [mHealth], and laboratory information management systems [LIMS]) on improving targeted public health outcomes for priority health problems in underserved communities. Finally, it is strengthening partnerships and capacity-building networks in the developing world that promote knowledge exchange about sustainable best-practices in HIT implementation at a local level" (Coloma, 2009).

Organizations, Stakeholders, And/Or Partners:

California Pacific Medical Center; OrderSmart.com; Genentech President; Panorama Research Inc. President; and Palo Alto Institute for Molecular Medicine.

University Involvement:

UCSF; University College Berkeley; Stanford; Washington University.

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

GLOBAL HEALTH INVESTMENT FUND (GHIF)

General Approach/Methods Applied:

(PUSH) Social impact investment fund that provides milestone payments and royalties to finance drug, vaccine, and diagnostic development and encourage global access agreements through 'mezzanine' debt funding.

Summary:

The Global Health Investment Fund (GHIF) "is a [US$] 108mm social impact investment fund designed to provide financing to advance the development of drugs, vaccines, diagnostics and other interventions against diseases that disproportionately burden low- income countries. This is achieved via milestone payments and royalties which will primarily be achieved from sales of the new products in developed markets, complementing global access agreements to bring the new products to the developing markets where they are critically required" (GHIF, 2015). According to the Fund's website, it "will make investments that will provide capital for the development of global health products, via a form of 'mezzanine' debt funding, to Product Development Partnerships (PDPs), pharmaceutical companies, contract research organizations and government bodies. The intention is to provide companies with investments structured to accelerate the development of products to address global health challenges, and to complete projects they might otherwise not pursue." However, "unlike a traditional mezzanine or private equity fund, the fund carry is not paid to the investment manager but will be held within a new not-for-profit entity and recycled back into global health research and development" (GHIF, 2015).

Main Project(s):

As of October 2014, GHIF had reviewed over 70 investment opportunities since its launch and had currently active pipelines for NTDs, TB, HIV, malaria, Vaccine Gen, Maternal Health and Diarrhea (Pagliusi, 2015).

Effectiveness:

Although not yet evaluated, it is expected that "drawing upon the scientific and financial expertise of its management and oversight teams, the Fund will seek a financial return for investors, thus creating a self-sustaining structure that can grow and continue to make meaningful investments over time. As this is a first-of-its-kind structure, the Gates Foundation and the Swedish International Development Cooperation Agency have committed to limit investors' downside if the Fund's investments are not successful" (Kemppainen-Bertram, 2013).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

The Global Health Investment Corporation (non-profit established to serve as the managing member of the fund by JP Morgan, BMGF); Lion's Head Global Partners.

Investors:
GSK; CIFF; Grand Challenges Canada; IFC; KfW; Merck; the Pfizer Foundation; JP Morgan Social Finance; Storebrand; and several high-net-worth individuals.

Co-Guarantor:
Sida (GHIF, 2015)

University Involvement:

None found.

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

HUMANITARIAN ASSISTANCE FOR NEGLECTED DISEASES (HAND)

General Approach/Methods Applied:

(PULL) Initiative focused on collaborative, non-commercial drug discovery and development, working to identify, evaluate and manage scientific projects and partnerships focused on neglected diseases.

Summary:

Genzyme established the HAND program in 2006 "to participate in efforts to discover and advance novel treatments for neglected diseases affecting the developing world. The company's new Humanitarian Assistance for Neglected Diseases initiative (HAND) will serve as a vehicle to identify, evaluate and manage scientific projects and partnerships focused on diseases that collectively affect hundreds of millions of people. These could include malaria, tuberculosis, leishmaniasis, Chagas disease, sleeping sickness and other diseases. Genzyme will focus on projects where it can play a defined role in the process of moving potential new treatments from discovery toward clinical testing. The company will not seek to profit from the commercialization of any products it helps to develop. It will grant all commercial and intellectual property rights in neglected disease areas to non-profit partners. The HAND initiative complements existing Genzyme programs that provide free medicines and help to build sustainable health care systems in developing countries" (Genzyme Corp., 2006).

Main Project(s):

One of HAND's first projects was in partnership with DNDi. "Genzyme and DNDi are working to develop and test novel compounds intended to treat African trypanosomiasis, Some testing under this agreement will also be done through an agreement with the Swiss Tropical Institute." The project initially focused "on seeking novel treatments that target the same biochemical pathways as those targeted by eflornithine"… "Genzyme's expertise in research on eflornithine and polyamine pathways for treatment of cancer may allow the company to contribute to this effort. Genzyme acquired certain rights to eflornithine, also known as DFMO, through its purchase of Ilex Oncology Inc." (Genzyme Corp., 2006).

A second project focuses on malaria in collaboration with the Broad Institute. With "a memorandum of understanding with Medicines for Malaria Venture (MMV)"… "MMV will provide clinical guidance, project management and coordination with other anti-malarial drug-development efforts, and will work with other parties to secure sources of funding for further work. MMV stated '[t]his collaboration with Genzyme and the Broad Institute will significantly enhance MMV's drug discovery capacity and further boost our ability to develop completely new anti-malarials'" (Genzyme Corp., 2006).

Additionally, Genzyme has "extended the [HAND] program to include a partnership with the Oswaldo Cruz Foundation, or Fiocruz, to tackle Chagas disease in Brazil" (BioWorld, 2008).

Effectiveness:

No information found.

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

Due to HAND's success, Genzyme has proposed a similar initiative to the Orphan Drug Act in 1988 would greatly contribute to accelerate drug development for NTDs along with "other incentive that can leverage the knowledge and resources of both innovator companies and humanitarian

A2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

HUMANITARIAN ASSISTANCE FOR NEGLECTED DISEASES (HAND)

groups to effectively address neglected diseases" (GHT HAND). HAND proposed bringing together a working group "to develop practical and innovative policies to ensure that the promise of breakthrough treatments can become a reality for individuals suffering from neglected diseases. Companies in the developed world can and should utilize their vast resources to develop new therapies and speed their delivery to affected patients in impoverished countries. Keeping in mind the dual concerns of access and development, the group should work to identify problems and propose solutions and incentives to bring to leaders in Congress" (GHT HAND).

Organizations, Stakeholders, And/Or Partners:

Founded by Genzyme

MMV; DNDi.

University Involvement:

Broad Institute of MIT; Harvard University.

A2

DRUG DISCOVERY INCENTIVES
D. VENTURE PHILANTHROPY FOR
DRUG DISCOVERY AND DEVELOPMENT

CQDM

General Approach/Methods Applied:

(COLLABORATIVE + PUSH) Pre-competitive research consortium with pharmaceutical companies and government members that funds the development of breakthrough tools and technologies to accelerate drug development and discovery.

Summary:

"CQDM is a pre-competitive research consortium driven by the mission to fund the development of breakthrough tools and technologies that enhance biopharmaceutical R&D productivity and accelerate the development of safer and more effective drugs. CQDM is also the catalyst where academia, governments, the pharmaceutical industry and the biotechnology converge to create practical solutions to complex medical challenges" (CQDM, 2015).

"CQDM's business model is based on a collaborative approach where all partners share the costs of biopharmaceutical research and benefit from its results, which can generate a financial leverage of up to 25-fold (each dollar invested in CQDM can generate up to 25 dollars in research) and allows funding of research that would be impossible to afford by a single organization itself. CQDM brings together nine of the world's top twelve pharmaceutical organizations, Quebec's provincial and Canada's national governments, and the very best public and private investigators to make unique, innovative drug discovery and development platforms reducing the cost and time required for the best health care solutions to reach the market. Investigators retain full ownership of all generated intellectual property" (CQDM, 2015). "CQDM launches several competitions each year related to its financing programs. Each targets "projects advocating enabling tools or technologies that are designed to accelerate drug discovery and develop safer and more effective treatments for patients." CQDM supports pre-competitive research where technological advances will drive biopharmaceutical R&D productivity" (CQDM, 2015).

Main Project(s):

CQDM's main initiatives include the EPLORE Program, to "fund five highly innovative and unconventional game-changing research and development projects to accelerate drug discovery in the Quebec-Ontario Life Sciences Corridor," the CQDM/CIHR Collaborative Funding Program in Personalized Medicine to Accelerate Drug Discovery, The FOCUS Program, and joint programs with Germany and France (CQDM, 2015).

CQDM Programs: **http://www.cqdm.org/en/programs-and-competitions/overview.php**

CQDM Project Portfolio: **http://www.cqdm.org/en/projects-portfolio/?lang=en&of=project_categories&option=all**

Effectiveness:

Since 2008, CQDM has managed to raise contributions of more than US$65m from Merck, Pfizer, AstraZeneca, Boehringer Ingelheim, Eli Lilly Canada, GlaxoSmithKline, Janssen, Novartis Pharmaceuticals Canada, Sanofi Canada, the Quebec Ministry of Economy, Innovation and Exports (MEIE), and the Business Led-Networks of Centres of Excellence (BL-NCE) program of the Government of Canada. CDQM has established 8 funding programs, launched 24 competitions and reviewed 649 projects, totaling over US$640m in funding requests.

CDQM has 50 research projects for a total of US$40m realized by a network of 610 researchers, including 100 graduate and post-graduate students in 68 research institutions (38 public and 30 private) mobilizing 100 mentors from CQDM pharmaceutical companies members.

A2 DRUG DISCOVERY INCENTIVES D. VENTURE PHILANTHROPY FOR DRUG DISCOVERY AND DEVELOPMENT

CQDM

In technologies that accelerate the discovery of new drugs and significant socioeconomic benefits, CDQM claims a success rate of 94 %, and 15 out of 16 projects completed to date have yielded the expected results. 85% of the developed technologies are used by CQDM pharmaceutical partners and there are 33 cooperation agreements, licenses or strategic partnerships with the private sector. CQDM pharmaceutical partners committed to provide significant additional contributions in various research laboratories to develop further CQDM technologies (CQDM, 2015).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

The Federal Government's Business-Led Networks of Centres of Excellence (BL-NCE) program; the Quebec Government's Minister of the Economy; Innovation and Exports (MEIE); Pfizer Canada; AstraZeneca; Merck; Boehringer Ingelheim; GlaxoSmithKline; Janssen; Eli Lilly Canada; Novartis Pharma Canada; and Sanofi Canada.

University Involvement:

University of Ottawa; Queen's University; University of Toronto; University of Montreal.

A2 DRUG DISCOVERY INCENTIVES
D. VENTURE PHILANTHROPY FOR
DRUG DISCOVERY AND DEVELOPMENT

CYSTIC FIBROSIS FOUNDATION THERAPEUTICS (CFFT)

General Approach/Methods Applied:

(COLLABORATIVE + PUSH) Non-profit collaborative network for drug development for cystic fibrosis employing venture philanthropy.

Summary:

"Established in 2000, Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) is the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation. CFFT supports and governs activities related to cystic fibrosis (CF) drug discovery through the many stages of drug development and clinical evaluation. The CF Foundation provides support to fund CFFT's operations, specifically the Therapeutics Development Program" (CFFT, 2015).

"Sound investment by the Foundation in cutting edge science has built an extensive base of knowledge about this disease. Some of these ideas have already led to innovative new therapies now in the Drug Development Pipeline" (CFFT, 2015). The Therapeutics Development Program (TDP) "model initiative has the infrastructure in place to support a virtual "pipeline" of CF therapeutics development from the discovery phase through several stages of clinical evaluation" (CFFT, 2015). "Through the Therapeutics Development Program, CFFT offers matching research awards to scientists, as well as access to a specialized network of CF clinical research centers. These awards provide support for the drug discovery phase through several stages of evaluation to complete the full-length drug development pipeline. The Therapeutics Development Program provides companies with a new opportunity to have investment capital during the early phases of drug research. And, it ensures the availability of new potential compounds for clinical investigation for the CF community" (CFFT, 2015). "The TDN promotes quality, safety and efficiency in CF clinical trials by centralizing and standardizing the research process. There is centralized review of clinical trial protocols; common policies to protect patient safety; standardized research procedures; shared expertise among top CF researchers; tools and training for clinical research staff; and a quality improvement program tailored for clinical research" (CFFT, 2015). Through CFFT, "funds are provided on a matching basis for preclinical and clinical development, awards are milestone driven, a scientific advisory council oversees progress, and upon approval of a drug, CFFT receives a multiple of its investment (or a royalty based on sales), which it can then reinvest in new products" (Wizemann, 2008).

Main Project(s):

CFFT has worked with Vertex "to support research and development activities related to potentiator compounds and corrector compounds, including ivacaftor, lumacaftor and VX-661" (Vertex AR, 2015).

CFFT drug development pipeline: **http://www.cff.org/research/DrugDevelopmentPipeline/**

Effectiveness:

"The TDN has conducted more than 100 clinical studies for CF in a wide range of therapeutic areas, including CFTR modulators, anti-infectives, anti-inflammatories, nutritional therapies and airway surface liquid hydrators. The studies have resulted in more than 175 publications" (CFFT, 2015).

Critiques/Questions Raised in the Literature:

There is concern that due to the venture philanthropy approach taken, drugs being discovered via CFFT are being overpriced and critics are hesitant to embrace the financial arrangement between the foundation and pharma as it essentially means the foundation is financially benefiting at the expense of patients and creates a conflict of interest (Fauber, 2013).

A2 DRUG DISCOVERY INCENTIVES
D. VENTURE PHILANTHROPY FOR DRUG DISCOVERY AND DEVELOPMENT

CYSTIC FIBROSIS FOUNDATION THERAPEUTICS (CFFT)

For example, CFF recently developed an incredibly expensive drug, argued to be one of the world's most expensive medicines, Ivacaftor (Kalydeco). While Ivacaftor was expected to be a "game changer" as it is "the first drug targeting the underlying cause of cystic fibrosis," not only did CFF allow the drug to be priced at over $300,000 PPY but they then engaged in advocacy efforts to get the UK and Australia to reimburse or pay for the drug on their national systems despite it not being cost-effective (Cohen, 2014).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Donors:
American Airlines; abbvie; Actavis; Novartis; Genentech; Wells Fargo; Vertex; Walgreens; Chubb.

University Involvement:

Various centers at the University of Colorado School of Medicine, the Seattle Children's Hospital and other universities associated with TDN.

TDN University Centers:
https://www.cff.org/Our-Research/Therapeutics-Development-Network/Working-with-the-TDN/CFFT-Therapeutics-Development-Centers/

A2 DRUG DISCOVERY INCENTIVES
D. VENTURE PHILANTHROPY FOR
DRUG DISCOVERY AND DEVELOPMENT

DEMENTIA DISCOVERY FUND

General Approach/Methods Applied:

(POOL + PUSH) Venture philanthropy capital fund to accelerate research on dementia drugs.

Summary:

The US$100 million Dementia Discovery Fund was announced by the UK government in 2015, designed as "a new venture capital fund dedicated exclusively to dementia research. With contributions from the British government, Alzheimer's Research U.K., and five major pharmaceutical companies, it aimed to support preclinical research to develop new drug targets. "Grants from the Dementia Discovery Fund will support small startups, perhaps even in academia, that have demonstrated strong proof of concept for a treatment but need capital for preclinical development . . . This fund allows pharmaceutical partners to pool their risk in that early phase…to bring investment into dementia . . . If a project is successful, companies can bid to develop it further. The assets will be sold on the open market . . . Proceeds will give contributors a return on their initial investment" (Zakaib, 2015).

Main Project(s):

Not yet active but funded.

Effectiveness:

Not clear yet. But "there is currently no drug which can halt or reverse [dementia] in the long term, and pharma industry research in the field has seen failure after failure in late-stage studies over the last 10-15 years. The UK has taken the lead in organizing new international initiatives to bring governments, academic researchers and the pharma industry together to pool resources to accelerate drug discovery and development" (PP DDF, 2015).

Critiques/Questions Raised in the Literature:

There is concern that the fund is not enough on its own and is simply a first step. "Even with the backing of the Dementia Discovery Fund, and even if the clinical trial process is accelerated to enable easier and faster access for patients to any new treatments, these will still be many years away and consequently too late for people who are currently on course for a diagnosis of dementia. What can be done now for this population? In answer to this question, some might argue that the time for a hierarchical strategy to tackle dementia, with investment in finding a cure at the apex, has now passed. Therefore, funds and effort might be better directed towards a more holistic approach that incorporates research and treatment, but also has a focus on better understanding of the factors that increase risk, and how these can be mitigated, as well as those that protect individuals from dementia" (Laneur, 2015).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

"Prime Minister David Cameron's government led the effort, pledging approximately US$22 million in the fall of 2014 to kick-start the fund. Alzheimer's Research U.K. promised another $5 million, GlaxoSmithKline $25 million, and Johnson & Johnson a further $10 million. Pfizer Inc., Biogen Idec, and Eli Lilly and Company will contribute the rest, while other investors will be able to join later on. The financial services firm J.P. Morgan will help manage the fund. A scientific advisory board with representatives from each investor will help select projects to support and offer advice throughout the investment period" (Zakaib, 2015).

University Involvement:

None found.

A3 DRUG LICENSING: DRUG PATENT POOLS AND RELATED INITIATIVES

UNITAID MEDICINES PATENT POOL

General Approach/Methods Applied:

(POOL) Patent pool currently focused on HIV/AIDS treatment implementing voluntary licensing of critical intellectual property in order to make patents work for public good.

Summary:

Established in 2010 with UNITAID, "the Medicines Patent Pool [MPP] works to bring down the prices of HIV drugs and encourage the development of desperately needed new formulations, such as medicines for children. The MPP does this through voluntary licensing of critical intellectual property – making patents work for public health, while giving pharmaceutical innovators compensation for their work"… "The [MPP] works to stimulate competition by saving generics companies the uncertainty of having to negotiate with several patent holders for the right to produce a particular medicine, making it easier for them to enter the market. The MPP works for rights-holders as it assures them fair royalty and gives them a concrete, visual way to contribute to global health. It works for innovators focused on developing countries by making it easier to access the patents needed to develop new products. Most importantly, it works for people living with HIV/AIDS by bringing prices to affordable levels and helping to provide the missing medicines they need to survive" (WIPO MPP, 2011).

The MPP works to "spread access to HIV/AIDS treatment by: Bringing medicines prices down by facilitating competition; fostering the development of better-adapted formulations for developing country contexts, such as medicines for children; and clearing the path for the development of needed fixed-dose combinations . . . The idea behind the patent pool is that patent holders – companies, researchers, universities and governments – voluntarily license their patents to the Pool under certain conditions. The MPP then makes licences available to qualified third parties, such as generic drug manufacturers, which then pay appropriate royalties on the sale of the medicines for use in developing countries" (WIPO MPP, 2011). Key features of the pool are that it is focused on HIV medicines, it is a voluntary mechanism, it targets developing countries, it requires producers getting licenses from the pool to meet agreed quality standards, and it offers various benefits to everyone involved (WIPO MPP, 2011).

Main Project(s):

"The Medicines Patent Pool agreed to its first license with the US National Institutes of Health in September 2010 for a patent on HIV drug darunavir. Significantly, the license allows any manufacturer to produce, and covers production and sale in all developing countries, including those called 'middle-income'" (MSF MPP). In 2011, MPP signed an agreement with Gilead, its first with a pharmaceutical company, "to improve access to HIV and Hepatitis B treatment in developing countries. The agreement allows for the production of the HIV medicines tenofovir, emtricitabine, cobicistat, and elvitegravir as well as a combination of these products in a single pill known as the "Quad." Cobicistat, elvitegravir and the Quad are products still in clinical development. The license also allows for the development and manufacture of other combinations that include these medicines. Tenofovir is also licenced for use in Hepatitis B" (UNITAID MPP, 2011). The agreement was stated to "be transparent; facilitate research on formulation including fixed doses combinations; [be] faster than bilateral negotiations between generator and generic pharmaceutical companies; [and] facilitate the practical implementation the trips flexibilities" (UNITAID MPP, 2015).

Effectiveness:

"To date, MPP has signed agreements for twelve antiretrovirals (ARVs) for countries home to 87-94% of people living with HIV in the developing world

A3 DRUG LICENSING: DRUG PATENT POOLS AND RELATED INITIATIVES

UNITAID MEDICINES PATENT POOL

and for one medicine for an HIV opportunistic infection." These are: "lopinavir/ritonavir (LPV/r) for paediatric use, tenofovir alafenamide (TAF), dolutegravir (DTG) for both paediatric and adult care, atazanavir (ATV), tenofovir disoproxil fumarate (TDF), emtricitabine (FTC), elvitegravir (EVG), cobicistat (COBI), abacavir (ABC) for paediatric use and darunavir (DRV)" (MPP, 2015).

"The MPP has also sub-licensed to generic manufacturers, who are already beginning to produce and supply HIV medicines at a lower cost. As of January 2015, the Medicines Patent Pool had signed sub-licensing agreements with ten key generic manufacturers: Aurobindo Pharma Limited, Cipla, Desano, Emcure Pharmaceuticals, Hetero Labs, Laurus Labs, Micro Labs, Mylan, Shasun Pharma Solutions and Shilpa Medicare" (MPP, 2015).

Additionally, "MPP, together with UNITAID, the Drugs for Neglected Diseases initiative (DNDi) and the Clinton Health Access Initiative (CHAI), is a partner in the Paediatric HIV Treatment Initiative (PHTI) to accelerate the development of appropriate paediatric FDCs for resource-limited settings" (MPP, 2015).

In theory the MPP "will help to speed up the availability of lower priced, newer medicines in developing countries because there will be no need to wait out the 20-year patent term. With licences covering low- and middle-income countries, the scope of the market will be large enough to encourage multiple producers to compete in the market and sustainably drive down prices" (WIPO MPP, 2015).

A recent article states that "over [US]$1 billion [will be] saved by 2028 through medicines patent pool licensing agreements" and "since 2010, UNITAID's investments in the MPP have yielded 2.6 times the value of its funding through such licensing deals"… "MPP now has licences that include all the patented ARVs recommended as preferred first line treatments by the WHO for adults and children of all age groups" (UNITAID MPP, 2014).

"Compared with TRIPS Compulsory Licensing and time-limited donation programs, the HIV patent pool is a groundbreaking strategy in addressing the accessibility of AIDS treatment within the international AIDS community. Through donating drug licenses, the generic versions can be manufactured by most developing countries at an affordable price, directly contributing to the globally general Antiretroviral Therapy (ARV) accessibility. Second, pooling the major patents can be a more sustainable method for authorized generic drug to be produced. Finally, the development of FDCs can become much more cost-efficient by sharing the patents among volunteer pharmaceutical companies in the pool" (Hu, 2011).

MPP Cost-benefit analysis: **http://www.keionline.org/misc-docs/1/cost_benefit_UNITAID_patent_pool.pdf**

Critiques/Questions Raised in the Literature:

"The major challenge facing the patent pool is that numerous major pharmaceutical companies expressed their hesitations on joining the patent pool. There are multiple factors contributing to the current situation. First, for pharmaceutical companies, donating patents would lead to a great profit loss due to the authorization of generic drug production. Second, although collaborative partnerships between the companies exist, the competitive relationships dominate the pharmaceutical market. However, the rationale of the HIV patent pool is largely grounded on the collaborations among different patent holders. Given this structural contradiction, which is difficult to challenge, pooling patents may not be realized if there are not powerful incentives for patent donators. One of the potential incentives is the patent sharing among volunteer pharmaceutical companies, which allows them to develop FDCs and broaden research area in a cost-efficient manner. However, this incentive is based on pharmaceutical companies' wide participation and donation.

A3 DRUG LICENSING: DRUG PATENT POOLS AND RELATED INITIATIVES

UNITAID MEDICINES PATENT POOL

Finally, although several companies have signed their voluntary license agreements with generic manufacturers, "most agreements so far are overly restrictive in terms of which regions they cover, and leave out too many people living with HIV and do not include enough generic companies to create the level of competition needed to sufficiently drive prices down" (Campaign For Access To Essential Medicines (CFATEM), 2011)" (Hu, 2011).

The pool is voluntary and often limited to low-income countries.

Specifically concerning darunavir, "the license itself does not allow for generic production of the drug, as Johnson & Johnson, which holds other key patents on the drug, so far refuse to put their patents in the Pool." In July 2011, pharmaceutical company Gilead agreed to put patents for four HIV medicines in the Pool, but "the licences disappointingly excluded several developing countries and restrict the number of companies that can produce the drugs. Pressure must be kept up to push Gilead to improve these licenses, as well as to push other companies to put their patents in the Pool" (MSF MPP).

Proposed Changes/Improvements:

According to a previous evaluation, "an alternative for promoting the collaborative relationship is to introduce multiple stakeholders concerning the AIDS medicine patent issues into the establishment and structure of the patent for example "an alternative is to introduce two other stakeholders into the pool – the US government and the global AIDS community – into the supporting structure of the patent pool"… "Two additional goals proposed are (1) ensuring increased participation of global AIDS community in policy implementation; and (2) motivating the participation of the federal government in order to facilitate more efficient operation of the patent pool" (Hu, 2011).

Organizations, Stakeholders, And/Or Partners:

With support from KEI and MSF, MPP was founded with funding from UNITAID.

University Involvement:

None found.

A3 DRUG LICENSING: DRUG PATENT POOLS AND RELATED INITIATIVES

GSK POOL FOR OPEN INNOVATION AGAINST NTDS (POINT)

General Approach/Methods Applied:

(POOL) A patent pool that makes technology that could be used to solve problems that arise in R&D available and that contributes know-how to the public domain that may assist in drug discovery or development, specifically for NTDs.

Summary:

GSK has made a commitment to open innovation and taking a flexible approach to IP, particularly in least developed countries for NTDs via the pool for open innovation started in 2009 (Hunter, 2011), GSK "make[s] available patented technology that could be used to solve problems that arise in R&D" and "contribute[s] available know-how that may assist discovery or development" (Skingle, 2010). The pool is administered by BVGH, which facilitates patent licensing, hosts disease-specific conferences, and partners to promote utilization (Skingle, 2010). The pool is comprised of all Open Laboratory Drug Discovery at GSK housed at the GSK Medicines Development Centre in Tres Cantos, Madrid and has focused on malaria, TB and NTDs in the past (Skingle, 2010). "Tres Cantos is a bioscience park based on an open innovation model in which companies located on the park . . . have shared access to specialist skills, equipment and expertise" (Hunter, 2010).

Main Project(s):

"GSK screened 2 million compounds vs the malaria parasite P.falciparum to generate 13,500 hits. It took 5 GSK scientists 1 year to complete; GSK to publish the chemical structures & associated assay data; data freely available via a user-friendly database; publication of Malaria work in high profile journal" (Skingle, 2010). This information was used in creating the malaria box with MMV (GPAH GSK, 2015). "In October 2012 [GSK] announced [it was] adopting the same open approach to TB research, by putting around 200 TB "hits" into the public domain" (GlaxoSmithKline, 2015).

The Tres Cantos "Open Lab has provided funding for three projects, totalling slightly over [US]$425,000. Since the launch, six projects have begun in the Open Lab, including one with South Africa-based iThemba Pharmaceuticals in multidrug-resistant TB (MDR-TB) and co-infection with HIV/AIDS; GSK provided in-kind contribution and the support of its scientists. iThemba was the first company to take advantage of the Pool for Open Innovation against Neglected Tropical Diseases (POINT)" (Phillippidis, 2011).

Effectiveness:

As of 2010, GSK had contributed over 800 patents/applications targeting NTDs. The first pool partner, Almylam, contributed key complementary discovery technology and fundamental RNAi technology involving over 1500 patents (Skingle, 2010). GSK places all chemical probes into the public domain with no IP and no restrictions during the pre-competitive phase (Skingle, 2010). As of 2011 there were over 2300 patents deposited in the pool (Hunter, 2011).

Critiques/Questions Raised in the Literature:

Following the addition of chemical probes and other compounds to the pool, "there were comments that these compounds are not 'drug-like', as claimed by GSK. This highlights the need for very clear communication about the value and the nature of what is being shared, as any perceived lack of transparency could easily create a negative impression for the consortia" (Hunter, 2011). Additionally, after the launch of the pool and Almylam's patent contributions, "the program

A3 DRUG LICENSING: DRUG PATENT POOLS AND RELATED INITIATIVES

GSK POOL FOR OPEN INNOVATION AGAINST NTDS (POINT)

seemed to languish in the following months, a situation seemingly caused by confusion over what to do with all that patent information" and skeptics have wondered " if the program is more about creating good will than substantial scientific progress"(Jarvis, 2010). Another concern is the limitation of the pool "on geographic coverage to only least developed countries as a starting condition" (So, 2012).

Proposed Changes/Improvements:

"In October 2011, GSK joined WIPO Re:Search as a founding member. WIPO Re:Search is an evolution of GSK's Pool for Open Innovation against Neglected Tropical Diseases (POINT). It brings together eight leading pharmaceutical companies in collaboration with the US National Institutes of Health (NIH) and multiple non-profit research organizations under the auspices of WIPO – a UN body – to help accelerate the development of new and better treatments against NTDs" (UCNTD GSK, 2015).

Organizations, Stakeholders, And/Or Partners:

The pool was founded by GSK and administered by BVGH. Following the first participant, Almylam, MIT became the first academic institution to join the pool, followed by the Technology Innovation Agency of South Africa, the first government agency. Additional partners include DNDi, MMV, TB Alliance, iThemba Pharmaceuticals, and Emory Institute for Drug Discovery (Skingle, 2010).

University Involvement:

MIT; Emory University.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

EUROPEAN VACCINE INITIATIVE (EVI)

General Approach/Methods Applied:

(COLLABORATIVE + PUSH) Non-profit PPP that works to bring vaccines to market, specifically focusing on fostering an environment in which potential vaccines can be brought to clinical trials and made accessible to low income populations. Houses TRANSVAC.

Summary:

The European Vaccine Initiative (EVI), founded in 1998 following the success of the European Malaria Vaccine Initiative, "fund[s] studies to bridge the gap between promising vaccine candidates and late-stage clinical trials. More broadly, [it] foster[s] an environment in which potential vaccines can be brought to clinical trials and made accessible to low income populations. In all this [EVI] collaborate with multiple stakeholders, to whom [it] offers a forum and focal point" (EVI, 2015). EVI works with partners including EDCTP to accelerate testing and clinical development of vaccine candidates (EVI, 2015). According to its site, EVI works in vaccine development, coordination, harmonization, R&D services, capacity strengthening, and policy activities alongside various partners (EVI, 2015). EVI's three main objectives are "to financially and technically support the accelerated development and clinical trials of vaccines for diseases of poverty in Europe and Developing Countries; to promote affordability and accessibility of vaccines for diseases of poverty in Europe and Developing Countries; and to engage European and international resources committed to research on vaccines for diseases of poverty" (TRANSVAC EVI, 2015). EVI's "three scientific pillars" are translational vaccine research, knowledge sharing, and harmonization of vaccine research efforts (Geels, 2011).

Main Project(s):

EVI began with work focused largely on malaria but has expanded "its scope to include vaccines directed against other diseases of poverty, such as Chagas, Dengue, HIV/AIDS, Leishmaniasis and Tuberculosis" (EVI, 2015). The TRANSVAC Consortium is one of EVI's many projects and works "to accelerate the development of promising vaccine candidates by bridging the gap between bench research and CTs" via research, networking, and additional services "through a peer-reviewed competitive process" (Geels, 2011). EVI developed the Malaria Vaccine Technology Roadmap in collaboration with the other members of the Malaria Vaccine Funders Group (Geels, 2011).
EVI has also recently signed MoUs with various international partners including USAID, PATH, TVI, and WHO (Geels, 2011).

The EVI Project index:
http://www.euvaccine.eu/portfolio/project-index

Effectiveness:

"During the first decade of its existence, EVI has successfully developed 24 malaria antigen combinations in 32 vaccine formulations and advanced 15 vaccine candidates into phase I a clinical trials, three of which have been transferred to partners for further clinical development" (EVI, 2015). "As of 2011, EVI ha[d] funded 29 different vaccine adjuvant/delivery formulations resulting in 13 vaccine candidates advanced into Phase I CTs" (Geels, 2011). "EVI has proven through its development of the GMZ2 and MSP3 blood-stage vaccine candidates that it can facilitate vaccine development through to Phase II clinical testing. Both concepts were deemed safe and tested in

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

EUROPEAN VACCINE INITIATIVE (EVI)

dose-finding CTs within 3–6 years" (Geels, 2011). Additionally, "EVI has coordinated the research networks EURHAVAC, PHARVAT, INYVAX and OPTIMALVAC, which are specific EC FP6-funded actions on harmonization of vaccine development in Europe and beyond" (Geels, 2011).

Critiques/Questions Raised in the Literature:

"Europe's position as the leader in different fields of vaccinology is now hampered by the decision of European governments, for economic reasons, to withdraw from funding state-owned vaccine production facilities. This withdrawal of funding is likely to slow down innovation in vaccine research, having an immediate effect on the pool of knowledge and competencies, and increasing the degree of fragmentation of know-how and facilities" (Geels, 2011).

Proposed Changes/Improvements:

"When innovation in research is not stimulated enough, then very few new vaccine candidates are available for proof-of-concept, that is, the EVI pipeline is drying up. In Europe it has classically been the role of the national research councils and of the Directorate General (DG) research of the EC to fund innovation. The risk associated with this has become evident over the last few years and to mitigate this risk it has been decided by the EVI Scientific Advisory Committee to broaden the strategy and commence funding of vaccine concepts and technical platforms that are still in the discovery phase of development" (Geels, 2011).

Organizations, Stakeholders, And/Or Partners:

Biomedical Primate Research Centre; Jenner Vaccine Foundation; National Institute for Public Health and the Environment (Intravacc); Royal College of Surgeons in Ireland (RCSI); Institut Pasteur (IP), etc.

Donors:
Republic of Ireland, Germany, the Netherlands, Sweden, and Denmark.

University Involvement:

Hosted by Heidelberg University; Stockholm University; University of Oxford.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

TRANSVAC (*UNDER EVI)

General Approach/Methods Applied:

(COLLABORATIVE) A collaborative project to create a network for vaccine R&D run by EVI that ended in 2013 and is currently being renewed.

Summary:

TRANSVAC was "a collaborative infrastructure project funded under the European Commission's (EC) 7th Framework Programme (FP7). The project is the joint effort of leading European groups in the field of vaccine development, and is coordinated by the European Vaccine Initiative (EVI). TRANSVAC was designed in order to enhance European research and training and foster the seamless implementation of a permanent research infrastructure for early vaccine development in Europe" (TRANSVAC, 2015). "TRANSVAC addresses knowledge transfer and capacity building by providing a transnational vaccine development platform accessible free of charge (OPEN CALL) or on a paid basis by innovative European vaccine research groups. Networking activities include a modular course on concepts in vaccine development, a workshop on Global Analyses Platforms, as well as a series of workshops on animal models. The consortium will be open to any interested party, should they be able to bring relevant resources and experience for mutual benefit" (TRANSVAC, 2015).

Main Project(s):

The research component of TRANSVAC targets the improvement of the use of (molecular) assays and standardised reagents, adjuvants, animal models and vaccine and cell bank production specific to the development of experimental vaccines. Seven of the 15 project Work Packages in TRANSVAC are dedicated to research into various aspects of vaccine development (TRANSVAC, 2015).

Effectiveness:

"By the time TRANSVAC ended in September 2013, partnerships were in place for 29 vaccine and vaccine-related studies on diseases such as Lyme disease, malaria, tuberculosis, dengue, influenza, mumps, whooping cough (Bordetella pertussis), pneumonia (Streptococcus pneumonia), HIV, plus two types of cancer . . . The TRANSVAC team granted free access to 29 projects, which were selected through a two-step peer review process, first on scientific excellence, and then on the feasibility and impact of the vaccines under development" (European Commission, 2015a).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

Developed by TRANSVAC and the broader EVI network, "the proposal for a European Infrastructure for vaccine R&D has been discussed and validated during a workshop held in June 2013, by 70 representatives of vaccine developers and manufacturers (academic researchers, biotech companies, large vaccine development companies, PDPs and other European vaccine-related projects), regulatory authorities, international and national policy makers, and funding agencies" (TRANSVAC, 2015). "The former [TRANSVAC] partners now plan to apply for EU research funding to establish a network of all stakeholders to promote even more collaboration – called the European Vaccine Research Development Infrastructure (EVRI). They are also applying for funding for a second project, similar to TRANSVAC" (European Commission, 2015a).

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

TRANSVAC (*UNDER EVI)

Organizations, Stakeholders, And/Or Partners:

European Vaccine Initiative (EVI); Biomedical Primate Research Centre (BPRC); Helmholtz Centre for Infection Research (HZI); Vakzine Projekt Management GmbH (VPM); LIONEX GmbH; Central Veterinary Institute; UK Department of Health; Centre for Emergency Preparedness and Response; Department of Health, Medicines and Healthcare Products Regulatory Agency, NIBSC; TuBerculosis Vaccine Initiative (TBVI), etc.

University Involvement:

Max Planck Institute for Infection Biology; University of Regensburg; London School of Hygiene & Tropical Medicine; University of Oxford, The Jenner Institute (UOXF); University of Lausanne.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

SABIN VACCINE INSTITUTE

General Approach/Methods Applied:

(COLLABORATIVE) Larger organization that houses a PDP focused on vaccine-preventable and NT diseases along with the Global Network for Neglected Tropical Diseases and other advocacy and fundraising entities.

Summary:

Founded in 2000 with funds from BMGF and originally called the Human Hookworm Vaccine Initiative (SABIN, 2015), "The Sabin Vaccine Institute Product Development Partnership (Sabin PDP) focuses on creating safe, effective, and low-cost vaccines to prevent human suffering from infectious and neglected tropical diseases that infect more than 1 billion people worldwide" (DSW, n.d.).

"The Sabin PDP collaborates with private, academic, and public institutions in low- and middle-income countries, Australia, the United States, and Europe for preclinical development, vaccine manufacturing, and clinical testing. It is the first and only vaccine development programme targeting human hookworm infection. In addition, the Sabin PDP is developing vaccines for schistosomiasis, leishmaniasis, Chagas disease, ascariasis, trichuriasis, and severe acute respiratory syndrome (SARS)—diseases that primarily affect people living in poverty around the world" (DSW, n.d.). "With over a decade of experience, Sabin PDP has produced a well-rounded model that serves as a blueprint for the development of safe and effective vaccines against vaccine preventable and neglected tropical diseases. Existing capabilities include: product development, technology transfer and manufacturing, epidemiological and clinical studies, and ethical and regulatory approvals . . . Sabin works on developing new vaccines, advocating for increased use of existing vaccines, and promoting expanded access to affordable medical treatments" (SABIN, 2015).

The Sabin PDP is part of the larger Sabin Vaccine Institute and operates alongside Sabin's Vaccine Advocacy and Education Program, its Global Network for Neglected Tropical Diseases, and the Sabin Foundation Europe. The Sabin PDP also contains the Michelson Neglected Disease Vaccine Initiative, which "supports a number of Sabin PDP activities" including the HHVI, the Pan-anthelminthic Vaccine Discovery Program, and the SVI, "and helps advance an innovative model" (SABIN, 2015).

Main Project(s):

Sabin's "Global Network for Neglected Tropical Diseases works to raise awareness, political will and funding necessary to control and eliminate the seven most common neglected tropical diseases (NTDs)"… "The Vaccine Advocacy and Education program at Sabin is dedicated to reducing the burden of preventable diseases by bringing together key stakeholders and leaders in government, private sector and civil society in order to foster cooperation, share information and best practices and develop improved vaccine policy and access" (SABIN, 2015).

"In 2008, Sabin PDP launched an initiative to develop a vaccine against schistosomiasis. The Sabin PDP recently initiated development for a new therapeutic vaccine for Chagas disease that will be undertaken with partners in Mexico. The vaccine is being developed in partnership with Baylor College of Medicine, and Texas Children's Hospital with support from the Slim Initiative for the Development of Neglected Tropical Disease Vaccines" (SABIN, 2015).

Sabin has a Human Hookworm Initiative (HHI), with two lead candidate antigens being developed to stimulate the human immune system to produce antibodies that inhibit parasite blood feeding: Na-GST-1 and Na-APR-1. Na-GST-1: Phase 1 clinical testing of the Na-GST-1 hookworm vaccine began in January 2012. Currently, clinical trials are being carried out in Minas Gerais, Brazil and Washington, DC. Na-APR-1: Na-APR-1 has also shown protection against adult hookworm in preclinical studies. Clinical testing began in September 2013. Sabin is a member of the HOOKVAC consortium, "led by the Academic Medical Center (AMC) at the University of Amsterdam, which has been awarded

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

SABIN VACCINE INSTITUTE

a grant from the European Commission to expand the development and testing of [the Hookworm] vaccine" (SABIN, 2015).
Under the Schistosomiasis Vaccine Initiative (SVI), "in collaboration with researchers at the James Cook University and The George Washington University, a promising new antigen, Sm-TSP-2 (Schistosoma mansoni Tetraspanin-2), was selected for development as a schistosomiasis vaccine. Then at Texas Children's Hospital and Baylor College of Medicine, Sabin and its partners developed the process for manufacture of the vaccine under cGMP, and was followed by technology transfer to Sabin's manufacturing partner, Aeras. Following final lot release, a toxicology study and subsequent regulatory filing for the vaccine are scheduled to take place in 2013 with a Phase 1 clinical trial slated to begin in late 2013/2014" (SABIN, 2015 – hasn't been updated).

"The PDP has also initiated a new project in early pre-clinical stages for the selection and discovery of antigens appropriate to advance into the development process of a leishmaniasis vaccine" (SABIN, 2015).

Effectiveness:

"With over a decade of experience, the program has produced a comprehensive, relatively low-cost model that serves as a blueprint for non-profit vaccine research and development and ongoing efforts to fight public health threats that adversely impact more than one billion people worldwide" (SABIN, 2015).

Critiques/Questions Raised in the Literature:

There has been concern in the past that Sabin's funding sources are not diverse enough, which could prevent reduction of transaction costs and up-front costs, even if pooling is implemented (Grace, 2011). As of 2011, Sabin, IAVI, and MMV were experiencing falling funding (Shetty, 2011).

Proposed Changes/Improvements:

Sabin's EVP believes that "in addition to quickening the pace of country and regional adoption of the Global Vaccine Action Plan (GVAP), "integration and cooperation are areas (where) [PDPs] could all do better" (Marine, 2014).

Organizations, Stakeholders, And/Or Partners:

Pharmidex Pharmaceutical Services Limited; Q-Biologicals; Amsterdam Institute For Global Health And Development (Aighd); Hôpital Albert Schweitzer; New York Blood Center; National Institutes Of Health; Laboratory Of Malaria And Vector Research, Vector Molecular Biology Section, Birmex; Center For Research And Advanced Studies Of The National Polytechnic Institute; The Institute Of Parasite Diseases, Chinese Centers For Disease Control And Prevention; Instituto Butantan; Fundacao Oswaldo Cruz; Sabin Vaccine Institute; and Texas Children's Hospital Center For Vaccine Development

Donors:
GHIT Fund and others.

University Involvement:

University Of Tuebingen; Leiden University Medical Center (Lumc), Academic Medical Center, University of Amsterdam (Amc); University Of Nottingham; University Of Texas Medical Branch; Autonomous University Of Yucatan; London School Of Hygiene and Tropical Medicine; James Cook University (Jcu); University Of Kansas; The George Washington University – Department Of Microbiology, Immunology And Tropical Medicine; and Baylor College Of Medicine.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

INTERNATIONAL AIDS VACCINE INITIATIVE (IAVI)

General Approach/Methods Applied:

(COLLABORATIVE + PUSH + PULL) Global non-profit organization working to ensure the development of AIDS vaccines for use throughout the world through research, development of consortia and partnerships, funding of external work, and product development services (houses a PDP and an innovation fund).

Summary:

"IAVI [The International AIDS Vaccine Initiative] is a global non-profit organization whose mission is to ensure the development of safe, effective, accessible, preventive AIDS vaccines for use throughout the world. Founded in 1996, IAVI works with governments, academia, civil society, and the private sector in 25 countries to design and evaluate novel AIDS vaccine candidates, advancing a portfolio of the most promising approaches in clinical testing, based on the latest scientific insights. It has a strong focus on the countries where HIV/AIDS has greatest impact, coordinating a network of research laboratories in five African countries and in India, building clinical research capacity, engaging with local communities and providing services such as free HIV testing and counseling. IAVI is dedicated to ensuring that a future AIDS vaccine will be available and accessible to all who need it, including those vulnerable groups (such as women and girls) who are often poorly served by existing HIV prevention tools. It also conducts policy analysis and serves as an advocate for the AIDS vaccine field, supported by generous donations from governments, private individuals, corporations, and foundations" (DSW, n.d.).

Essentially, IAVI "supports a comprehensive approach to addressing HIV and AIDS that balances the expansion and strengthening of existing HIV prevention and treatment programs with targeted investments in the design and development of new tools to prevent HIV" (IAVI, 2015). IAVI is comprised of experts in policy research, social science research, observational epidemiology, and clinical trials (IAVI, 2015). "IAVI serves as a bridge between sectors and has forged many longstanding partnerships with researchers in government, academia, industry and the non-profit sector to advance AIDS vaccine development. IAVI provides its partners with support in translational research—the processes essential to converting scientific concepts into products that can be manufactured on a large scale and evaluated in humans. At the same time, the organization seeks to harness the unique expertise and resources of industry to design and develop vaccine candidates, in part through partnerships in which IAVI assumes much of the risk associated with the early stages of such efforts. These partnerships are instrumental to IAVI's efforts to quickly advance the most promising candidates forward. IAVI also partners with civil society groups around the world to advocate for continued investment in new tools and strategies to prevent HIV transmission. The organization works closely with policymakers, HIV-prevention advocates and communities in which vaccine trials are conducted to sustain support for AIDS vaccine development. IAVI also conducts policy analyses in partnership with government agencies and other organizations to model the potential impact of HIV vaccines on the AIDS pandemic and monitors funding trends in HIV-prevention research" (IAVI, 2015).

Main Project(s):

"Over the past decade, IAVI and its partners have launched research consortia to address some of the major challenges of the field. The Neutralizing Antibody Consortium continues to make significant contributions to the design of vaccine candidates that have the potential to neutralize a broad spectrum of HIV variants. The engagement of developing countries, where the AIDS pandemic has taken its greatest toll, is essential to IAVI's model" (IAVI, 2015).

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

INTERNATIONAL AIDS VACCINE INITIATIVE (IAVI)

"IAVI and its partners in Africa have established a highly regarded clinical research network to evaluate AIDS vaccine candidates and conduct related epidemiological research. More recently, the Government of India's Translational Health Sciences and Technology Institute has partnered with IAVI to establish an HIV Vaccine Discovery Program" (IAVI, 2015). IAVI's science, "pursued with many partners, focuses on: Discovery and development of vaccine candidates capable of eliciting broadly neutralizing antibodies (bNAbs) to prevent HIV infection; Discovery and development of replicating viral vector-based vaccine candidates capable of preventing and controlling HIV infection; and providing product development services to the broader AIDS vaccine field to help advance the most promising candidates into clinical development" (IAVI, 2015).

IAVI also runs the IAVI Report, a publication on AIDS Vaccine Research (IAVI Report, 2015).

All IAVI studies can be found here including clinical trials, observational and epidemiological research, policy research, and social research:
http://www.iavi.org/who-we-are/experts/our-studies

Effectiveness:

"In September 2009, a global group of researchers led by IAVI published a study in the journal Science identifying PG9 and PG16, two highly powerful broadly neutralizing antibodies against a wide variety of HIV variants. The site on the virus to which PG9 and PG16 attach revealed a vulnerability on HIV. PG9 and PG16 were the first new broadly neutralizing antibodies against HIV discovered in more than a decade and are the result of a global effort launched in 2006" (IAVI Wikipedia).

Critiques/Questions Raised in the Literature:

As of 2011, IAVI's funding was falling (Shetty, 2011).

Proposed Changes/Improvements:

Sabin's EVP believes that "in addition to quickening the pace of country and regional adoption of the Global Vaccine Action Plan (GVAP), "integration and cooperation are areas (where) [PDPs] could all do better" (Marine, 2014).

Organizations, Stakeholders, And/Or Partners:

Member of the Global HIV vaccine Enterprise and the Global Health Technologies Coalition.

Donors:
Irish Aid; NIAID; USAID; UK DFID; The World Bank; BMGF; Robert Wood Johnson Foundation; The Starr Foundation; Bristol-Myers Squibb; GSK, Google; and others found here:
http://www.iavi.org/what-we-do/partner/donors

University Involvement:

None found.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

INTERNATIONAL VACCINE INITIATIVE (IVI)

General Approach/Methods Applied:

(COLLABORATIVE) International non-profit housing PDPs focused on development of vaccines for cholera, typhoid, and dengue fever.

Summary:

"The International Vaccine Institute (IVI) is an international nonprofit organization that was founded on the belief that the health of children in developing countries can be dramatically improved by the use of new and improved vaccines. Working in collaboration with the international scientific community, public health organizations, governments, and industry, IVI is involved in all areas of the vaccine spectrum – from new vaccine design in the laboratory to vaccine development and evaluation in the field to facilitating sustainable introduction of vaccines in countries where they are most needed. Created initially as an initiative of the United Nations Development Programme (UNDP), IVI began formal operations as an independent international organization in 1997 in Seoul, Republic of Korea. Currently, IVI has 35 countries and the World Health Organization (WHO) as signatories and/or state parties to its Establishment Agreement. The Institute has a unique mandate to work exclusively on vaccine development and introduction specifically for people in developing countries, with a focus on neglected diseases affecting these regions" (IVI, 2015). IVI is able to accomplish a great deal due to "its in-house capacity in basic and translational research and its extensive network of field sites and collaborations with various private-sector, public-sector and governmental partners in countries in Asia, Africa, and Latin America" (IVI, 2015).

Main Project(s):

IVI "has [PDP] vaccine programs focused on cholera, enteric fever, and dengue. It also conducts work on Shigella, rotavirus, polio, and hepatitis E" (IVI, 2015). IVI's main projects have included: The Diseases of the Most Impoverished (DOMI) Program, to generate scientific evidence on the burden of cholera, typhoid fever, and dysentery; The Pediatric Dengue Vaccine Initiative (PDVI) to accelerate the development and introduction of new dengue vaccines in dengue-endemic countries; The Cholera Vaccine Initiative (CHOVI) to develop and introduce new oral cholera vaccines into countries afflicted by cholera; The Vi-based Vaccines for Asia (VIVA) Initiative to develop and introduce new and improved Vi-based typhoid vaccines; The Supporting National Independent Immunization and Vaccine Advisory Committees (SIVAC) Initiative, a partnership between IVI and Agence de Medecine Preventive, to help developing countries in making informed decisions about vaccine introduction and immunization programs; The Biosafety Level 3+ (BSL3+) laboratories at IVI headquarters, which will allow vaccine research on dangerous pathogens such as those that cause avian influenza and tuberculosis; The Typhoid Fever Surveillance in sub-Saharan Africa Program (TSAP), supported by BMGF, to assess the burden of typhoid in 10 countries in Africa; Clinical development of the world's first universal dysentery vaccine with support from BMGF and in collaboration with PATH; The Dengue Vaccine Initiative (DVI), a continuation of PDVI (IVI, 2015).

IVI Vaccine Profile:
http://www.ivi.int/web/www/02_04

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

INTERNATIONAL VACCINE INITIATIVE (IVI)

Effectiveness:

In 2009, "the killed whole-cell oral cholera vaccine developed through IVI [wa]s licensed in India (as Shanchol™), making it the first vaccine developed through IVI to achieve licensure" (IVI, 2015). IVI has "major research programs in 21 countries in Asia, Africa and South America. IVI fills a niche in global efforts of vaccine research, development, training and technical assistance. The success of IVI is linked to its successful collaboration with universities, Ministries of Health, local biotechnology companies, WHO, and vaccine developers in both industrialised and developing countries" (SIDA IVI, 2009).

Critiques/Questions Raised in the Literature:

IVI "had to overcome initial opposition from WHO, which saw it as impinging on its own Western Pacific Regional Office in Manila in the Philippines. Some US vaccine manufacturers were also apparently concerned that it might become a commercial competitor. WHO's opposition abated after three of its officials were appointed to the 16-member board of trustees, including the head of the Western Pacific Regional Office. And one of the new board's first actions last week was to pass an amendment to IVI's constitution explicitly stating that it will not engage in the sale of vaccines, although it may prepare test vaccine lots for evaluation and clinical trials" (Swinbanks, 1997).

Proposed Changes/Improvements:

In a 2009 evaluation conducted by SIDA, further geographical expansion beyond Asia was recommended. SIDA also recommended "that IVI's laboratories primarily should provide support to the translational research and reduce the number of smaller projects." (SIDA IVI, 2009). "In order to further strengthen the translational research and the use of the knowledge that is generated [SIDA] propose[d] that IVI establishes a policy unit that could strengthen its unique contributions among present international vaccine initiative players. [It] also propose[d] that IVI's programs of transfer of technologies be expanded beyond Asia to include Africa and South America. A further expansion of the unique monitoring work of vaccine safety is another recommended priority area" (SIDA IVI, 2009). Additionally, SIDA recommended that IVI diversify its funding sources in order to achieve financial sustainability (SIDA IVI, 2009).

SIDA IVI Report: **http://www.sida.se/contentassets/9173f760cbb14b80b515606abbeb4e32/0709-the-relevance-and-future-role-of-the-international-vaccine-institute-ivi_2000.pdf**

Organizations, Stakeholders, And/Or Partners:

GAVI; BMGF; Sanofi Pasteur in DVI; Sabin Vaccine Institute; World Health Organization.

Donors:

Funding from Republic of Korea and Sweden (IVI, 2015). Additional donors are listed here: **http://www.ivi.int/web/www/do**

University Involvement:

Johns Hopkins University.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

PROGRAM FOR APPROPRIATE TECHNOLOGY IN HEALTH (PATH)

General Approach/Methods Applied:

(COLLABORATIVE + PUSH) Large organization known for partnering with the private sector to develop lifesaving health technologies with global impact through five large programmes dedicated to product development including the Malaria Vaccine Initiative and the Meningitis Vaccine Project. Incorporated **the Institute for OneWorld Health**, a PDP, in 2011. Houses the PATH Global Health Innovation Hub, which directly supports innovators in India and South Africa and incorporates startups, impact equity investors, and the transfer of knowledge from local to global.

Summary:

Founded in 1977 to address women's health issues such as contraception and originally named the Program for the Introduction and Adaptation of Contraceptive Technology before being renamed the Program for Appropriate Technology in Health in 2014 (PATH, 2015), "PATH is an international non-profit organization that transforms health through innovation. Its mission is to improve the health of people around the world by advancing technologies, strengthening systems, and encouraging healthy behaviors. PATH's work spans five platforms: vaccines, devices, diagnostics, drugs, and system and service innovations. PATH is known for partnering with the private sector to develop lifesaving health technologies with global impact and has five large programmes dedicated to product development. PATH works across the R&D spectrum, from development to delivery, channeling the tremendous potential of inventive ideas, scientific discovery, and groundbreaking collaborations into better health and opportunity for all" (DSW, n.d.).

PATH has its own state-of-the-art laboratory and product development shop in Seattle from which to conduct work on health technologies tailored to low-resource settings (PATH, 2015). Additionally, "Numerous PATH publications—including the reproductive health newsletter Outlook, started in 1983—share updated information and research with global health colleagues" (PATH, 2015). PATH's "Global Health Innovation Hub adapts [its] partnership model to directly support innovators in India and South Africa" and incorporates start-ups, impact equity investors, and the transfer of knowledge from local to global into the PATH model (PATH, 2015).

"Headquartered in Seattle, Washington, [PATH has] more than 1,200 staff members and offices in 40 cities in 22 countries: Bangladesh, Belgium, Cambodia, China, DR Congo, Ethiopia, France, Ghana, India, Kenya, Mozambique, Myanmar, Peru, Senegal, South Africa, Switzerland, Tanzania, Uganda, Ukraine, Vietnam, Zambia, and the United States" (PATH, 2015). There is also an affiliated non-profit, "PATH Vaccine Solutions (PVS) . . . that funds some projects conducted by PATH's Vaccine Development Program" (PATH, 2015). PATH now works in advocacy and policy, child health, HIV and AIDS, Malaria, Non-communicable diseases, Nutrition, Reproductive health, Safe birth and newborn care, TB, and Women's cancers (PATH, 2015).

Main Project(s):

"One of PATH's flagship product development programmes is the PATH Malaria Vaccine Initiative (MVI) was established in 1999 to accelerate the development of malaria vaccines and catalyze timely access in endemic countries"… "MVI identifies potentially promising malaria vaccine approaches and systematically moves them through the development process. Since its founding, MVI has moved dozens of projects through its pipeline, with half a dozen in clinical development in 2014—including the RTS,S malaria vaccine candidate, under development with GlaxoSmithKline, which is currently in late-stage development" (DSW, n.d.).

MVI portfolio:
http://www.malariavaccine.org/rd-portfolio.php

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

PROGRAM FOR APPROPRIATE TECHNOLOGY IN HEALTH (PATH)

A second primary initiative of PATH is the Meningitis Vaccine Project (MVP), which was established in 2001 in collaboration with the WHO. The MVP has "developed a needed vaccine to address a specific strain common in Africa's 'meningitis belt.' Technology was licensed through the U.S. National Institutes of Health to the Serum Institute of India, which agreed to provide the vaccine at an affordable price in exchange for transfer of know-how support for clinical trials in Africa and India, and the prospect of a GAVI-supported market. The total project cost amounted to just [US]$60 million, excluding plant costs" (Wilson, 2010). The Meningitis A Vaccine, MenAfriVac, is now available across Africa.

In addition to MVI and MVP, PATH has had or currently has programs for other vaccine and pharmaceutical technologies including a Rotavirus Vaccine Access and Delivery Program, a Pneumococcal Vaccine Project, and a Japanese Encephalitis Program (PATH, 2015).

Effectiveness:

"The Meningitis Vaccine Project has been a highly-effective and cost-efficient model that has resulted in an innovative adaptation of an existing vaccine. This model should be replicated where appropriate" (Wilson, 2010). PATH is partially responsible for the creation of the first ever malaria vaccine and the creation of the vaccine vial monitor, both of which have the potential for great impact (PATH, 2015).

"Previously used meningitis vaccines had low efficacy and cost US$80 per dose. The new vaccine has high efficacy against the type of meningitis that is most prevalent in Africa and costs less than $0.50 per dose. The entire vaccination research and development project cost less than US$100 million, about one-fifth the typical cost for developing a vaccine" (PATH WIkipedia).

"The new [malaria] vaccine has the backing of the UN's Swiss-based WHO which states that it will recommend the use of RTS,S for use starting in 2015, providing it gets approval" (PATH WIkipedia).

Critiques/Questions Raised in the Literature:

"The [MVP] model will mainly be useful for adaptations of existing vaccines with known technologies, rather than for the development of entirely new and more complex vaccines, such as those for TB, malaria and AIDS" (Wilson, 2010).

Proposed Changes/Improvements:

"Looking forward, MVI's R&D strategy is to develop a second-generation malaria vaccine that would support achievement of the longer-term goals of malaria elimination and eradication" (DSW, n.d.).

Organizations, Stakeholders, And/Or Partners:

MVI: Crucell; Gennova Biopharmaceuticals Ltd.; GlaxoSmithKline Biologicals; Malaria Vaccine Development Program; National Institute of Allergy and Infectious Diseases; Seattle BioMed; and Walter Reed Army Institute of Research; MVP: GAVI; Serum Institute of India; WHO; Synco Bio Partners B.V.; Center for Biologics Evaluation and Research; B.Y.L. Nair Charitable Hospital; Nizam's Institute of Medical Sciences; King Edward Memorial Hospital (KEM); the Medical Research Council Laboratories (MRC); Navrongo Health Research Center (NHRC); Center for Vaccine Development-Mali; Institut de Recherche pour le Développement;

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

PROGRAM FOR APPROPRIATE TECHNOLOGY IN HEALTH (PATH)

DiagnoSearch Life Sciences Pvt Ltd.; CDC; FDA; UK HPA; Norwegian Institute of Public Health; MSF; and UNICEF; GHIH: South African Medical Research Council; Unitus Seed Fund; Infectious Disease Research Institute; International Centre for Genetic Engineering and Biotechnology; Vac4All; and Villgro

University Involvement:

Johns Hopkins University; University of Oxford; Emory University; Imperial College London; Loyola University College; University of Miami; Radboud University Medical Centre; and University of Maryland; University of Siena; Norwegian Institute of Public Health; University of Maryland School of Medicine.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

INSTITUTE FOR ONEWORLD HEALTH (IOWH – NOW PART OF PATH)

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on orphan drugs and NTDs, now part of PATH Drug Discovery Program.

Summary:

The Institute for OneWorld Health was formerly a non-profit drug development organization founded in San Francisco in 2000 with seed funding from BMGF that worked to develop "new, affordable medicines for infectious diseases that disproportionately affect people in the developing world, including visceral leishmaniasis, malaria, diarrhea and Chagas disease" (Cecil, 2005). IOWH identified promising drug candidates in late stage R&D, completed animal and human studies, secured quality manufacturing in disease endemic countries, and obtained regulatory approval in disease endemic countries (Hale, 2005).

In 2011, OneWorld Health was absorbed by PATH and became part of PATH's Drug Development Program, which has continued working to develop and ensure availability and accessibility of safe and effective new medicines for diseases disproportionately affecting people in resource-limited settings. It works with partners around the globe to identify potential new medicines for diseases affecting vulnerable populations, assess the safety and effectiveness of investigational medicines, honor international ethical standards for research, collaborate to manufacture and distribute new medicines, and ensure that medicines will be affordable and available for distribution. PATH's current drug development efforts are focused on targeting diarrheal disease, ensuring the supply of malaria treatments, and developing a new tool to stop the spread of HIV (OWH Wikipedia). OneWorld Health was "the first nonprofit pharmaceutical company in the U.S." (Cecil, 2005).

IOWH's principles included the following: "Do not compete[with pharma/biotech/PPPs], Do not duplicate available resources, Focus on D, versus R when possible, Be the bridge – industry & public sector" (Woo) and "do not allow paths to sustainability to influence decision-making" (Hale, 2005). IOWH strived to "find new approaches to old diseases, focus on high-risk, high-reward projects, start with parasitic diseases (for which there are no vaccines), and seek to find new uses for older, off-patent drugs" (Wizemann, 2008).

Main Project(s):

As of 2005, "IOWH had received a grant of nearly US$10 million from the Bill & Melinda Gates Foundation to continue advancing its promising drug for visceral leishmaniasis (VL), paromomycin, through the approval and post-approval process. Specifically, the company [was going to] seek regulatory approval in India th[at] year, execute a post-approval Phase IV study, and complete a clinical trial of shorter duration of administration to optimize the use of paromomycin. A Gates Foundation grant supporting this work was also expected to "support the company's work with partners to manufacture paromomycin at an affordable cost" (Cecil, 2005).

In addition to VL, IOWH worked extensively on malaria, "evaluating a biotechnology process to make artemisinin, the anti-malarial compound of choice, affordable and widely abundant in parts of the world where current therapies are ineffective" and "developing a program focused on the assessment of the safety and efficacy of anti-malarial drugs for use by pregnant women in malaria-endemic areas" (WTN OWH, 2005).

Effectiveness:

IOWH got "regulatory approval granted for Paromomycin IM to treat visceral leishmaniasis and expansion of the treatment program from India to

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

INSTITUTE FOR ONEWORLD HEALTH (IOWH – PART OF PATH NOW)

Bangladesh and Nepal. Established pioneering use of synthetic biology to produce a reliable supply of artemesinin – a key component of malaria treatment – at an affordable price. Semisynthetic artemesinin (PMIM) registered with national drug development agencies of India, Nepal and Bangladesh and included on WHO Essential Medicines List" (SF OWH). IOWH also increased "clinical trial capacity and knowledge in resource-constrained settings in India to conduct GCP-compliant studies and access research with Paromomycin IM Injection" and established mutually beneficial collaborations with leading academic institutions, industries, and local partners that integrate academic and commercial interests with global health concerns. IOWH created "[i]nnovative agreements with Roche and Novartis allow access to highly-restricted IP for promising technologies to address diarrhoeal diseases, enabling iOWH to move rapidly into critical drug development. Also Sanofi-aventis is actively and exclusively partnering with iOWH to develop and commercialize high quality, low cost semi-synthetic artemisinin on a no-profit/no-loss basis" (R4D OWH).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

"By becoming a PATH affiliate, OneWorld Health [was expected to] be able to scale and accelerate its successful drug development efforts, which include developing a semisynthetic version of artemisinin, a key component in treating malaria, to help provide an affordable, stable source of the drug, alleviate shortages, and meet global demand. OneWorld Health remain[s] a nonprofit organization operating out of its South San Francisco headquarters" (PATH OWH, 2011). IOWH had planned to work on "cutting edge technology platforms with potential to transform a unique sector of global health treatment, appropriately-designed treatment strategies that can prolong the useful lifespan of existing drugs for neglected diseases, [and] combination and/or co-administration product strategies in VL and diarrhea to prevent resistance" (Woo).

Organizations, Stakeholders, And/Or Partners:

IOWH worked with Sanofi Aventis, Amyris, and the University of California, Berkeley, Novartis, BMGF, QB3, WHO/TDR, Int'l Dispensary Association, Gland Pharmaceuticals, Janani, Walter Reed, and other large pharmaceutical companies (Hale, 2005).

University Involvement:

"The University of California, Santa Barbara (UCSB), donated a patent that covers the novel use of an established class of cardiovascular medicines, calcium channel blockers, as a potential new drug against the parasitic disease, schistosomiasis, to non-profit pharmaceutical company, the Institute for OneWorld Health, in February 2004" (Gerhardsen, 2006).

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

THE CRITICAL PATH TO TUBERCULOSIS (TB) DRUG REGIMENS

General Approach/Methods Applied:

(COLLABORATIVE + OPEN) PPP with an open source and open innovation collaborative database and Drug Development Coalition to speed the development and impact of new and markedly improved drug regimens for tuberculosis.

Summary:

A public-private partnership, "the Critical Path to TB Drug Regimens (CPTR) initiative, aims to speed the development and impact of new and markedly improved drug regimens for tuberculosis [through formation of innovation partnerships]. Co-founded by the Bill & Melinda Gates Foundation, the Critical Path Institute, and the TB Alliance in 2010, CPTR is a coalition comprised of the world's leading pharmaceutical companies, product development sponsors, diagnostic companies, regulatory agencies, and civil society organizations which support and catalyze advances in regulatory science, the development of infrastructure, and other progress needed to accelerate the pace of development and introduction of novel regimens" (CPTR, 2015b). According to CPTR, "The undersigned partners commit to work together to accelerate the development of new TB drug regimens. Within this initiative, the partners agree to: Encourage information sharing and collaboration among international organizations, industry, and regulatory agencies to innovate and accelerate TB drug development and get important new therapies to patients; Promote the development of new regulatory approaches that support innovative research into TB therapeutics, evaluate new TB drug combinations safely and effectively, and reinforce current guidelines for development of effective drug combinations; Work together, using industry best practices, to test TB drug candidates in combination regimens beginning early in the development process; Create a collaborative coordinating structure to oversee this initiative; Explore creative new funding streams for developing novel combination TB therapies; Advance efforts to utilize existing clinical trial sites for TB while also building clinical trial site capacity for late-stage combination TB drug trials; [and] Support relevant organizations and stakeholders in accelerating procurement of and access to new TB drug therapies for patients in need" (CPTR, 2015b).

Main Project(s):

CPTR's work is broken up into the Drug Development Coalition, led by the TB Alliance, the Rapid Drug Susceptibility Testing Group (RDSTG), the Regulatory Science Consortium, led by the Critical Path Institute, and the Research Resources Group, led by the BMGF (CPTR, 2015b). "The Drug Development Coalition consists of drug developers who allow their TB drug candidates to be tested in combination with one another with the goal of assembling the most effective TB drug regimens, regardless of sponsor" (CPTR, 2015b). Via the RDSTG, "CPTR partners collaborate to advance the field of drug-susceptibility testing by facilitating development of new diagnostic tools to complement novel drug regimens, thereby ensuring the maximum impact of new tools on the disease" (CPTR, 2015b).

"The Regulatory Science Consortium focuses on integrating a combination drug development framework; creating innovative tools, such as data standards, databases, biomarkers and clinical endpoints, and disease progression models; establishing consensus on preferred tools for developing TB drug regimens; and obtaining qualification of such tools for specific content of use from regulatory authorities" (CPTR, 2015b). Lastly, "the Research Resources Group works to create the framework and infrastructure that will support the development of novel TB regimens. This Group

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

THE CRITICAL PATH TO TUBERCULOSIS (TB) DRUG REGIMENS

is responsible for increasing clinical trial capacity, raising funding for late-stage clinical development, promoting understanding of the potential ethical challenges along the path to TB drug development, expanding regulatory guidance globally, providing relevant information on TB drug markets, and ensuring effective and appropriate stakeholder and community engagement" (CPTR, 2015b).

The six projects across drug-development stages being conducted by the Modeling and Simulation Work Group are the Hollow-Fiber System platform for Mtb, the Physiologically-Based Pharmacokinetic Modeling, the Risk Stratification Modeling for drug-induced cardiac arrhythmias, the Liquid Culture Empirical Modeling, the Systems Pharmacology Modeling, and the Population Pharmacokinetic/ Pharmocodynamic Modeling (Romero, 2014).

Effectiveness:

Since its launch, CPTR "has actively engaged the FDA, which has released updated regulatory guide-lines for developing new TB drug regimens with continued efforts to create a more favorable environment for combination regimen development. In 2011, CDER head Dr. Janet Woodcock authored an opinion piece in the New England Journal of Medicine expressing support for "co-development" of therapies for life-threatening diseases such as TB. In addition, the TB Alliance launched the first-ever clinical trial of a novel combination drug regimen for TB in October 2010. The trial tested new TB drug candidates in combination with an existing antibiotic. The study met its milestones, validating the approach to regimen development set forth by CPTR and highlighting the promise of a novel regimen. A new TB drug regimen known as PaMZ designed to treat both drug sensitive and multi-drug resistant TB is moving to a landmark global phase III clinical trial named STAND" (CPTR, 2015a).

By engaging collaborators across the world, CPTR has established a "legal framework allowing data sharing among scientists from the pharmaceutical industry, academia and regulatory authorities" (CPTR, 2015a). Two products are currently in the project pipeline at CPTR, in vitro hollow fiber model for tuberculosis (HFS-TB) and liquid culture (CPTR, 2015a).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Critical Path Institute; US CDC; European Medicines Agency and Chair of CPTR Advisory Panel; National Institute of Allergy and Infectious Diseases, US NIH; TB Drugs, Global Health, Bill & Melinda Gates Foundation; Treatment Action Group; US FDA; TB Alliance; Janssen; Stop TB Department, World Health Organization; CAPRISA; TB Proof; Takeda Pharmaceuticals.

University Involvement:

None found.

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

THE AFRICAN NETWORK FOR DRUGS AND DIAGNOSTICS INNOVATION (ANDI)

General Approach/Methods Applied:

(COLLABORATIVE + PUSH) PPP working on formation of an R&D network and product innovation initiative in disease-endemic regions. Responsible for the proposal for the ANDi Health Technology Fund, which would be equipped with grant making and social venture arms to support ANDi to ensure development, implementation and commercialization of technologies emanating from African Centres of Excellence and other sources.

Summary:

"The African Network for Drugs and Diagnostics Innovation (ANDi) was launched in Abuja in 2008." It was promoted by African governments, the African Diaspora and numerous African research centers and received the immediate support of key partners that are the African Development Bank (AfDB), the European Union (EU), and the World Health Organization (WHO). ANDI is now hosted by the United Nations Office for Project Services (UNOPS) in Addis Ababa (Ethiopia).

The goal of ANDi "is to promote and sustain African-led product R&D innovation through the discovery, development and delivery of affordable new tools, including those based on traditional medicines. ANDI also support[s] capacity and infrastructural development" and to "create a sustainable platform for R&D innovation in Africa to address Africa's own health needs" with the expected outcome being "the discovery, development and delivery of affordable new health tools including those based on traditional medicine, as well as the development of capacity and establishment of centres of research excellence" (ANDi, 2015).

ANDi recognizes "32 African institutions as ANDi Centres of Excellence in health innovation" and, following mapping of the health R&D landscape in Africa, there is now capacity for product R&D and innovation to capitalize upon through broader and more coordinated collaboration: (ANDi, 2015). The business plan for ANDi "call[ed] for a US $ 600 million endowment fund in Africa that can complement other, more classical, donations to generate a sustainable income of up to US $30 million annually to support African health product innovation including a portfolio of 15 network projects, capacity building and support for infrastructural development" (WHO ANDi).

"Discussions are under way with the African Development Bank to host this fund. ANDI aims to partner, fund and coordinate research through the creation of portfolio of collaborative project networks and partnerships" (WHO ANDi). During ANDi's mapping project, it was found that there is "need for IP management" so WIPO is working with ANDi to develop an IP strategy with the potential to design a network IP policy (Botros, 2009). ANDi works with other innovation networks including the Asian and Americas Network for Drugs and Diangostics Innovation (Asian-NDI, South American-NDI). Additionally, a similar approach is being applied among the Association of South East Asian Nations (ASEAN). These regional networks originally formed the basis of activities falling under the TDR Business Line on Innovation for Product Development in Disease Endemic Countries. However, the TDR Business Line is no longer existent although TDR continues to remain engaged in each network's activities.

Main Project(s):

At the last stakeholder meeting it was announced that the review process had been finalized and 2 stand-alone projects had been recommended as well as 5 network projects. News of further verification still outstanding but should be published soon (ANDi, 2015).

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

THE AFRICAN NETWORK FOR DRUGS AND DIAGNOSTICS INNOVATION (ANDI)

Effectiveness:

As of 2009, the projected annual budget for ANDi was USD 31 million by 2015 for 15 network projects (Botros, 2009). Mapping conducted by ANDi identified several hot spots or competency centers in existence in 2009 where a great deal of research and related publications were being generated and in some cases, patent activity was found (Botros, 2009).

ANDi Value Proposition:
http://www.andi-africa.org/index.php/component/content/article/9-about-us/264-why-andi?highlight=YToxOntpOjA7czoxMToicHJvcG9zaXRpb24iO30=

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

There is a current proposal for a Health Technology Fund to make it possible for sustainable development to take place within the ANDi network. “This new African-based fund, equipped with grant making and social venture arms to support the initiative, would ensure development, implementation and commercialization of technologies emanating from African Centres of Excellence and other sources. It will also support partnership building, the operationalization of the African regulatory harmonization activities, and promote local research into Ebola and other emergent infectious diseases. Establishment of incubators for innovation and engagement with the private sector will be pivotal for realizing this ambition” (UNICEF ANDi, 2015).

Organizations, Stakeholders, And/Or Partners:

AfDB; TDR/WHO; UNOPS; Novartis; Ministry of Health, Burkina Faso; LIFElab; Pharmaceutical Product Development (PPD) Inc; Pasteur Institute, etc.

Donors:
European Union

University Involvement:

Theodor Biharz Research Institute; University of Nairobi, Kenya; and University of Yaoundé

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

BIOVENTURES FOR GLOBAL HEALTH (BVGH)

General Approach/Methods Applied:

(COLLABORATIVE + PULL) Non-profit organization that provides incentives and fosters collaboration and partnerships in various areas of global health. Supports the GSK patent pool and WIPO Re:Search.

Summary:

BIO Ventures for Global Health (BVGH) was "founded in 2004 by the Biotechnology Industry Organization (BIO) with financial and in-kind support from the Bill & Melinda Gates Foundation, the Rockefeller Foundation, and BIO." It "is a results-oriented nonprofit organization dedicated to solving global health issues by forming connections between people, resources, and ideas" (BVGH, 2015). BVGH's key activities involve identifying opportunities, finding partners, establishing relationships, and conducting alliance management while engaging stakeholders as well as supporting research and development and knowledge production (BVGH, 2015). This is achieved via capacity building, fellowship programs, provision of access to funding and equipment donation (BVGH, 2015). BVGH's three key objectives are to "synthesize and disseminate information and analysis, increase biotechnology and global health innovator collaborations and partnerships, and design and advocate for market-based incentives" (BVGH, 2015).

Main Project(s):

BVGH supports WIPO Re:search, the Funders Database and other partnerships. Additional current programs include its Membership Program, Fellowship Programs, the Nigerian Capacity Building Initiative, the Ebola R&D Consortium, and the Neglected Disease Product Pipelines (BVGH, 2015). As part of the NTD project BVGH conducts review of pipelines for Ebola, TB, Malaria, and other NTDs and in April 2014, BVGH reviewed the drug and diagnostic pipelines for the 10 neglected tropical diseases selected as priorities by Uniting to Combat NTDS in the London Declaration.

BVGH also completed a similar survey of drugs and diagnostics for tuberculosis and malaria in late 2014, as well as a survey of drugs, diagnostics, and vaccines for Ebola in early 2015.

Prior work, last updated by BVGH in June 2012, "examined the drug, diagnostic, and vaccine pipelines for 25 neglected diseases (including the 10 London Declaration NTDs) under the rubric of the Global Health Primer. The Global Health Primer is now maintained by Emory University" (BVGH, 2015). BVGH's "case studies reveal the progress to date for research in specific diseases and also provide market assessments of the market potential of R&D and the potential return on investment" (RDI BVGH, 2015).

Effectiveness:

Besides working in many countries to support R&D capacity-building, BVGH has done a great deal of mapping of current innovations in and gaps in global health R&D, and more specifically NTDs.

For example:
http://www.bvgh.org/LinkClick.aspx?fileticket=867bPGw-kYo%3D&tabid=79

Critiques/Questions Raised in the Literature:

As of 2010 there was concern that BVGH was moving away from its client base of biotech companies, that its "mission statement [w]as weak and uninformative," that its resource list had not been updated in two years, and that there was not enough progress on its "Global Health Connect Plan" (Dippel, 2013).There is criticism of the primer project, it has been called "passive and marginally helpful to companies wanting to enter or build their global health businesses" (Dippel, 2013).

A4 DRUG ADVANCEMENT: LARGER PPPS OR ORGANIZATIONS THAT HOUSE MULTIPLE INNOVATIVE R&D INITIATIVES

BIOVENTURES FOR GLOBAL HEALTH (BVGH)

Proposed Changes/Improvements:

One critic "recommended that BVGH provide tools and information more useful in business development; for example, for "each project, BVGH should report the quality of participation (e.g., funds, personnel) of each partner and which party was the originator so one can follow the money and figure out who is funding what. BVGH could find and list technologies relevant to global health products that are available for companies to license from academic and research institutions and opportunities for PDPs to work with biotech companies as partners rather than contractors. It could also report on which major pharma companies have experience in developing and commercializing which products, which developing world companies are seeking biotech partners, and, most importantly, identify whom to contact" (Dippel, 2013).

Organizations, Stakeholders, And/Or Partners:

Merck; Pfizer; WHO; GlaxoSmithKline; Novartis; Sanofi; BIO; WIPO; BMGF.

University Involvement:

Emory; Broad Institute of MIT; Harvard; London School of Hygiene and Tropical Medicine; Pace University; and University of Oxford (GHI BVGH, 2009)

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS CHALLENGING CURRENT R&D SYSTEM

A NOTE ON PRODUCT DEVELOPMENT PARTNERSHIPS

Many Product Development Partnerships evaluated were found to implement alternative mechanisms that can and should be considered as types of push, pull, pool, and/or open mechanisms. For instance they may provide funding for researchers or ensure open licensing or promote open data-sharing. However, while these mechanisms are often elements of their work, the PDPs are not based on applying those them in all their activities. However, these PDPs are designed to be collaborative in all that they do. We therefore categorized them as collaborative and noted their work where these other mechanisms were met.

MEDICINES FOR MALARIA VENTURE (MMV)

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on drug development for malaria treatment without in-house product development capacity.

Summary:

Founded in 1999 via US$4 million initial seed financing, the "Medicines for Malaria Venture [MMV] is a leading product development partnership (PDP) in the field of antimalarial drug research and development" (DSW, n.d.). MMV manages "the largest portfolio of antimalarial R&D projects ever assembled, of over 65 projects, MMV has nine new drugs in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria, and drugs that could support the elimination/eradication agenda. MMV's success in research and access & product management comes from its extensive partnership network of over 375 pharmaceutical, academic and endemic-country partners in 50 countries" (DSW, n.d.).

R&D activities are not conducted on MMV's premises but in its partners' facilities with all activities relying solely on outsourcing to external hi-tech laboratories and technical expertise via partners or contract research organizations (CROs). According to MMV, its 'virtual' R&D portfolio is efficient, cost-effective and generally "more flexible than the conventional R&D found in pharmaceutical companies" (MMV, 2015). Furthermore, MMV claims to promote and protect access and affordability via socially responsible agreements with partners. This is achieved via the following principles applied to all MMV contracts:

Exclusivity via worldwide exclusive licenses for programme and background IPR, Royalty-free, particularly in malaria-endemic countries, and Transferable so that IP rights can be transferred to any partners(s) if necessary, specifically for out-of-house manufacturing (MMV, 2015). MMV has in place various policies and is extremely transparent about its operations as well as its funding and expenditure (**http://www.mmv.org/about-us/our-policies**).

MMV's standards of practice: **http://r4d.dfid.gov.uk/Project/60659/**

Main Project(s):

MMV currently works "to develop products that will provide: efficacy against drug-resistant strains of *Plasmodium falciparum*, potential for intermittent treatments (infants and pregnancy), safety in small children (less than 6 months old), safety in pregnancy, efficacy against *Plasmodium vivax* (including radical cure), efficacy against severe malaria, and transmission-blocking treatment" (MMV, 2015).

Although MMV is highly focused on malaria, its research has been expanded beyond antimalarials and includes the Malaria Box, specific to malaria, and the Pathogen Box, a box of 400+ compounds that include actives against parasites, bacteria and other pathogens as well as "development of other technologies that complement antimalarials" (WHO MMV). MMV does a great deal of open source work with projects such as the malaria box and the open source drug discovery initiative (**http://www.mmv.org/research-development/open-source-research**).

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

MEDICINES FOR MALARIA VENTURE (MMV)

MMV's complete R&D portfolio: **http://www.mmv.org/research-development/rd-portfolio**

Effectiveness:

"MMV has developed and brought to registration four new medicines: Pyramax®, co-developed with Shin Poong; Eurartesim® with Sigma-Tau; Guilin's artesunate injection for the treatment of severe malaria, Artesun®; and Coartem® Dispersible, a child-friendly formulation developed with Novartis" (DSW, n.d.).

"Since 2009, over 200 million courses of Coartem Dispersible treatment have been supplied to 50 malaria-endemic countries; and since prequalification in 2010, an estimated 12 million vials of artesunate injection have been delivered, saving 80,000 – 90,000 additional lives" (DSW, n.d.).

MMV's website (2015) lists numerous additional achievements in malaria. These include the screening of over 5 million compounds and the releasing of data from three projects into the public domain, as well as the dispatching of 250 million treatments of Coartem and 36 million vials of artesunate injection (MMV, 2015). According to a 2007 evaluation of MMV conducted by the World Bank, MMV has made "tremendous progress" and "it [was] likely to achieve its specific objective of registering one new malarial drug before 2010," which it did accomplish (GPR MMV, 2007).

Critiques/Questions Raised in the Literature:

"The challenge for MMV is no longer to prove that PDPs can deliver new antimalarials – that has been accomplished. Future success rests on maintaining a healthy portfolio adapted to the new agenda of malaria eradication. Achieving this will require increased international funding. In addition, beyond R&D lies the challenge of access, delivering new antimalarials to those who need them" (MMV, 2015). "MMV is fully aware that, despite its considerable fundraising success, it needs to expand the number of its donors, and that it faces substantial financial gaps even for currently planned R&D activities."

As of 2007, "while the relevance, efficacy, and efficiency of MMV's R&D activities [we]re evident, it [was] too early to reach conclusions on the relevance, efficacy and efficiency of MMV's new and highly demanding downstream access and delivery activities. This work demands individual and organizational skills, and involves interfaces that are not traditional for MMV. It remain[ed] to be seen to what extent and how MMV w[ould] be able to reconcile its private sector entrepreneurial style with the public sector requirements for resolution of policy and institutional issues in access and delivery" (GPR MMV, 2007). "[S]uch PD-PPPs raise particular issues including achieving legitimacy, establishing an appropriate planning and monitoring framework, and ensuring financial sustainability" (GPR MMV, 2007).

Proposed Changes/Improvements:

Following an evaluation conducted by FSG in 2008, MMV revised its business plan and began focusing more on upstream groundwork and downstream access, looking beyond core drug discovery and development and further emphasizing "the role of MMV's access component in complementing other global health actors to support key downstream activities, such as product introduction and enhancing reach" (FSG, 2015). In the TWB evaluation of MMV, "recommendations included supporting the expansion of MMV's mandate to access and delivery, strengthening MMV's engagement with the Roll Back Malaria Partnership

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

MEDICINES FOR MALARIA VENTURE (MMV)

(RBM) and the Special Program of Research and Training on Tropical Diseases (TDR), strengthening MMV's portfolio management with new expertise, new tools and additional staff, and undertaking special efforts to establish effective collaborative mechanisms between MMV and WHO. The evaluation proposed an independent review of MMV's interaction with TDR and RBM, but no such review has been carried out" (GPR MMV, 2007).

Organizations, Stakeholders, And/Or Partners:

Shin Poong; Sigma-Tau; Guilin; Novartis, etc.
List of all External Partners: **http://www.mmv.org/partnering/meet-our-partners**

Donors:
GHIT; BMGF; The WHO; The World Bank; Wellcome Trust; USAID; UKAID; UNITAID; The Rockefeller Foundation; and several governments including Switzerland and the Netherlands

University Involvement:

"University of Nebraska has assigned the Medicines for Malaria Venture the rights to the patent applications and patents on synthetic peroxide technologies to develop medicines for malaria, with no licences involved or payment to the university" (Gerhardsen, 2006).

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES (IPM)

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on preventing HIV among women using products based on microbicides.

Summary:

Founded as a non-profit organization in 2002 (IPM, 2015), "IPM is uniquely focused on preventing HIV infection using products based on microbicides, compounds that can be applied internally to protect against sexually transmitted infections (STIs) including HIV," specifically for women (Mostert, 2014; DSW, n.d.). IPM works with the public, private, and philanthropic sectors to "prevent HIV transmission by accelerating the development and availability of safe and effective microbicides for use by women in developing countries. Microbicides in the form of vaginal rings, films, and gels could help empower women with discreet, safe, effective, and long-acting tools they can use to protect their own health" (DSW, n.d.). "Using a "best practices" approach to its work, IPM: evaluates promising compounds; designs optimal formulations; conducts preclinical and clinical trials; identifies appropriate regulatory pathways for products; establishes manufacturing and distribution capacity to ensure access to future products; and IPM also engages and collaborates with advocates and global health leaders to raise awareness about microbicides and HIV prevention products worldwide" (IPM, 2015).

More specifically, IPM implements access principles including architecture, availability, acceptability, affordability, and appropriate use and supports access by: Acquiring intellectual property rights for drugs in development; Developing products that meet women's needs and preferences; Conducting clinical trials to international regulatory and ethical standards with strong country and community participation; Interacting with African, European and US regulatory authorities, and the WHO to outline a global drug development plan for regulatory decision-making for IPM's novel products; Identifying high-quality, cost-effective manufacturing options; Undertaking social and policy research to inform product introduction and use; Facilitating strategic partnerships in manufacturing, distribution and marketing; and Developing the IPM Strategic Access Plan (IPM, 2015)

Main Project(s):

"IPM's most advanced product is a monthly vaginal ring that slowly releases the antiretroviral drug dapivirine. The dapivirine ring is now in two parallel Phase III studies—the first efficacy studies of a microbicide ring for HIV prevention. These studies are expected to provide the evidence needed to secure regulatory approvals and licensure when results become available in 2016" (DSW, n.d.).

Additionally, since 2004, IPM has partnered with "five major pharmaceutical companies — Bristol-Myers Squibb, Gilead, Merck & Co., Pfizer and Janssen Sciences Ireland UC (formerly Tibotec Pharmaceuticals), one of the Janssen Pharmaceutical Companies — entered into six non-exclusive, royalty-free licenses with IPM to develop, manufacture and distribute eight antiretroviral (ARV) products as microbicides in developing countries" (IPM, 2015). Most recently, "in 2014, the royalty-free license for the ARV dapivirine expanded to an exclusive worldwide rights agreement with Janssen" (IPM, 2015).

List of IPM-licensed ARVs:
http://www.ipmglobal.org/products-development

Effectiveness:

"IPM [has expanded] the microbicide pipeline with the development of multipurpose prevention technologies that provide simultaneous protection against HIV infection and unintended pregnancy

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES (IPM)

in order to address women's multiple sexual and reproductive needs" (DSW, n.d.). IPM also stresses the role that industry can play in microbicide development and introduction: providing financial backing; "[l]inkages for formulations development; [l]ong-term seconded technical expertise; [s]ite development support in overlapping areas; [s]upport for access: [s]haring experience in resource limited settings and product forecasting tools & procurement management; [g]uidance on: Relations with regulatory bodies for product approval, issues of product liability and pharmacovigilance, selecting outside technical expertise and vendors, and managing organizational growth" (Rosenberg, 2008). "Based on the original 2002 business plan goals, IPM has performed effectively, achieving the 8 out of 10 of the original goals and addressing parts of the remaining two" (IPM Eval, 2008).

Full IPM evaluation:
http://www.ipmglobal.org/sites/default/files/IPM-Evaluation-Report.pdf

Critiques/Questions Raised in the Literature:

"IPM's value-for-money proposition is difficult to evaluate due to the lack of available benchmarks. General product and clinical development costs were not relevant for comparison and peer microbicide trial costs were not available" (IPM Eval, 2008).

Proposed Changes/Improvements:

"IPM can improve the way it manages risk in its scientific decision-making and operational implementation. Ultimately, IPM's long-term success will be measured by whether safe and effective microbicides are approved. [It is] believe[d] that if IPM progresses its portfolio and conducts clinical trials while controlling risk to the greatest extent, it will have performed admirably. Second, IPM can apply even greater emphasis on the partnership component of its work. As a virtual organization, dependent upon others to complete many of the key activities in its strategy, it is critical that IPM have strong, positive relationships that will withstand the inevitable ups and downs in clinical research" (IPM Eval, 2008).

Organizations, Stakeholders, And/Or Partners:

Bristol-Myers Squibb; Gilead; Merck & Co.; Pfizer and Janssen Sciences Ireland UC; PHIVA; Qhakaza Mbokodo; Desmond Tutu HIV Foundation; Ndiovu Medical Centre; MRC/UVRI Uganda Research Unit on AIDS; BMS; Viiv Healthcare; QPharma; Omnichem; Particle Sciences, Inc.; Huntington Life Sciences; Almac; CONRAD; Global Health Technologies Coalition; Planeta Salud; Open Society Initiative for Southern Africa, etc.

Donors:
Belgian Development Cooperation; BMGF; Canadian International Development Agency; Ministry of Foreign Affairs Denmark; Flanders Department of Foreign Affairs; Ministry of Foreign and European Affairs of France; Irish Aid; OPEC; NORAD; SIDA; UK AID; DFID; UNFPA; USAID; PEPFAR; and World Bank.

University Involvement:

Queen's University; Imperial College; Albert Einstein College of Medicine; Drexel University; and the Madibeng Centre for Research, Maternal, Adolescent and Child Health (Univ. of the Witswatersand).

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

TB ALLIANCE

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on drug development for TB treatment.

Summary:

Founded in 2000 and based in NYC and Pretoria, SA, "TB Alliance is a non-profit organization dedicated to the discovery and development of better, faster-acting, and affordable drugs for TB"… "Through innovative science and with partners around the globe, it leads a global effort to ensure development of and equitable access to faster, better TB [and drug-resistant TB] cures that will advance global health and prosperity. The TB Alliance combines the unparalleled R&D expertise of its staff with the skills and resources of its highly accomplished network of partners to efficiently leverage the most promising science around the world" (DSW, n.d.).

"As a virtual drug developer, TB Alliance manages a portfolio of candidate TB compounds, from both public and private sector sources, using a variety of licensing and partnership agreements. This model minimizes costs, including overhead and investments in infrastructure, while optimizing scientific capability to speed new TB drug development"… "To ensure [its] products reach the hands of those who need them most urgently, the TB Alliance and its partners are working with global, regional, and national stakeholders to facilitate regulatory approval, adoption by TB programs, and widespread availability of new drug regimens" (TBA, 2015). TB Alliance works to advance what it calls "AAA", adoption, availability and affordability, in addition to innovation of new TB medications and regimens (TBA, 2015).

The TB Alliance screens for and selects projects based on their potential impact using scientific criteria that include: "potential to shorten and simplify duration of treatment; effectiveness against multidrug-resistant strains; compatibility with anti-retroviral therapy for people with TB-HIV co-infection; suitability for pediatric populations; and ability to improve the treatment of latent infection" (TBA, 2015).

Main Project(s):

"The TB Alliance currently manages more than 20 projects in its pipeline, including several multi-drug regimens in late-stage clinical trials" (DSW, n.d.).

"The TB Alliance supports community participation in its development work through its Community Engagement program. These initiatives serve as a bridge between trial participants, community members, and researchers" and help establish two-way communication channels to discuss and manage TB Alliance's in-country work (TBA, 2015). The program includes "site-level activities ranging from the establishment of formal community advisory structures, to workshops and trainings on TB drug research, to public education and awareness campaigns" (TBA, 2015).

Past work: TB Alliance has "worked with IMS Health to understand the TB market including [its] Pathway to Patients study in 2007 and [its] research on the private sector in 2010-2011"… "The Liverpool School of Tropical Medicine is now working with [TB Alliance] to conduct patient studies in Bangladesh and Tanzania and Treatment Action Group has helped [them] keep in touch with patients who have TB." TB Alliance also works "with the STOP TB Partnership's DOTS Expansion Working Group particularly in the areas of Public-Private Mix (PPM) and Introducing New Approaches and Tools (INAT)" (TBA, 2015).

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

TB ALLIANCE

Effectiveness:

The TB Alliance has "Assembled and manage the largest portfolio of potential new TB drugs in history, which includes more than 20 active development programs and 9 novel classes of drugs; Launched the first clinical trials to test multiple new TB drugs in combination, and new TB regimens in TB and multidrug-resistant tuberculosis (MDR-TB) patients simultaneously. Novel regimens show promise in curing both drug-sensitive and drug-resistant disease with the same treatment, which would simplify delivery and global scale-up of MDR-TB treatment; Reinvigorated global TB drug development by being a central resource for and lowering the barriers associated with the field — there are now 10 clinical TB drug candidates in the global portfolio, many managed by some of the world's largest pharmaceutical companies; Worked in partnership with Janssen Pharmaceuticals to help develop Sirturo, the first new drug approved for the treatment of MDR-TB; Co-founded the Critical Path to TB Drug Regimens (CPTR) initiative, and leads the drug development arm of the program. This initiative is working to tackle a broad array of challenges, including reducing the timeline needed to develop novel TB regimens by as much a 75%; Established a robust Community Engagement program surrounding TB drug trials that create important links between the local clinical trial sites and the TB research community; Mapped the global capacity to conduct TB clinical trials, and helped to develop this global infrastructure, including many sites in endemic countries; and Established, with DNDi, the first-ever royalty-free license agreement between two not-for-profits, enabling TB Alliance compounds to be tested and developed for therapy of multiple additional neglected diseases" (TBA, 2015).

TB Alliance is "committed to advancing a new drug development paradigm that will telescope the time needed to develop markedly improved TB cures. This approach evaluates novel combinations of TB drugs — instead of single drugs — as part of a single development program, enabling the development of novel TB drug regimens that have potential to transform treatment for drug-sensitive and drug-resistant tuberculosis"… "The TB Alliance is in a unique position to bring together TB drug developers under the Critical Path to TB Drug Regimens (CPTR) initiative to test their drugs together and advance the best TB regimens, regardless of sponsor" (TBA, 2015).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

IMS Health; CPTR; Janssen; STOP TB Partnership; Treatment Action Group.

Donors:
Australian Aid; BMGF; European Commission; GHIT; Irish Aid; National Institute of Allergy and Infectious Disease; UK Aid; UNITAID; USAID; the FDA.

University Involvement:

Liverpool School of Tropical Medicine; University College London (Ginsberg, 2011).

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

AERAS GLOBAL TB VACCINE FOUNDATION

General Approach/Methods Applied:

(COLLABORATIVE) Biotech firm and PDP focused on TB vaccine development.

Summary:

Founded in 2003, "Aeras is a nonprofit biotech advancing the development of new TB vaccines that will be accessible and affordable to all who need them, with a particular focus on developing countries where the need is most urgent. Aeras is a fully integrated R&D organization with the expertise to conduct the full spectrum of vaccine development—vaccine construction, vaccine evaluation, manufacturing, clinical development, and regulatory submission for licensure. New vaccines sit at the center of future TB elimination efforts" (DSW, n.d.). Aeras has offices in the U.S., Africa, and Asia with a total staff of 100+ people. "Aeras has capabilities in finance, portfolio management, immunology, assay development, clinical trials, regulatory affairs and policy, advocacy and resource mobilization, as well as in-house capacity to conduct pilot manufacturing" (Aeras, 2015).

"Together with experts throughout the world, Aeras has established comprehensive, measurable and globally acceptable criteria for selecting, assessing and advancing the best vaccine candidates in the pipeline. These "stage-gate" criteria at each phase of the R&D lifecycle provide a data-driven framework that maximizes the chances of developing new vaccines to prevent TB. The criteria are based on the novelty of the scientific approach; phase of development; and data showing whether the product is technically feasible, safe and effective against TB. Aeras and [its] partners have developed target product profiles (TPPs) for each vaccine candidate in the product pipeline to maximize the public health impact and serve as a guidepost on whether or not to move forward with a candidate. The TPP criteria could include the target population, specific number of doses, a certain percentage of efficacy and a clear safety profile" (Aeras, 2015).

Main Project(s):

"In collaboration with [pharmaceutical and academic] partners worldwide, Aeras is supporting the clinical testing of six experimental vaccines, as well as the development of a robust portfolio of second generation vaccine candidates" (DSW, n.d.).

Aeras' Clinical Portfolio:
http://www.aeras.org/candidates

Effectiveness:

"In collaboration with partners, Aeras has conducted over 30 clinical trials of new TB vaccines, enrolling thousands of subjects at multi-country trial sites. Together with experts from around the world, Aeras has established comprehensive, measurable, and globally acceptable criteria for selecting, assessing and advancing only the most promising vaccine candidates through the pipeline with the goal of bringing more effective TB vaccines to the market" (DSW, n.d.). Aeras is furthermore a partner in six active clinical development programs (Aeras, 2015).

Evaluation of Aeras:
http://r4d.dfid.gov.uk/Project/60702/

Critiques/Questions Raised in the Literature:

None found.

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

AERAS GLOBAL TB VACCINE FOUNDATION

Proposed Changes/Improvements:

As of 2006 shortage of trial sites was a concern. "Despite significant progress by the Aeras Global TB Vaccine Foundation in setting up clinical trial sites in India and South Africa, there [was] still a need for additional sites to support the current pipeline of TB vaccines . . . Only one to two Phase III trials [could] be started in the next two to three years, creating a serious bottleneck." At the time, "plans by the European and Developing Countries Clinical Trials Partnership to fund development of additional trial sites" was expected to ease this bottleneck but it is unclear whether this took place (BVGH, 2006).

Organizations, Stakeholders, And/Or Partners:

Australian AID; BMGF; FDA GHIT; NIAID; UK Aid; FDA; Rjiksoverheid; Crucell; GSK; IDRI; Sanofi Pasteur; Statens Serum Institut; CDC; Institut Pasteur; TBVI; Okairos; China National Biotech Group; South African TB Vaccine Initiative; Wellcome Trust; EDCTP, etc. (Aeras, 2015).

University Involvement:

Albert Einstein College of Medicine; Colorado State University; Cornell University; Dartmouth University; Harvard University; Imperial College London; Johns Hopkins University; London School of Hygiene & Tropical Medicine; Oregon Health & Science University; University of Oxford; Rutgers University; St. Louis University; Tulane University; University of California, Los Angeles; University of California, Berkeley; University of British Columbia; University of Cape Town; University of Maryland; University of Pittsburgh; University of Wales; Wuhan University

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

TUBERCULOSIS VACCINE INITIATIVE (TBVI)

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on development and delivery of a TB vaccine.

Summary:

"[O]n suggestion of the European Commission [,] in 2008 Tuberculosis Vaccine Initiative (TBVI) was founded" as a source of increased funding for TB vaccine research. TBVI "is a non-profit foundation that facilitates the discovery and development of new, safe and effective TB vaccines that are accessible and affordable for all people. As a Product Development Partnership (PDP), TBVI integrates, translates and prioritizes R&D efforts to discover and develop new TB vaccines and biomarkers for global use. TBVI provides essential services that support the R&D efforts of its consortium partners – 50 partners from academia, research institutes and private industry in the TB vaccine field. These services include: project identification, design and development; project management; resource mobilization; knowledge development, exchange and networking; technical advice and support for product and clinical development; TBVI does not have its own commercial interests. Ownership of vaccine candidates and biomarkers, and any intellectual property rights remain with researchers and vaccine developers. Access and affordability of TB vaccines for the developing world is a statutory objective of TBVI and will be a commitment that is part of each project grant agreement supported by TBVI. TBVI innovates and diversifies the pipeline for TB vaccines. It accelerates the most promising vaccine and biomarker candidates through the pipeline, applying portfolio management to support decision-making in an objective and transparent manner and to use the available financial resources effectively. It seeks to align its portfolio management approach with other global efforts, in particular with the portfolio management approach foreseen by the Global TB Vaccine Partnership (GTBVP)" (TBVI, 2015).

Main Project(s):

"With the establishment of TBVI [the EC was] able to sustain and accelerate vaccine and vaccine related developments of TBVAC and its successors, such as NEWTBVAC (2010-2014) and TBVAC2020 (2015-2019)."

Additionally, "TBVI projects have delivered 6 vaccine candidates moving from discovery to the preclinical phase, and 4 vaccine candidates going to Phase I clinical trials; TBVI supports new antigen discovery, including protein and non-protein (e.g. glycolipid) targets novel formulations and delivery systems alternative routes and methods of vaccine administration development of safer and more effective live vaccines; [and] TBVI has a special project to accelerate pre- and early clinical development of TB vaccine candidates, funded by the Bill & Melinda Gates Foundation. Another, very related project, is the 'R&D of TB vaccines' project, funded by the Norwegian Agency for Development Cooperation (Norad)" (TBVI, 2015).

"The TBVI consortium has established a novel pre-clinical prime-boost model to evaluate innovative prime-boost strategies." Furthermore, "a series of new TB biomarker signatures has been identified through candidate testing as well as through unbiased biomic approaches. Assays suitable for use in large-scale monitoring studies (e.g. in TB endemic areas) have been developed" and "the Phase I trial of vaccine candidate MTBVAC, conducted at the University of Lausanne, was completed in 2014. The safety and immunogenicity results of this trial were satisfactory. MTBVAC is planned to move forward to a Phase Ib trial in South Africa in 2015" (TBVI, 2015).

TBVI Projects: **http://www.tbvi.eu/projects.html**

A5 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS

TUBERCULOSIS VACCINE INITIATIVE (TBVI)

Effectiveness:

"TBVI's strategy in the coming four years is expected to result in support for 20 new discovery approaches, up to 6 candidates at preclinical stages and up to 6 candidates at early clinical stages. In addition, it will identify, optimize and evaluate 15 innovative approaches on biomarkers and TB" (TBVI, 2015).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

From 2015-2017 TBVI plans "to innovate and diversify the vaccine and biomarker pipelines and to move promising candidates through preclinical and early clinical development. TBVI will strengthen its knowledge-sharing platform, expand its research and strategic partner network and diversify its funding sources" (TBVI, 2015).

Organizations, Stakeholders, And/Or Partners:

WHO; University of Groningen; GFATM; TB Europe coalition; Stop TB Partnership; Results UK; MSF; Global Health Advocates; European Vaccine Initiative; EDCTP; and Case Western Reserve University TB Research Unit

GSK-Biologicals; Scientific Institute of Public Health; Statens Serum Institut (SSI); Centre National de la Recherche Scientifique (CNRS); Institut National de la Santé et de la Recherche Médicale (INSERM); Institut Pasteur de Lille; Institut Pasteur (Paris); Institut Mérieux; PX'Therapeutics; Max-Planck-Institute for Infection Biology; Paul Ehrlich Institut; Vakzine Projekt Management GmbH; IRCCS Lazzaro Spallanzani; Istituto Superiore Di Sanità (ISS); International Tuberculosis Research Center; Espoir pour la Santé; K-Rith Kwazulu-Natal Research Institute for Tuberculosis; Biofabri/CZ Veterinaria; Fundació Institut d' Investigació en Ciències de la Salut Germans Trias i Pujol; ETH Zürich, Institute of Molecular Systems Biology; Institute for Research in Biomedicine; Medical Research Council; Biomedical Primate Research Centre (BPRC); Intravacc; National Institute for Biological Standards (NIBSC/ MHRA); Public Health England, Porton Down; Veterinary Laboratory Agencies (DEFRA); and Aeras

Donors:
EU Horizon 2020 Programme; BMGF; Norad, Biofabri; GSK; and DFID.

University Involvement:

University of Oxford; Leiden University Medical Center (LUMC); Aston University; Bangor University; Imperial College of Science Technology and Medicine; London School of Hygiene and Tropical Medicine; University of Geneva; University of Lausanne; University of Zürich; University of Basel; University of Sydney; Ghent University; Université Libre de Bruxelles; University of Ulm; Universidad de Zaragoza; Free University Medical Centre (VUMC); University Hospital of Basel; Centre Hospital Universitaire Vaudois; SATVI/University of Cape Town; Stellenbosch University; Centre Hospitalier Universitaire Le Dantec; Università Degli Studi Di Padova; University of Palermo; Norwegian University of Life Sciences; Educational Foundation Yonsei University; and University College Dublin.

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

DRUGS FOR NEGLECTED DISEASES INITIATIVE (DNDI)

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on drug development for neglected diseases treatment without in-house product development capacity.

Summary:

Established in 2003, "as a non-profit R&D organization, DNDi [Drugs for Neglected Diseases Initiative] works to deliver new treatments for neglected diseases, in particular leishmaniasis, human African trypanosomiasis (sleeping sickness), Chagas disease, malaria, specific filarial infections, and paediatric HIV. DNDi has established regional disease-specific platforms, which bring together partners in disease-endemic countries to strengthen existing clinical research capacity, as well as to build new capacity where necessary" (DSW, n.d.). According to the DNDi website (2015c), "DNDi will manage R&D networks built on South-South and North-South collaborations. While using the existing support capacities in countries where the diseases are endemic, DNDi will help to build additional capacity in a sustainable manner through technology transfer in the field of drug R&D for neglected diseases." DNDi now has 5 regional offices (Africa, Latin America, Japan, Malaysia, India) and 1 affiliate (North America) as well as 1 project support office (DRC) with its headquarter in Geneva (DNDi, 2015c). DNDi's work is oriented around R&D but also includes fundraising and advocacy as well as a robust access strategy (DNDi, 2015c).
"DNDi does not have any research facilities and does not directly conduct research to develop its treatments. DNDi . . . follow[s] the virtual research mode, whereby most research is outsourced with the R&D projects actively managed by DNDi personnel experienced in different aspects of pharmaceutical development" (DNDi, 2015c).

"During its first years of existence, DNDi developed an intellectual property (IP) policy to guide its R&D activities and associated contractual agreements with the following objectives: The need to ensure that treatments are ultimately affordable to patients who need them and that access to these treatments is equitable; [and] The desire to develop drugs as public goods when possible" (DNDi, 2015c). According to DNDi's website (2015), "licenses should be: royalty-free to ensure the lowest possible price; sub-licensable, or in other terms, contain the authorization to disclose the obtained information to another party in order to continue product development; worldwide coverage both for R&D and for manufacture; non-exclusive to enable third parties to enter the field (included in [its] most innovative agreements)" and should require limited confidentiality.

DNDi Fundraising, access, regulatory, research misconduct, scientific communications, and procurement policies: **http://www.dndi.org/about-us/dndis-policies/access-policy.html**

Main Project(s):

"The primary objective of DNDi is to deliver a total of 11 to 13 new treatments by 2018 for leishmaniasis, sleeping sickness, Chagas disease, malaria, paediatric HIV, and specific helminth infections and to establish a strong R&D portfolio that addresses patient needs" (DNDi, 2015c). DNDi also has an open innovation portal to "disseminate the scientific knowledge gained through research projects" via WIPO Re:Search and ChEMBL (DNDi, 2015c).

DNDi has set up two platforms in Africa: the Leishmaniasis East Africa Platform (LEAP) and the Human African Trypanosomiasis (HAT) Platform, and in Latin America, DNDi has created the Chagas Platform" (DSW, n.d.). Furthermore, "DNDi has built the largest ever R&D portfolio

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

DRUGS FOR NEGLECTED DISEASES INITIATIVE (DNDI)

for the kinetoplastid diseases and has currently underway five projects in Implementation stage, seven in the clinical, and seven in the pre-clinical" (DNDi, 2015c).

"Recently DNDi formed a consortium with four pharmaceutical companies [AstraZeneca, Takeda, Eisai, and Shionogi & Co, Ltd.] to hasten the development of drugs for leishmaniasis and Chagas disease," called the *Neglected Tropical Diseases Drug Discovery Booster Consortium* and supported by funds from GHIT, for more information the press release for the Consortium can be found here: **http://www.dndi.org/media-centre/press-releases/2156-pr-drug-discovery-booster.html** (Asian Scientist Newsroom, 2015).

DNDi's Project Portfolio:
http://www.dndi.org/diseases-projects/portfolio.html

Effectiveness:

"Since its inception in 2003, DNDi has delivered six treatments: two fixed-dose anti-malarials (ASAQ and ASMQ), nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness, sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa, a set of combination therapies for visceral leishmaniasis in Asia, and a pediatric dosage form of benznidazole for Chagas disease" (DSW, n.d.).

More information on DNDi's accomplishments can be found here: **http://www.dndi.org/about-us/overview-dndi/key-accomplishments.html**

Proposed Changes/Improvements:

"In December 2011, the Board of Directors decided that while maintaining its full commitment to neglected diseases such as sleeping sickness, leishmaniasis, and Chagas disease, DNDi [would] conclude its malaria activities by 2014, maintaining emphasis on technology transfer and sustained access, and take on new activities in the fields of paediatric HIV and specific helminth infections" (DNDi, 2015c). "With its pipeline maturing, DNDi will increasingly focus on access, with the ultimate aim of facilitating maximum impact via appropriate use of treatments, assuring their effective transition to relevant access partners and implementers, and leveraging success for future steps. A critical component of the updated strategy is the further empowerment of Regional Offices, aiming at their transition from a support role to a more active contribution to all DNDi activities" (DNDi, 2015c).

"A main DNDi challenge is to build a solid R&D portfolio for neglected diseases and to deliver preclinical candidates in a timely manner using an original model based on partnership. To address this challenge DNDi has remodeled its discovery activities from a project-based academic-bound network to a fully integrated process-oriented platform in close collaboration with pharmaceutical companies. This discovery platform relies on dedicated screening capacity and lead-optimization consortia supported by a pragmatic, structured and pharmaceutical-focused compound sourcing strategy" (Ioset, 2011).

In September 2015, DNDi introduced their new business plan for 2015-2023. Its goal is to introduce a more flexible and dynamic portfolio approach that integrates various operating models in order to better respond to the needs of patients, particularly those in low- and middle-income countries (DNDi, 2015c). The plan facilitates the uptake of new diseases into DNDi's portfolio, not only immediately but also as new patient needs and opportunities for innovation, such as AMR, become apparent. The Business Plan continues DNDi's current commitment "to develop treatments for African sleeping sickness, leishmaniasis, and Chagas disease as well as filarial

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS WORKING ACROSS DISEASES

DRUGS FOR NEGLECTED DISEASES INITIATIVE (DNDI)

diseases and paediatric HIV. Having transferred its malaria activities to the Medicines for Malaria Venture (MMV), DNDi is also undertaking new research and development (R&D) projects for hepatitis C and mycetoma, two very different diseases that share one key challenge: the existing system of biomedical innovation has failed to deliver safe, effective, quality products that are affordable to poor populations" (DNDi, 2015c).

DNDi's new business plan aims to reinforce the following principles within the organization: "a patients' needs-driven approach; a steadfast commitment to promote open sharing of research knowledge and data while ensuring an access-oriented approach to intellectual property (IP) management and licensing; the fostering of innovative, collaborative partnerships; and the diversification of funding sources to ensure scientific independence" (DNDi BP, 2015). DNDi also plans to "take concrete steps in analyzing, piloting, and bringing evidence from its alternative and open models of innovation; pro-access management of intellectual property and licensing; practice of de-linking product pricing from R&D costs; and promotion of innovative regulatory pathways" (DNDi BP, 2015).
2015-2023 DNDi Business Plan:
http://www.dndi.org/images/stories/pdf_publications/DNDi_Business_Plan_2015-2023.pdf

Organizations, Stakeholders, And/Or Partners:

Founding Partners:
Institut Pasteur; MSF; TDR; Fiocruz; The Kenya Medical Research Institute (KEMRI); the Indian Council of Medical Research; and the Malaysian Ministry of Health. The majority of these partners are from the public sector (DNDi, 2015c).

All current partners including pharmaceutical, biotech, PDPs and PPPs, NGOs, National Research Centers, Contract Research Organizations, Ministries of Health and Government Organizations, Hospitals, and Research Institutes:
http://www.dndi.org/partnership/partners.html

University Involvement:

Addis Ababa University; Antwerp University, Laboratory of Microbiology, Parasitology and Hygiene (LMPH); Baylor College of Medicine; Bonn University Hospital, Institute of Medical Microbiology, Immunology and Parasitology; Brasilia University; Dundee University, Research and Innovation Services; FAPUNIFESP, Fundaçao de Apoio Universidade Federale de Sao Paolo; Gondar University Hospital; Imperial College; London School of Pharmacy ; LSHTM, London School of Hygiene and Tropical Medicine; Makerere University and Amudat Hospital; McGill University; Michigan State University; Monash University, Centre for Drug Candidate Optimization; Murdoch University, School of Veterinary and Biomedical Science; Pace University; Stellenbosch University; UCSF, University of California, San Francisco; University of Antoquia, PECET – Programme for the study and control of tropical diseases; University of Auckland; Universidade Estadual de Campinas UNICAMP; Universidad Mayor de San Simon; University of North Carolina, Office of Technology Development; Universidade Ouro Preto; University of Oxford, Worldwide Antimalarial Drug Resistance Network; University Sains; Utrecht University.

University "Spin-off" Partners:
Epichem and Eskitis, The Eskitis Institute for Cell and Molecular Therapies, Griffith University.

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

General Approach/Methods Applied:

(COLLABORATIVE) PDP focused on development of diagnostic tools for poverty-related diseases without in-house production capacity.

Summary:

Founded in 2003, FIND [the Foundation for Innovative New Diagnostics] is an international non-profit that focuses on R&D of innovative diagnostic solutions to fight diseases of poverty. "The scope of [FIND's] activities is rapidly expanding: [its] disease programmes now include tuberculosis (TB), malaria and human African trypanosomiasis (HAT), also known as sleeping sickness" (FIND, 2015). "FIND builds and sustains effective partnerships with all those involved in diagnostics – both the public and private sectors. These partnerships and a quality-assured project management framework enable [FIND] to accelerate products through a well-defined value chain – from discovery and proof of principle, to development, evaluation, WHO endorsement and implementation of new technologies" (FIND, 2015). FIND operates "as facilitator, mobilizer, and bridge builder to support complete diagnostic solutions, with linkage to treatment and care paramount in everything that [it does] . . . It has also supported quality assured scale-up of diagnostics through implementation, quality assurance, and lab-strengthening work" (DSW, n.d.). "FIND also undertakes laboratory strengthening and scale up projects to facilitate the rapid uptake of new tools in disease endemic countries. All of this is aimed at one thing – a people-centered approach that focuses on diagnostics as a platform to shorten the delay between disease and treatment, halt transmission, and minimize the impact of disease on families" (FIND, 2015). FIND "headquarters are located in Geneva, Switzerland, and [it has] offices in Kampala, Uganda, and New Delhi, India" (FIND, 2015).

"Over the years, [FIND has] developed and refined a skill-set including: End-to-end product development experience that allows [it] to anticipate bottlenecks or missteps in development before they occur and to help product developers avoid them; Technical expertise covering the spectrum from early product development to implementation that allows us to act as translator between developers and end-users; Clinical trial experience and know-how that allow FIND to shape the entire clinical process (from specimen collection to coordinating clinical trials) and dramatically reduce the time for test development and validation; In-country knowledge and the ability to identify and act on the true needs, constraints and behaviours of end-users in endemic regions; Proven mechanisms to create feedback loops that enable communication between end-users, product developers, and everyone in between; and strong relationships with country governments, laboratories, and implementers that allow FIND to support rapid uptake of products and transmit lessons learned to product developers." In addition, "FIND has developed a novel commercial model based on a segmented intellectual property (IP) policy that overcomes the usual barriers to product availability and motivates some of the very best biotechnology companies to innovate in high tech diagnostics " (FIND, 2015).

FIND's Project Objectives:
http://r4d.dfid.gov.uk/Project/60703/

Main Project(s):

"Over the past 11 years, FIND has delivered 11 new tests and created an enabling environment for countless more through specimen banks, reagent development, and better market visibility.

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

It has conducted clinical trials and supported the development of policy guidances for 6 novel TB diagnostics and the new human African trypanosomiasis rapid test" (DSW, n.d.). FIND is currently working on Ebola, NTDs, Malaria and acute febrile syndrome, HIV, TB, and general access issues. FIND also "scouts for innovative, new diagnostic approaches for poverty-related diseases. You can submit your technology, biomarker and/or product proposal via [its] submission webform" (FIND, 2015).

FIND has co-developed products endorsed by WHO for implementation for TB including Liquid Culture and DST, Rapid Speciation, Line Probe Assay (1st line), LED microscopy, and Xpert MTB/RIF and has available a TB Diagnostic Pipeline and Specimen Bank. For malaria FIND has catalyzed development of a blood transfer device (BTD) for lateral flow assays and a LAMP kit as well as supporting introduction and access to antenatal screening and RDTs. For NTDs FIND has specifically supported the development of new diagnostics for Leishmaniasis, Chagas, and Buruli ulcer. FIND has focused on development of antigen detection tests and LAMP for VL, development of a LAMP assay for Chagas, and point-of-care tests and district hospital or microscopy level laboratory tests for Buruli ulcer. FIND has also partnered with the WHO to develop a Human African Tryposomiasis (HAT) Specimen Bank and is working to develop an RDT as well as a molecular test for diagnosis of HAT, disease staging tools and improved parasite detection (FIND, 2015).

FIND's Programs:
http://www.finddiagnostics.org/programs/

Effectiveness:

FIND has already contributed to the introduction of five new diagnostic tools for TB already in use in endemic countries (FIND, 2015). FIND also utilizes a Support for Success (S4S) platform, a collaborative and confidential tool which provides access to FIND's sample bank and its worldwide network of clinical study sites in return for partners "providing their services and products to targeted markets under agreed upon conditions" (FIND, 2015).

"Achievements To Date include: . . . endorsement by WHO of three diagnostic technologies that were evaluated and demonstrated within national TB programmes by FIND; . . . completion and publication, in collaboration with WHO, of the largest-ever independent, laboratory-based evaluation of rapid diagnostic tests for malaria in April 2009; [and] successful transfer of manufacturing of the mini Anion Centrifugation Technique from Europe to Africa, the successful rollout of a strategic plan for advocacy for HAT with the backing of the African Union in all HAT-endemic countries, and the first ever pipeline of new diagnostic tools for HAT" (R4D FIND, 2014).

Proposed Changes/Improvements:

"Since 2003, the landscape has shifted significantly. There is more industry engagement in emerging markets. Small and medium enterprises, especially from middle-income countries, are playing a greater role in global health and more donor and venture capital funding is directly available to manufactures. In many countries, laboratories remain the weakest link of health systems but governments are increasingly willing to invest in their improvement. Private healthcare service providers have an expanding role to play in addressing public health problems. While new challenges have emerged – for example, the threat of antibiotic resistance – [FIND] also sees new opportunities: the information technology revolution may for the first time allow us to fully capture the value of diagnostics. Overall, since the landscape has become more complex, a more holistic, nuanced response is required" (FIND, 2015).

A5

DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Organizations, Stakeholders, And/Or Partners:

"FIND has active collaborations with over 150 partners, including ministries of health, bilateral and multilateral organizations, research and academic institutes, commercial partners, NGOs and over 80 clinical trial sites," among them WIPO Re:Search and BVGH.

Donors:
BMGF; the governments of the Netherlands and Germany; the UK's Department for International Development; the European Union; USAID; Irish Aid; UNITAID (FIND, 2015).

University Involvement:

University of Geneva; Makerere University.

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

INFECTIOUS DISEASE RESEARCH INSTITUTE (IDRI)

General Approach/Methods Applied:

(COLLABORATIVE) Biotech firm and PDP focused on drug development for infectious diseases, specifically tuberculosis, leishmaniasis, leprosy, malaria, and Chagas Disease.

Summary:

IDRI, established in 1993 and based in Seattle, develops "products that solve intractable global health challenges." Its "unique product-based approach to fighting infectious diseases has already yielded novel diagnostics, vaccines, and treatment strategies that are protecting and saving lives. With deep relationships in the academic and corporate arenas, IDRI unites the best of the research and product development communities. [Its] partnerships with businesses, nonprofit foundations, and government agencies give [IDRI] unprecedented access to cutting-edge technology and financial support. [IDRI believes its] holistic approach – combining the high-quality science of a research organization with the product development capabilities of a biotech company – will help [it] reach [its] goal of creating new diagnostics, drugs and vaccines to help those who need it most" (IDRI, 2015). IDRI is currently "focused on eradicating tuberculosis, leishmaniasis, leprosy, malaria, and Chagas Disease" and operates based on its values of "compassion, scientific excellence, and impact" (IDRI, 2015). IDRI works with collaborators on antigen discovery, adjuvant discovery and delivery, general product development via the Process Science group, Adjuvant Formulation group, and Clinical Development Team, and general drug discovery via the Drug Discovery Research Group (IDRI, 2015).

Main Project(s):

IDRI's Good Manufacturing Practices include: "Formulation development services with a focus on liquid, emulsion, and liposome formulations; cGMP drug product manufacturing for preclinical, Phase 1 and 2 clinical studies with a batch capacity of up to 15,000 vials of drug product in compliance with U.S. and EU regulations; and stability studies performed in compliance with ICH guidelines" (IDRI site, 2015).

"IDRI helped develop a tuberculosis vaccine being tested by the Aeras Global TB Vaccine Foundation. It also developed a blood test for Chagas disease in collaboration with Corixa and is working on a possible vaccine" (GHP IDRI). "In addition to [their TB] vaccine program, [IDRI is] also focused on developing a rapid and effective TB diagnostic test. [Its] efforts in this area are supported by [its] expansive collection of TB antigens — the world's largest" (IDRI site, 2015).

"[IDRI] also acquired exclusive rights to MicronJet, an intradermal delivery system that enables improved tuberculin skin testing" and has "developed a prototype diagnostic test that rapidly detects active TB and would provide significant advantages over current diagnostic methods. [IDRI's] commitment to discovering and developing new TB therapies extends beyond [its] participation in the Lilly TB Drug Discovery Initiative. [It] have built a state-of-the-art assay development, screening, and chemistry group to support [its] in-house discovery activities and also have in-licensed several promising mid-stage TB drug candidates" (IDRI, 2015).

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

INFECTIOUS DISEASE RESEARCH INSTITUTE (IDRI)

As part of its leishmaniasis program, IDRI's "scientists also identified a recombinant antigen (rK39) that is useful for diagnosing more than 98% of human visceral leishmaniasis cases with no more than a drop of blood" and "[IDRI's] partner InBios International has received FDA approval for an rK39-based blood test, which is now being used extensively in India. Another diagnostic partner, Chembio Diagnostic Systems, is developing an antigen-based test for human and canine leishmaniasis in Brazil, in conjunction with Fiocruz" (IDRI, 2015).

For its leprosy program, "IDRI has identified an expansive panel of recombinant antigens for specific detection of *M. leprae* infection. Working with [its] manufacturing partners [IDRI] ha[s] developed prototype tests that enable rapid diagnosis of *M. leprae* infection even before the appearance of clinical symptoms . . . Development of a successful vaccine is also critical to leprosy eradication efforts. Toward this end, IDRI has identified the largest panel of M. leprae antigens that are relevant to human disease. IDRI has also "developed and refined systems for testing vaccine candidates and [it is] working with partners in areas where leprosy is endemic as well as national health centers around the world to assess vaccine efficacy" (IDRI, 2015).

Within the malaria program, "preclinical studies have shown that [IDRI's] adjuvant technology, in concert with key malaria antigens, provide a broad level of protection against multiple malaria strains" (IDRI, 2015).

IDRI is also applying its "expertise in adjuvants to the development of an effective vaccine against H5N1" and "IDRI is pursuing a multi-faceted approach to eliminating Chagas Disease that includes diagnostic tests to detect infection as well as a prototype vaccine that might be effective against both Chagas and Leishmaniasis (IDRI, 2015).

IDRI's product pipeline:
http://www.idri.org/products.php

Effectiveness:

"IDRI was instrumental in the discovery and early evaluation of the first protein-based TB vaccine candidate. Even as this vaccine candidate continues to advance through the development process, [IDRI's] team is working on a next-generation vaccine that could prevent and potentially treat multi drug-resistant TB" (IDRI, 2015). Additionally, "IDRI developed the world's first defined vaccine candidate for leishmaniasis. It has been tested in the U.S., Peru, Brazil and Colombia, and is currently being tested in Sudan and Peru" (IDRI, 2015). "More than 13 million IDRI diagnostics are on the market for leishmaniasis, Chagas disease & leprosy. IDRI has vaccines in clinical trials, including a promising tuberculosis candidate currently in trials in South Africa, which has one of the world's largest burdens of TB. [This includes] 10 trials for leishmaniasis vaccines and 3 trials for tuberculosis vaccines. IDRI scientists have screened over 500,000 chemical compounds, feeding a pipeline of new drugs for tuberculosis" (SF IDRI).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

"IDRI generally relied on grants, but found that the funds were typically designated for a particular development program and had specific underlying rules governing their use. Accordingly, most grant support could not be used to develop IDRI's infrastructure or to explore new projects that might enhance current research platforms. These

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

INFECTIOUS DISEASE RESEARCH INSTITUTE (IDRI)

funding constraints made sustaining the company challenging and limited its strategic growth. IDRI needed to generate additional revenue streams that would allow its management team more freedom in allocating funds to strategic, forward-looking activities." At the below link there is a "mini-case study [that] describes how Reed devised a model to create for-profit development arms to commercialize select IDRI vaccine technologies that had first-world applications, and thus significant profit potential, to help continue funding IDRI's larger portfolio of projects": **http://csi.gsb.stanford.edu/idri-neglected-disease-rd-nonprofit-model** (Zenois, 2012).

Organizations, Stakeholders, And/Or Partners:

IDRI has numerous non-university partners and affiliates including InBios International, Chembio Diagnostic Systems, the Lilly TB Drug Discovery Initiative, Washington Global Health Alliance, Washington Biotechnology & Biomedical Association, and Northwest Association for Biomedical Research (**http://www.idri.org/collaborate.php**).

Donors:
American Leprosy Missions; Army Research Office; BARDA; BMGF; DARPA; Eli Lilly Co.; MJ Murdock Charitable Trust; NY Community Trust; NIH/NIAID; Paul G. Allen Family Foundation; and Renaissance Health Service Corporation.

University Involvement:

University of Washington is an affiliate of IDRI and many other universities are collaborators.

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

MEDICINES DEVELOPMENT FOR GLOBAL HEALTH (MDGH)

General Approach/Methods Applied:

(COLLABORATIVE) PPP focused on drug development for infectious diseases such as onchocerciasis with in-house production capacity.

Summary:

Founded in 2005 and based in Australia, Medicines Development for Global Health (MDGH) is "a not for profit [biopharmaceutical] organization with the mission to put new and improved medicines into the hands of people who need them most" via development of "affordable medicines and vaccines . . . that may have limited commercial opportunity, but which address important unmet medical needs," particularly in low- and middle-income settings (MDGH, 2015). MDGH employs "a differentiated pricing model so that funds from commercial sales can be used to make medications accessible to those most in need. This model allows [MDGH] to deliver on [its] social goals while also ensuring financial return for [its] funders" (MDGH, 2015). MDGH's "core expertise is in designing and running the complex regulatory-standard product development process at all stages, from candidate compound selection through to clinical development" (Sullivan, 2014).

Main Project(s):

Most recently, "Medicines Development for Global Health sign[ed] a US$10 million funding deal with the Global Health Investment Fund for the registration of moxidectin for onchocerciasis"… "Upon successful registration of moxidectin, [MDGH] ha[s] committed to deliver moxidectin for onchocerciasis treatment on a cost recovery basis and, with GHIF, to continue to research other potential human uses of moxidectin" (MDGH, 2015).

MDGH's development programs, in addition to the Moxidectin Program wherein MDGH works towards the registration of Moxidectin for river blindness, are considered its Global Health Programs and include development of a live attenuated Pertussis vaccine, a long acting penicillin G depot for prevention of acute rheumatic fever, multipathogen hyperimmmune colostrum in an oral tablet form to be used as an antidiarrheal, a sublingual interferon alpha tablet for the treatment of chronic hepatitis B and C, a low cost neonatal rotavirus vaccine, registration of ivermectin for the treatment of scabies, and separate consulting services (MDGH, 2015).

Effectiveness:

MDGH "is contributing to the development of more than 40 technologies, of which 13 primarily affect the developing world" (Sullivan, 2014).

PRV connection:

"The Priority Review Voucher (PRV) programme run by the US Food and Drug Administration (FDA) is a critical part of Medicines Development for Global Health's efforts to tackle neglected diseases–and involves the work of many other companies. As part of an initiative proposed by scientists at Duke University and signed into law by President George W Bush in 2007, vouchers for priority drug reviews are issued to companies that develop drugs and vaccines targeting certain neglected diseases with little profit potential. These vouchers entitle the bearer to an expedited drug review for their next candidate, which speeds the approval process by four months. When the programme was first established, there were 16 neglected diseases that could qualify for a voucher, but since then the list has grown and today it includes a number of rare paediatric conditions. In order to be eligible, the treatment must show significant safety or efficacy

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

MEDICINES DEVELOPMENT FOR GLOBAL HEALTH (MDGH)

benefits over current competitors, and be the first human registration of the product. This is no small task, and only four vouchers have been issued so far – but the benefits are great. Recently, BioMarin Inc. became the first to sell a voucher, receiving US $67.5 million from a large pharmaceutical company. For companies such as Medicines Development for Global Health sponsoring products like moxidectin, the voucher programme offers an attractive incentive and a potential route towards funding" (Sullivan, 2014).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

While MDGH does not have a comprehensive list of partners or donors available on its website, it has worked with many organizations, institutions, and companies including GHIF, the Kirby Institute, bioCSL Ltd, Cytopia, and WHO TDR (MDGH, 2015).

University Involvement:

Monash University (MDGH, 2015).

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

EUROPEAN COMMISSION'S INNOVATIVE MEDICINES INITIATIVE (IMI)

General Approach/Methods Applied:

(COLLABORATIVE) PPP focused on drug development for neglected health needs in both LMICs and HICs and providing grants for research.

Summary:

Launched in 2008 and now in its second phase, "The Innovative Medicines Initiative (IMI) is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. IMI supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe. IMI is a joint undertaking between the European Union and the pharmaceutical industry association EFPIA" (IMI, 2015). More specifically, "the Innovative Medicines Initiative (IMI) is working to improve health by speeding up the development of, and patient access to, innovative medicines, particularly in areas where there is an unmet medical or social need. It does this by facilitating collaboration between the key players involved in healthcare research, including universities, the pharmaceutical and other industries, small and medium-sized enterprises (SMEs), patient organisations, and medicines regulator" (IMI, 2015). "IMI is the world's biggest public-private partnership (PPP) in the life sciences; Through the IMI 2 programme, it has a €3.3 billion budget for the period 2014-2024. Of this: €1.638 billion (half the budget) comes from Horizon 2020, the EU's framework programme for research and innovation; €1.425 billion is committed to the programme by EFPIA companies; [and] up to €213 million can be committed by other life science industries or organisations that decide to contribute to IMI 2 as members or Associated Partners in individual projects. EFPIA companies and other Associated Partners do not receive any EU funding, but contribute to the projects 'in kind', for example by donating their researchers' time or providing access to research facilities or resources" (IMI, 2015).

"The goal of the Innovative Medicines Initiative 2 (IMI 2) programme is to develop next generation vaccines, medicines and treatments, such as new antibiotics . . . The IMI 2 programme will provide Europeans, including the increasing numbers of older people, with more efficient and effective medicines and treatments. Cost savings will ease the burden on public healthcare systems and greater coordination across industry sectors will result in more reliable and faster clinical trials, and better regulation. IMI 2 research and innovation efforts will also open new commercial possibilities based on new services and products. The research, industry and societal sectors involved in IMI 2 programmes will benefit from the cooperation and knowledge sharing which take place in these projects. In particular, IMI 2 aims to deliver: a 30% better success rate in clinical trials of priority medicines identified by the WHO; clinical proof of concept in immunological, respiratory, neurological and neurodegenerative diseases in just five years; [and] new and approved diagnostic markers for four of these diseases and at least two new medicines which could either be new antibiotics or new therapies for Alzheimer's disease"… "IMI launches a number of research and/or training projects every year. Project participants are recruited through open and competitive Calls for research proposals. The selection of the winning proposals is based on independent peer review and concluded by a Grant Agreement and Project Agreement" (IMI, 2015).

Additionally, "the IMI2 Partnering Platform facilitates networking among universities, research and patient organizations, SMEs and industry interested in participating in the Innovative Medicines Initiative Joint Undertaking (IMI JU)"… "By completing and activating [a] profile you publish your partnering profile to all users and present your collaboration offers" which can then be found via the IMI Partner Search Tool (IMI Partnering, 2015).

Objectives of IMI:
http://www.imi.europa.eu/content/objectives

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

EUROPEAN COMMISSION'S INNOVATIVE MEDICINES INITIATIVE (IMI)

Main Project(s):

IMI "currently has over 50 projects, with more in the pipeline. Some focus on specific health issues such as neurological conditions (Alzheimer's disease, schizophrenia, depression, chronic pain, and autism), diabetes, lung disease, oncology, inflammation & infection, tuberculosis, and obesity. Others focus on broader challenges in drug development like drug and vaccine safety, knowledge management, the sustainability of chemical drug production, the use of stem cells for drug discovery, drug behaviour in the body, the creation of a European platform to discover novel medicines, and antimicrobial resistance. In addition to research projects, IMI supports education and training projects.

The Strategic Research Agenda for IMI2 "identifies four major axes of research: target validation and biomarker research (efficacy and safety); adoption of innovative clinical trial paradigms; innovative medicines; [and] patient-tailored adherence programmes"… "The priorities are: antimicrobial resistance; osteoarthritis; cardiovascular diseases; diabetes; neurodegenerative diseases; psychiatric diseases; respiratory diseases; immune-mediated diseases; ageing-associated diseases; cancer; rare/orphan diseases; [and] vaccines" and following the 2014 Ebola outbreak, IMI introduced the Ebola+ Programme (IMI, 2015).

Ongoing IMI projects:
http://www.imi.europa.eu/content/ongoing-projects

Effectiveness:

"IMI projects have already shown a positive impact on research and development: By pooling resources, the NEWMEDS project has created the largest known database of studies on schizophrenia. The New Drugs for Bad Bugs Programme has launched project to tackle the growing threat of anti-microbial resistance – a growing public health threat. The eTox project is developing a drug safety database based on both industry and public toxicology data, in a step towards greater safety for patients" (EFPIA IMI, 2013). According to a separate review article, "projects conducted by IMI consortia have already delivered meaningful results, providing proof-of-concept evidence for the efficiency of this new model of collaboration" (Goldman, 2012).

Critiques/Questions Raised in the Literature:

"The funding scheme has been criticised, requiring universities to invest more money than with EU FP7 programs. Besides the non-competitive financial aspects of participation in IMI projects for academia, this criticism also discusses that intellectual property is freely flowing to industry" (IMI Wikipedia). A recent evaluation noted several problems with IMI including a growing gap between essential medicines and profitable fields of business, inadequate monitoring, lack of transparency, divergence of IMI research from WHO goals, patients becoming industry lobbyists, hitches in IMI rules, and Europe being the center of focus. Key issues identified were: "The European Union pays while industry cashes in; Participating universities and research institutions have little influence over what happens at IMI; In practical terms, IMI's main purpose is to conduct research in areas that benefit the pharmaceutical industry, as opposed to its original purpose, which was to develop treatments and essential medicines; The control mechanisms lack transparency, and reports are only disseminated within IMI; [and] Pharmaceutical companies are not providing controllers who represent the EU and the public with access to the details of individual IMI research projects" (Elmer, 2015).

A5

DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

EUROPEAN COMMISSION'S INNOVATIVE MEDICINES INITIATIVE (IMI)

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Health, Demographic Change and Wellbeing Societal Challenge of Horizon 2020; EFPIA companies; JDRF; The Leona M. and Harry B. Helmsley Charitable Trust; BMGF; and other life science industries or organizations as well as many Partners in Research (IMI, 2015).

Going to the ongoing projects page and clicking on a given project will lead to a Participants list with all universities as well as non-academic institutions and organizations involved in the given IMI project.

University Involvement:

Emory University; Leiden University Medical Centre; Università degli Studi di Siena; University of Geneva; University of Gothenburg; University of Oxford; University of Tübingen; Mendel University in Brno; Kobenhavns Universitet; Stockholms Universitet; Université d'Aix-Marseille; University of Helsinki; University of Stirling (UK).

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

UCSF/UCSD CENTER FOR DISCOVERY & INNOVATION IN PARASITIC DISEASES (CDIPD)

General Approach/Methods Applied:

(COLLABORATIVE) NTD-focused drug discovery and development research center.

Summary:

"The Center for Discovery and Innovation in Parasitic Diseases (CDIPD) is an interdisciplinary research center based at UC San Diego. CDIPD targets diseases affecting hundreds of millions of people worldwide, but which are largely ignored by traditional drug and vaccine discovery companies because they primarily affect the poor and underserved. CDIPD was inaugurated as the Tropical Disease Research Unit at UC San Francisco in 1985 . . . In 2002, Herb and Marion Sandler made a groundbreaking gift to the University of California to expand the TDRU into the Sandler Center for Basic Research in Parasitic Diseases. This now allowed the interdisciplinary research group to branch into several other parasitic diseases of global health importance. By 2009, the focus of this research team became the discovery and development of drugs for several neglected parasitic diseases. The Sandler Center became the Sandler Center for Drug Discovery. The transition in 2012 to the Center for Discovery and Innovation in Parasitic Diseases (CDIPD) reflected a broader interdisciplinary research effort that now includes not only drug discovery and development, but also vaccine development.

Beginning July 2014, CDIPD is administered at the Skaggs School of Pharmacy and Pharmaceutical Sciences, UC San Diego" (CDIPD, 2015). Currently, "the focus of CDIPD is on the parasitic organisms that are responsible for neglected tropical diseases (NTDs). [Its] research includes studying the basic biology and biochemistry of these parasites as well as key aspects of the biology of the host-parasite relationship. [CDIPD] use[s] the information gathered from these studies to discover and develop new drugs, diagnostics and vaccines targeting NTDs. [CDIPD's] major efforts are in drug discovery and development including translational research to develop drug leads into clinical candidates" (CDIPD, 2015).

Main Project(s):

CDIPD currently has ongoing projects focused on Amebiasis, African sleeping sickness, Chagas, Filariasis, Hookworm, Leishmaniasis, Naegleriasis, Onchocerciasis, and Schistosomiasis. CDIPD also recently worked with the UCSF Small Molecule Discovery Center to screen for molecules to use against Ebola and other diseases (McKerrow, 2015).

Most of CDIPD's work involves lead optimization, drug screening, and/or drug development. Current projects include collaboration with DNDi "on the preclinical development of K777, a novel small molecule targeting cysteine proteases, for use in treatment of Chagas disease." Additionally, "Acea Biosciences and CDIPD are collaborating on development of Corifungin as a new drug to treat Primary Amebic Meningoencephalitis caused by Naegleria fowleri and visceral leishmaniasis. CDIPD successfully petitioned for Orphan Drug Status for Corifungin with the FDA" (CDIPD, 2015).

Ongoing CDIPD projects:
http://globalprojects.ucsf.edu/organizations/center-discovery-and-innovation-parasitic-disease-cdipd

Effectiveness:

CDIPD has achieved success in various areas of NTD research. For example, "Bioventures for Global Health has identified pharmaceutical companies with an interest in neglected tropical diseases. A promising collaboration has begun between researchers at CDIPD and AstraZeneca

A5 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS
WORKING ACROSS DISEASES

UCSF/UCSD CENTER FOR DISCOVERY & INNOVATION IN PARASITIC DISEASES (CDIPD)

to explore compound libraries against of a number of pathogenic parasites" and "CDIPD and the Broad Institute have joined in an effort to identify new drug leads for neglected tropical diseases. An ongoing collaboration between CDIPD and the Broad Institute has led to promising leads for new chemotherapy targeting Chagas disease. A follow-up program to screen compounds produced at the Broad Institute against Leishmania parasites is imminent." Additionally, "[a] collaboration with Anacor led to the identification of a potent lead series effective against trypanosomes in culture, as well as in an animal model of acute infection. CDIPD Director, James McKerrow, introduced Anacor to DNDi to facilitate further development of this series. With synthetic chemistry and PK support from Scynexis, a lead compound has been developed into a clinical candidate, oxaborole SCYX-7158. This drug candidate is now in clinical trials and was declared "Project of the Year 2011" by DNDi" (CDIPD, 2015).

Furthermore, "CDIPD member, Dr. Anjan Debnath, developed the first high-throughput screen for identifying drugs effective against Entamoeba histolytica. While screening a library of FDA-approved drugs and bioactives, Dr. Debnath discovered auranofin as an FDA-approved drug with better efficacy than the current treatment for amebiasis. This drug, originally developed for rheumatoid arthritis, has received Orphan Drug Status from the FDA, and is also effective against Giardia, Trichomonas, Cryptosporidium, Onchocerca and Brugia. For more details see recent press releases and publications.

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

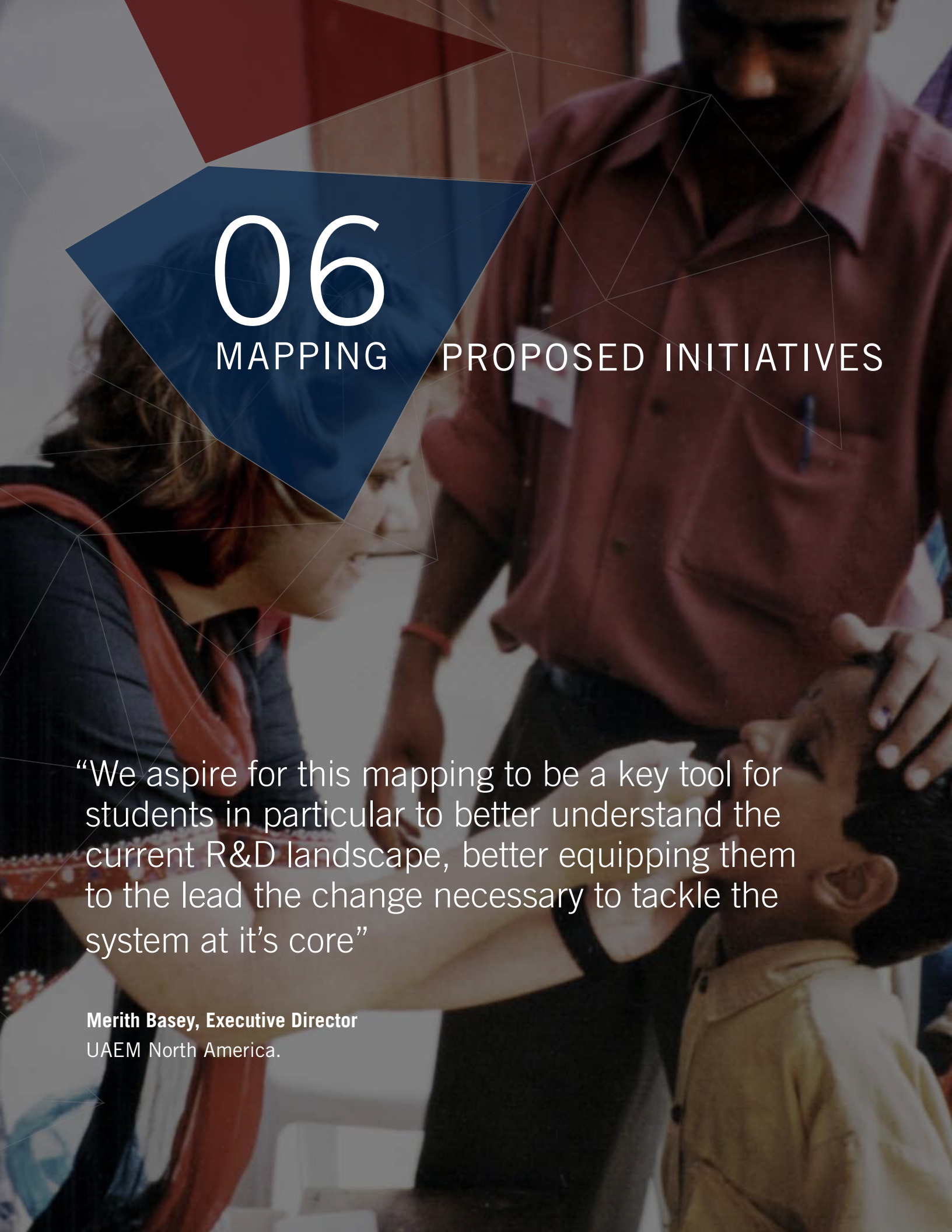
None found.

Organizations, Stakeholders, And/Or Partners:

Anacor Pharmaceuticals; DNDi; The Genomic Institute of the Novartis Foundation (GNF); Acea Biosciences; the CDC; AstraZeneca; BioVentures in Global Health (BVGH); New York Blood Center; St. Jude Hospital, Scripps Florida; Intervet Innovation GmbH; Pharmadyn; the Broad Institute; Khepri Biosciences; the National Institutes of Allergy and Infectious Diseases; The Sandler Foundation; the Institute for OneWorld Health, etc.

University Involvement:

Based at UCSD Skaggs School of Pharmacy and Pharmaceutical Sciences; University of California, San Francisco; University of California, Santa Cruz; Stanford University; Northeastern; University of Cape Town; Yale University; UCLA; Justus-Liebig-University; Georgia Institute of Technology; Johannes Gutenburg Universität Mainz; University of East Anglia; The University of Queensland; McGill University, etc.



06 MAPPING PROPOSED INITIATIVES

"We aspire for this mapping to be a key tool for students in particular to better understand the current R&D landscape, better equipping them to the lead the change necessary to tackle the system at it's core"

Merith Basey, Executive Director
UAEM North America.

A NOTE ON CEWG DEMONSTRATION PROJECTS

The WHO's CEWG (Consultative Expert Working Group) Demonstration Project Proposals were reviewed and, via a thorough selection process, the four projects considered most promising were ultimately selected for further development during a global technical consultative meeting and are expected to be funded with support from **the pilot Pooled International Fund** discussed below. The proposed projects must specifically work to develop health technologies including but not limited to medicines, diagnostics, medical devices, and vaccines, "for diseases that disproportionately affect developing countries and for which identified R&D gaps remain unaddressed due to market failures." According to the WHO, "the projects must [also] demonstrate effectiveness of alternative, innovative and sustainable financing and coordination approaches to address identified R&D gaps" (WHO CEWG 2015).

The original Criteria for Selection for submitted projects used by the CEWG were based on public health impact, efficiency/cost-effectiveness, technical feasibility, financial feasibility, IP management, potential for de-linking, governance and accountability, and impact on capacity-building.

In 2014, the selection of demonstration projects was organized by the World Health Organization through a call for proposals though its 6 Regional Offices. 22 projects were initially shortlisted and an independent panel of experts recommend 8 projects for further development. This included:

1. The Visceral Leishmaniasis (VL) Global R&D & Access Initiative (DNDi)
2. Development Of Class D Cpg Odn (D35) As An Adjunct To Chemotherapy For Cutaneous Leishmaniasis And Post Kala- Azar Dermal Leishmaniasis (PkdI) (FDA)
3. Exploiting the Pathogen Box: an international open source collaboration to accelerate drug development in addressing diseases of poverty (MMV).
4. Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases (ANDI)
5. Multiplexed Point-of-Care test for acute febrile illness (Translational Health Science and Technology Institute, India
6. Demonstration of the potential of a single dose malaria cure of artemether-lumefantrine through reformulation in a nano-based drug delivery system (Council for Industrial and Scientific Research, South Africa)
7. Development Of A Vaccine Against Schistosomiasis Based On The Recombinant Sm14 A Member of The Fatty Acid Binding Protein: Controlling Transmission Of A Disease of Poverty. (Fiocruz, Brazil)
8. Dengue vaccine development (Health Systems Research Institute (HSRI), Thailand) – this project was subsequently withdrawn from the process.

The 8 projects chosen were asked to submit additional information based on the following six elements, as defined by the CEWG: (1) Utilizes open knowledge innovation approaches; (2) Utilizes licensing approaches that secure access to research outputs and final products; (3) Proposes and fosters financing mechanisms including innovative, sustainable and pooled funding; (4) Fosters effective and efficient coordination mechanisms amongst existing organizations/initiatives; [and] (5) Strengthens capacity for research, development and production, including through technology transfer, in developing countries"; and (6) Intends to delink the price of the final product from the cost of R&D (Jahn, 2014).

After consideration of additional information (**http://www.who.int/phi/implementation/Meeting_to_Examine_Revised_Proposals_Results.pdf?ua=1**), four projects were then selected to be developed further. The two VL projects decided to collaborate meaning three projects were deemed suitable for funding. In June 2015, an Ad Hoc Advisory committee recommended the following funds to be awarded to the projects for the first 12 months of operation:

A NOTE ON CEWG DEMONSTRATION PROJECTS

1+2. The Visceral Leishmaniasis (VL) Global R&D & Access Initiative - Drugs for Neglected Diseases initiative (DNDi), submitted via AFRO and EMRO joined up with the Development of Class D Cpg Odn (D35) as an Adjunct to Chemotherapy for Cutaneous Leishmaniasis and Post Kala-Azar Dermal Leishmaniasis (Pkdl) - United States Food and Drug Administration (US FDA), et al., submitted via AMRO. Awarded: Euro 2.34 million

3. Exploiting the pathogen box: an international open source collaboration to accelerate drug development in addressing diseases of poverty (MMV) submitted through EURO. Awarded: US$1.36 million

4. Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases - African Network for Drugs and Diagnostics Innovation (ANDI), et al., submitted via AFRO. Awarded US1.6 million.

The three remaining projects (5, 6 and 7) remain under development. However, projects 6 and 7 were left out of this mapping because, based on the information publicly available, their current stage of development did not to meet our inclusion criteria.

In total, 22 proposals were submitted as potential demonstration projects. The mapping includes those which met one or more of the aforementioned inclusion criteria beyond collaboration, did not meet any exclusion criteria, and were found to have sufficient enough information publicly available to facilitate evaluation.

For more information on the CEWG Demonstration Projects and Selection Process: **http://www.who.int/phi/implementation/cewg_background_process/en/**

Critiques/Questions Raised in the Literature:

"Many proposals addressed the need for better diagnostics technologies that can be used in resource poor settings" (Love, 2013). According to KEI, "this may reflect (1) the growing recognition that diagnostics are a key element of health systems, (2) [that] there are opportunities for innovations in diagnostics, particularly as it relates to resource poor settings, and (3) that the R&D costs associated with diagnostics are generally lower than for drug development, and people are trying to be realistic about the resources available for the demonstration projects" (Love, 2013).

"Critics are upset that novel and more risky ideas that would have helped to unlink the cost of drug development from prices were eschewed in favour of the eight shortlisted proposals, which were seen as more viable because they build on existing efforts and focus on specific diseases" (Hayden, 2014). Specifically, "critics worry that the eight shortlisted pilot projects are not actually testing new ways of funding, and that more innovative ones have been shelved. One proposal, rejected last month, would have used two tools — milestone payments and patent pools — to spur the development of tuberculosis medicines. Milestone payments would reward early-stage successes of potential drugs, such as proof of activity in humans. Recipients of the payments would then place intellectual property on these potential drugs into a patent pool. Drug developers could license these patents at low cost and would agree to put further patents back in the pool. Another rejected proposal involved taxing antibiotic use to fund the development of antimicrobials. In their deliberations, reviewers were asked to score the projects' public-health impact and scientific merit ahead of their novelty. Some neglected-disease advocates say that those priorities should have been reversed" and, as Katy Athersuch from MSF explained, there is concern that the selected projects will not allow us to tell how well a completely different approach to R&D can work (Hayden, 2014).

A NOTE ON CEWG DEMONSTRATION PROJECTS

"In response to this criticism, the WHO asked the backers of the [top] eight projects — five of which focus on developing vaccines or medicines for specific neglected diseases, one on fever diagnostics and two on basic research — to explain . . . how they will test methods for funding the work" (Hayden, 2014).

Mapping:

For the purposes of this mapping, we reviewed all of the CEWG proposals submitted, along with other proposals. Only those with one or more truly innovative mechanisms and/or incentives clearly delineated in the proposal submitted, beyond collaboration, were included.

- BLUE = A proposal not related to the *CEWG Demonstration Project Proposals*
- GREEN = One of the four *CEWG Demonstration Project Proposals* selected to first be further developed
- RED = Submitted as a *CEWG Demonstration Project Proposal* but not selected as one of the final four to pursue further.

B1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

EXPLOITING THE PATHOGEN BOX: AN INTERNATIONAL OPEN SOURCE COLLABORATION TO ACCELERATE DRUG DEVELOPMENT IN ADDRESSING DISEASES OF POVERTY

General Approach/Methods Proposed:

(COLLABORATIVE + OPEN) Collaborative and open source platform to provide start points for the discovery of new medicines.

Summary:

"The Medicines for Malaria Venture (MMV)'s Demonstration Project "Exploiting the Pathogen Box: an international open source collaboration to accelerate drug development in addressing diseases of poverty" has the aim to deliver new drug discovery projects for numerous neglected diseases that disproportionately affect developing countries and for which identified R&D gaps remain unaddressed due to market failures. This project builds on the "Open Source Pathogen Box" designed to provide start points for the discovery of new medicines against a range of Type II and Type III diseases" (WHO PB, 2015), which is modeled after MMV's earlier Malaria Box, and will ultimately contain "400 diverse compounds against a range of pathogens" (Reddy, 2015), made available "free-of-charge to researchers"… "with the understanding that results are placed in the public domain within two years" (McCarthy, 2014).

"This demonstration project seeks to exploit "hits" from the Pathogen Box through target identification and chemical optimization to deliver series available for robust drug discovery . . . ready for further [uptake] by the community. The specific objectives of the project are to identify the mechanisms of resistance and modes of action on up to 25 Pathogen Box compounds and to deliver, in open source collaboration, up to 25 robust "hit" series against relevant pathogens" (WHO PB, 2015). "The total budget for the project is USD 11,500,000" (WHO R&D, 2015). Target diseases will include "Malaria, *Mycobacterium Tuberculosis*, Leishmaniasis, Cryptosporidiosis, Chagas, Human African Trypanosomiasis, Lymphatic filariasis, Onchocerciasis, Schistosomiasis and other orphan or neglected tropical infectious diseases" (WHO Box template).

For additional information about Medicines for Malaria Venture and the Malaria Box refer to the MMV section under existing initiatives.

Critiques/Questions Raised in the Literature:

For drugs developed based on results of the Pathogen Box project, there is not yet any specific plan to guarantee affordability and access beyond the expectation that non-profit and PDP partners will be willing to implement equitable licensing policies (WHO Box template).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Proposed by and "will be overseen by MMV scientific leaders and will be evaluated through contributions from MMV's expert scientific advisory committee (ESAC) . . . This project is based on "The Pathogen Box", which is funded by a grant from The Bill and Melinda Gates Foundation" (WHO R&D, 2015) and will be further funded through "in-kind support from partners (pharmaceutical companies and universities) and local agencies in the form of screening, expertise and as well, potentially, matched funds (EDCTP, IMI)" (WHO PB, 2015).

St Jude; Eskitis; UCSD; EPFL, Lausanne; NIAID; GATB; TBDA; Oxford University CPU Vietnam; University of Antwerp; LSHTM, STPH, Basel; London School of Hygiene and Tropical Medicine; DNDi (McCarthy, 2014).

B1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

ESTABLISHING A DRUG DISCOVERY PLATFORM FOR SOURCING NOVEL CLASSES OF ANTIBIOTICS AS PUBLIC GOODS

General Approach/Methods Proposed:

(PULL + OPEN) Creation of a Drug Discovery Platform for Antibiotics with milestone monetary prizes for early stage antibiotic developments, non-exclusive licensing for promising antibiotics, and an open source platform to share intellectual property and data.

Summary:

"The Antibiotics as Public Goods Model . . . combines an open-source discovery platform, milestone prizes, PDPs, and patent buyouts . . . This mechanism is unique because it prioritizes early research of natural molecules, which are the basis for over 75% of antibiotics reaching the market. At the core of this model is an open-source platform that fosters an international research community that pools human, technical, and material resources. This strategy is particularly beneficial to SMEs because milestone prizes and funding through PDPs help them overcome early-stage development barriers. Furthermore, patent buyouts serve to add promising intellectual property to the research commons. These public patents can be licensed out to generic firms, which can price close to marginal cost in the poorest countries. Moreover, by decoupling sales volume from revenue, firms are no longer incentivized to over-market their drug" (Renwick, 2014).

The Public Goods "proposal is a variant of patent buy-out prize funds with an emphasis on open source R&D into antibiotics derived from natural products. The treatment of continued antibiotic effectiveness as a public good is thoughtful, with application to all potential models" (Outterson, 2014). "By shaping the conditions under which these compounds are made available, various R&D pathways for innovation might be tested, for example: 1) milestone prizes for creating promising, druggable leads for novel antibiotics; 2) non-exclusive licensing to publicly funded product development partnerships for generic production and scale up limited to rational use, thereby ensuring conservation of the effectiveness of antibiotics produced; or 3) open source, online collaboration platform for sharing annotation data in a research commons, with a clickwrap license ensuring that the intellectual property generated belongs to the community contributing to the repository"… "From the drug discovery platform, a range of approaches for managing intellectual property, publicly financing the R&D, and scaling the project could be piloted" (WHO Public Goods template).

Critiques/Questions Raised in the Literature:

"This proposal is problematic for several reasons. First, given the early-stage focus of this model, the funder is exposed to high risk that the purchased IP or cash injection does not contribute to any meaningful development. Second, it is technically challenging to calculate a patent buyout price that is both social[ly] optimal and large enough to entice developers. Third, it may be difficult to stimulate successive innovation on publicly owned intellectual property. Finally, it is a significant implementation hurdle to establish a new international entity that will govern acquired IP, operate the discovery platform, and manage the prize fund" (Renwick, 2014).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Submitted by ReAct – Action on Antibiotic Resistance, Uppsala University, and the Program on Global Health and Technology Access, Sanford School of Public Policy, Duke University. "This proposal has the potential of engaging a broad range of stakeholders. These include: 1) research institutions from high-, low- and middle-income institutions, such as US-NIH, UK-MRC, India's Council on Scientific and Industrial Research, the Kenyan Medical Research Institute, Brazil's Farmanguinhos, or China's National Center for Drug Screening; 2) research networks like the African Network for Drugs and Diagnostics Innovation and ASEAN-NDI; 3) product development partnerships like the Drugs for Neglected Diseases Initiative, Medicines for Malaria Venture and the Global Alliance for TB Drug Development; and 4) pharmaceutical firms, including those from low- and middle-income countries and small biotechnology companies" (WHO Public Goods template).

B1 DRUG DISCOVERY AND DATA-SHARING PLATFORMS

BUILDING A DIAGNOSTIC INNOVATION PLATFORM TO ADDRESS ANTIBIOTIC RESISTANCE

General Approach/Methods Proposed:

(POOL + PUSH + PULL) Creation of a diagnostic innovation platform to address antibiotic resistance with pooling of resources and use of push and pull mechanisms to incentivize research.

Summary:

"This proposal for a diagnostic innovation platform to address antibiotic resistance would pool R&D inputs at three key points in the value chain: 1) a specimen bank that serves as a reference against which to test diagnostics; 2) a patent portfolio license bundling key components of the diagnostic platform technology; and 3) a clinical trial network for testing diagnostics. The technology platform discussed here as an exemplar is a microfluidic, paper-based analytic device. Both the paper and patterning for diagnostic purposes have a very low marginal cost. The goal would be to develop a non-instrumented, disposable, point-of-care test particularly well suited for low-resource settings at the base of the pyramid of care. Applying [delinkage] here, this would make the approach of upfront public funding in exchange for an end-product priced close to marginal cost very attractive" (WHO Dx template).

"Access to the public infrastructure of a specimen bank, a technology platform, and a clinical trial network could derisk the R&D pipeline, but also be made available to manufacturers willing to accept push or pull financing in exchange for close-to-marginal cost pricing in low- and middle-income countries . . . The target product profiles would shape the criteria for awarding grants from push financing or milestone prizes from pull financing" (WHO Dx template).
The "Dx Platform is treated as a hybrid model . . . because the scope of [delinkage] is strictly limited to diagnostics. Improved diagnostics are certainly an important component to appropriate use and therefore continued antimicrobial effectiveness" but this project does "not fully or exclusively embrace antibiotic [delinkage]" (Outterson, 2014).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Submitted by ReAct – Action on Antibiotic Resistance, Uppsala University, and the Program on Global Health and Technology Access, Stanford School of Public Policy, Duke University.

B2 DRUG DISCOVERY INCENTIVES
A. PRIZES

MEDICAL INNOVATION PRIZE FUND (MIPF) AND PRIZE FUND FOR HIV/AIDS

General Approach/Methods Proposed:

(PULL) Proposed *patent buy-out end product prize fund* to delink R&D costs from drug prices.

Summary:

The Medical Innovation Prize Fund (MIPF) was proposed by Senator Bernie Sanders via the Medical Innovation Prize Act of 2007. The bill "proposes a non-voluntary replacement for the existing monopoly patent system that would eliminate market exclusivity for patented products in favor of a government fund that would reward innovators for the health impact of their patented innovations. It is intended to impact the domestic US pharmaceutical market exclusively." The MIPF "would incentivize research into new medicines that improve health outcomes, especially in essential areas, and would expand access to new medicines by separating rewards for innovation from monopoly pricing. Patents would no longer serve to guarantee market exclusivity, but would instead be used only to determine eligibility for reward funds. Patent holders would be immediately forced to allow the open use and production of the patented innovations, and the patentee would be rewarded by the government according to the positive health impact of the innovation, much as in the Health Impact Fund. The distribution of prize payments to innovators would be made by a panel consisting of government officials and representatives of stakeholder groups according to the criteria of the incremental therapeutic benefit of a drug and access improvement as compared to the baseline of existing drugs and the degree to which the drug meets health priorities including global infectious diseases, neglected diseases, and rare diseases and conditions" (Hollis, 2008). "The proposal also contains provisions for special payments to be made for drugs treating neglected diseases" (Hollis, 2008).

The Medical Innovation Prize Fund would create a prize fund equal to .55 percent of U.S. GDP, which is more than US$80 billion per year at current levels of U.S. GDP (Love, 2011) and, similarly to the HIF, "new products would participate in the fund for ten years" (Love, 2009). "The Medical Innovation Prize Fund proposal has been introduced to Congress multiple times, as the Medical Innovation Prize Act of 2007, the Medical Innovation Prize Fund Act of 2011, and the Prize Fund for HIV/AIDS Act of 2011" (Williams, 2012). The Prize Fund for HIV/AIDS Act is very similar to the MIPF Act except that where the MIPF would apply to all prescription drugs, the Prize Fund for HIV/AIDS would solely apply to HIV/AIDS treatments and would therefore be funded at .02 percent of the U.S. GDP, which amounts to approximately US$3 billion per year currently (Love, 2011).

Critiques/Questions Raised in the Literature:

According to some critics, "the Medical Innovation Prize Act is problematic in some respects. The fact that it is a mandatory, comprehensive system for all pharmaceuticals, not just for those products which opt in, means that its implementation requires a substantial reorganization of the entire pharmaceutical industry, which is unlikely to be politically feasible. At the same time, its comprehensive approach would create problems for innovators developing drugs with relatively small measured health impact but which patients were willing to pay for. In such cases, a willing exchange between innovator and patient could be blocked, since the Act would require only small payments to the innovator, inadequate to incentivize the innovation. There are also questions regarding whether the act would be compliant with the TRIPS agreement" (Hollis, 2008). HIF proponents argue that it is a more appropriate proposal as "it does not aspire to be a comprehensive, mandatory system" (Hollis, 2008).

B2 DRUG DISCOVERY INCENTIVES
A. PRIZES

MEDICAL INNOVATION PRIZE FUND (MIPF) AND PRIZE FUND FOR HIV/AIDS

Concerning prize funds like the MIPF, the "primary objection has been that the "administration would give rise to partiality, arbitrariness, or even corruption—the dangers of all institutions giving discretionary power to administrators" (Wei). "Under the proposed Act, the government will encounter certain nuanced problems involved with comparing drugs whenever it attempts to evaluate the benefits of a drug or medical product. First, the proposed Act remains silent on whether off-label drug use will be considered when calculating the overall social benefit of the drug . . . Second, administrators of the MIPF must confront the difficulty of drawing a line between medically necessary drugs and drugs that provide lifestyle benefits (e.g. acne medication or Viagra) . . . Third, administrators rewarding drug discovery based simply on the total number of patients served or QALYs might unfairly disadvantage certain minorities . . . Fourth, the Board would have to decide how to handle negative information about the drug that emerges after prize payment has already been awarded." Finally, "in addition to valuation problems, the government may struggle with administrative problems" (Wei).

Proposed Changes/Improvements:

"The proposed Act does not provide a formula for how the Board will determine the amount of each prize payment. Most companies will be forced to bear the risk of innovation because these companies will not know what to expect. The factors that the proposed Act does mention, like number of people treated by the medicine, are rough guidelines (at best) and over-simplistic standards (at worst) for judging the benefits of different drugs. This lack of clarity, which is partly attributable to the difficult task of measuring the value to health in the first place, opens MIPF prize payments up to major disputes and to political influence. Commentators are split on whether a predetermined, complex formula to measure the "social value" of a drug or product would be helpful or any less costly to administer than an open-ended approach" (Wei).

In the 2011 proposal it was explained, "the new version of the Medical Innovation Prize Fund will introduce two new features. One is the "open source dividend." In response to criticism that prizes would result in too much secrecy, the open source dividend would set aside some of the prize money to be shared with those who openly share knowledge, materials and technology that were instrumental in the development of the new product. A second is a system of intermediaries rewards, managed by competitive intermediaries" (Love MIPF, 2009).

Organizations, Stakeholders, And/Or Partners:

Based on Love and Hubbard's 2007 prize fund proposal and adapted by Bernie Sanders (Spulber, 2014).

B2 DRUG DISCOVERY INCENTIVES
A. PRIZES

THE BANGLADESH, BARBADOS, BOLIVIA, AND SURINAME (BBBS) OPEN SOURCE DIVIDEND PROPOSAL

General Approach/Methods Proposed:

(PULL) Proposed *open source dividend and milestone prizes* given to reward openness and sharing of knowledge, materials and technologies as part of larger innovation inducement prize efforts.

Summary:

"The "open source dividend" approach, which was embraced in several of the five Bangladesh, Barbados, Bolivia, and Suriname proposals," all of which are described below, "would share a percentage of end product prize money with those who openly, freely and without discrimination shared knowledge materials and technology. This new feature in the prize funds would extend the benefits to thousands of individuals, academic researchers, universities, government agencies, non-profit institutions and businesses that open source knowledge. It is an incentive to share" (Love PF, 2010). Introduced first in 2009 and most recently in 2015, "in the BBBS proposal 10% of the total final product prize envelope for a TB diagnostic [or other drug] would be reserved for entities making useful information contributions to the end product, in this case a TB diagnostic. To qualify for the open source payment, entrants must make their work freely available" (HRP BBBS, 2015).

The BBBS proposals have included "prizes for different neglected diseases: on Chagas treatments, diagnostics and vaccines – on which there is "almost no" private sector research, the proposal says – and for treatments on HIV/AIDS and TB, malaria, tuberculosis diagnostics, cancer and other major diseases. The prize funds include proposals to support innovation incentive mechanisms to solve technical challenges, such as InnoCentive, and also for licensing pools for IP rights related to those medical solutions" (Mara, 2009). As determined by an Openness Dividend Jury, "to qualify for the Openness Dividend, knowledge, materials and technology must be made freely available on a non-remunerative basis. To the extent intellectual property rights exist, the knowledge, materials and technology must be licensed on a royalty free basis for a field of use and geographic region that is consistent with the field of use and geographic region covered by the Prize Fund rewards" (BBBS, 2015).

"Some of the Bangladesh, Barbados, Bolivia and Suriname proposals include the obligation to grant open, reasonable and non-discriminatory licenses to patent pools (such as the UNITAID patent pool), licensing agencies or similar mechanisms in order to claim the rewards. Some also include Standards for Access to Technologies and proposals for price ceilings and market penetration tests" (BBBS, 2009).

General BBBS prize fund proposal:
http://www.who.int/phi/news/phi_2_kei_prizes_cewg_22june2011_en.pdf

Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis Proposal:
http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_TBPrize.pdf
Via the proposed fund, "the entire [US]$100 million prize, administered by the WHO, would be awarded once a submission meets the minimum criterion specified by the fund. The proposal suggests investing the endowment in income-generating securities and using the earnings for the fixed costs of clinical trials for the final product. A licensing pool would manage the Intellectual Property and guarantee that the diagnostic would be made available at an accessible price" (HRP BBBS, 2015).

B2 DRUG DISCOVERY INCENTIVES
A. PRIZES

THE BANGLADESH, BARBADOS, BOLIVIA, AND SURINAME (BBBS) OPEN SOURCE DIVIDEND PROPOSAL

Prizes as a Reward Mechanism for New Cancer Treatments and Vaccines in Developing Countries Proposal:
http://www.who.int/phi/Bangladesh_Bolivia_Suriname_CancerPrize.pdf
Proposal in which "developing countries de-monopolize the entire sector of medicines and vaccines for cancer, and permit free entry by generic suppliers. In return for ending the monopoly, the governments should agree to provide a domestic system of rewards for developers of new medicines and vaccines for cancer that is funded as a fixed proportion" of a specified base (KEI cancer, 2008).

Chagas Disease Prize Fund for the Development of New Treatments, Diagnostics and Vaccines Proposal:
http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_ChagasPrize.pdf
"The [proposed] prize would be endowed with [US]$250 million and incentivize product development and information sharing. The fund would reward the development of vaccines, diagnostics and medicines that improve health outcomes for populations at risk for Chagas disease. New medicines and vaccines would be eligible for final product prizes, whereas solutions for technical challenges would receive awards in a "best contributions" category. A portion of the "best contributions" funding would be set aside for developing country researchers, and the winners of any of the awards would have to license their intellectual property to a patent pool. In the interim when the prize money is unclaimed, the fund would invest the endowment in income-generating securities" (HRP Chagas, 2015).

Prize Fund to Support Innovation and Access for Donor Supported Markets Proposal:
http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_DonorPrize.pdf
The proposal "suggest[s] that the best way to induce valuable innovation for global health is to divorce the reward from product prices and sales. The reward payments would be divided among competitors and proportional to the incremental health benefit offered by the products. The proposal calls for donors to set aside 10% of their development assistance (DAH) for health that is used to procure drugs for the fund. Theoretically, increasing generic production of global health treatments in developing countries could help drive down the DAH required in the long run" (HRP Donor, 2015).

Priority Medicines & Vaccines Prize Fund Proposal:
http://keionline.org/misc-docs/b_b_igwg/prop3_pmv_pf.pdf
Proposal for both final product and upstream prizes specifically targeting treatment and prevention of type II and III diseases, new antibiotics, and any other emerging public health threats with minimum allocations for each category of interest.

Critiques/Questions Raised in the Literature:

"How do you address the aspiration of small businesses, researchers or non-profit organizations to win prizes, if they can't realistically manage the whole drug development process? Can you offer lots of smaller prizes, for interim progress toward drug development or scientific progress? The answer is, yes you can, and you probably should, but you also have to address the management of those prize programs, and address issues such as the criteria for the selection of winning projects, standards and

B2 DRUG DISCOVERY INCENTIVES
A. PRIZES

THE BANGLADESH, BARBADOS, BOLIVIA, AND SURINAME (BBBS) OPEN SOURCE DIVIDEND PROPOSAL

mechanisms to address conflicts of interest, how to value the prizes, the licensing of IP rights, and other issues. Several of the Bangladesh, Barbados, Bolivia, and Suriname proposals include interim prizes, such as the TB diagnostics or the Chagas disease prize fund proposals, for example" (Love PF, 2010) as well as a Donor Prize, a Cancer Prize, and a Priority Medicines and Vaccines Prize (Love CoI, 2009). Some concerns are specific to certain prize proposals. For example, "some treatment activists are concerned that the donor prize fund would divert money from treatment. However, this would only be true if the funding of the prize fund was more expensive than alternative ways of obtaining access to newer AIDS drugs" (KEI WHO, 2011).

Proposed Changes/Improvements:

For the donor prize fund proposal, "the CEWG might consider requesting the WHO, UNAIDS or the Global Fund to simulate the costs and benefits of the donor prize fund, with regard in particular to efforts to provide sustainable access to newer generation drugs for HIV/AIDS" (KEI WHO, 2011).

Organizations, Stakeholders, And/Or Partners:

Supported by BBBS, KEI, and James Love.

B2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW VOUCHERS

THE NEGLECTED DISEASE TAX CREDIT PROPOSAL

General Approach/Methods Proposed:

(PUSH) Proposed tax incentives to subsidize and encourage R&D on neglected diseases, specifically applicable for large firms.

Summary:

Also known as HR316 and "referred to the House Ways and Means Committee in 2009" (Rao, 2011), "the Neglected Disease (NTD) Tax Credit proposal is designed to help encourage companies to conduct the vital research necessary to develop treatments and possibly cures for neglected diseases and the millions of persons affected by them. While the proposal certainly will not make the development of neglected disease treatments profitable, it will allow companies to recoup a portion of their research and development expenditures. The proposal is modeled after the successful and well-known Orphan Drug Tax Credit" (GHT NTD tax credit). "The [NTD] Tax Credit proposal would: Provide a 50 percent tax credit for pre-clinical (before human clinical testing) research expenditures incurred for the development of "neglected disease" treatments;"… "Restore the full deduction for research costs that are eligible for the 50 percent neglected disease tax credit; Require a charitable non-deductible donation of the rights to the neglected disease treatment to an organization the principal purpose of which is to research, develop or administer treatments for neglected diseases;"… "Not be refundable or tradable; [and] Contain anti-abuse language to ensure that only expenses incurred for neglected disease research would qualify for the credit" (GHT NTD tax credit).

This proposal was "put forward by the biotechnology company ("biotech") Genzyme with the sponsorship of Representative Donald Payne and others" (Rao, 2011). The NTD Tax Credit "could avoid some of the problems encountered with direct funding and could complement pull mechanisms by stimulating early-stage R&D. A tax-credit approach could avoid the administrative costs of funding program infrastructures and the transaction costs of application procedures, which often deter for-profit companies from applying for modest funds that they may see as being more trouble than they're worth . . . A major advantage of this approach is that it could ensure that the property rights of the innovation become widely available" (Anderson, 2009).

Critiques/Questions Raised in the Literature:

"This proposed credit, as currently designed, will likely only interest the small number of established firms that are already conducting neglected-disease R&D for philanthropic reasons and have revenues to offset against the credit. Since startup biotech companies without revenue-generating commercial products cannot make use of the proposed credit, the measure is unlikely to bring many new innovator firms to the table. Furthermore, for the established firms with philanthropic motivations that are already performing neglected-disease R&D, it is unclear whether the proposed credit would induce them to increase their level of effort and investment or would [it] simply subsidize spending that would have occurred anyway? Without provisions for more generous expenditure eligibility and for refundability that could improve the credit's appeal to firms, the credit on its own is unlikely to have broad uptake, either in expanding the number of companies involved in this kind of R&D or in persuading those who are already doing neglected-disease R&D to deepen their efforts. One outstanding question is whether HR 3156 might change the profit equation for firms pursuing a drug against the subset of neglected diseases that may have a significant paying market in middle- and high-income countries, such as Chagas disease, dengue, malaria, and tuberculosis. In other words, might the credit turn what would otherwise have been an unprofitable R&D investment into a profitable venture?" (Rao, 2011).

B2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW VOUCHERS

THE NEGLECTED DISEASE TAX CREDIT PROPOSAL

Additionally, "as targeted R&D tax credits subsidize research inputs for a specific pharmaceutical product rather than rewarding successful product development, they are subject to monitoring problems similar to those for other push mechanisms" and "a targeted R&D tax credit could be claimed by a pharmaceutical company pursuing R&D for versions of the pharmaceutical product that are not appropriate for poor countries" (Mueller-Langer, 2013).

Proposed Changes/Improvements:

"If a tax credit is to have a positive impact for neglected-disease R&D, [a previous] assessment suggests that it would have to be redesigned in several ways, including (a) broadening the credit's eligibility to include clinical as well as nonclinical expenditures; (b) making the credit refundable for companies that do not have offsetting revenues; and (c) modifying the intellectual property (IP) and licensing stipulations so that companies can retain their IP for the more affluent markets, while ensuring access at affordable prices in lower-income markets. The level of the credit might also need to be raised above the 50% level proposed in this bill. In addition, experience with biomedical incentive packages, such as the Orphan Drug laws in the United States, indicates that to achieve its goals, a neglected-diseases tax credit might have to be bundled with other measures such as government R&D grants to firms and certain forms of market commitments (price and/or volume guarantees)" (Rao, 2011).

Rao's evaluation provides more insight into necessary steps towards determining the potential effectiveness of an R&D tax credit: **http://bit.ly/1NabgSH**

Organizations, Stakeholders, And/Or Partners:

Proposed in 2009 by Genzyme with the sponsorship of Representative Donald Payne.

B2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW VOUCHERS

OPTIONS MARKET FOR ANTIBIOTICS (OMA)

General Approach/Methods Proposed:

(PULL) Proposed market-based incentive supplied via OMA for any antibiotic-related innovation, or creation of a guaranteed subsidized market funded by donors and available at various stages of the development process.

Summary:

Proposed in 2013, the Options Market for Antibiotics (OMA) "seeks to incentivize development [of antibiotics] early on, while sharing risks between developers and payers. The goal of the OMA is to allow the market to function effectively at different points in a drug's life cycle, instead of simply at the time of marketing. The OMA model effectively takes the subsidy proposed by the AMC, and transfers that to companies at earlier stages, appropriately discounting it for the time value of money, as well as the risk assumed. The underlying tenets of the need for a subsidy are the same; however, this hybrid mechanism simply advocates this subsidy at different stages in the product life cycle." In the OMA proposal, "if new IP is developed during a project in which options are purchased, it would be paramount that a portion of any subsequent dividends stemming from that IP be shared with the holders of the initial options . . . The goal of the OMA is to allow the market to function effectively at different points in a drug's life cycle, instead of simply at the time of marketing" (Brogan, 2013). "Call options would be sold by drug firms and purchased by payers. Depending on the contract terms, OMAs might function more like insurance, which is an important aspect of antibiotic policy. OMAs could be designed with delinkage features since the option payment and the strike price are not necessarily tied to marginal unit sales" (Outterson, 2014).

Critiques/Questions Raised in the Literature:

"It is possible that promising drugs might be conceived by companies ill-equipped to carry their development through. This must be taken into account when making the decision to invest." In such, the OMA model "would rely heavily on full disclosure of all relevant documents" and "free exchange of information between potential purchasers and developers" (Brogan, 2013). "Access to all results from animal testing and preliminary clinical trials would be essential to allow proper evaluation of the viability and efficacy of the drug. This sort of evaluation would require a multi-disciplinary team with representatives suited to evaluate the medical efficacy, pharmacologic profile and cost effectiveness of purchasing options. Corporations may prove hesitant to disclose such sensitive data, but appropriate steps could be taken to ensure confidentiality" (Brogan, 2013).

An additional "critique of the model is that the premium price of any antibiotic outside of the discounted price may be substantial" (Brogan, 2013). Furthermore, there is concern that under the OMA proposal "option sellers [will] hold most of the information needed to price the option; contract terms will determine whether it is a delinkage mechanism; [and] option holders will have first claim on scarce supplies (Outterson, 2014). Finally, it "does not directly encourage follow-on innovation unless multiple projects are funded in early stages" and it would be "technically challenging to price the call options" (Renwick, 2014).

B2 DRUG DISCOVERY INCENTIVES
B. TAX SUBSIDY/PRIORITY REVIEW VOUCHERS

OPTIONS MARKET FOR ANTIBIOTICS (OMA)

Proposed Changes/Improvements:

"This model is not without risk to the developer as well, as additional hidden costs may manifest at the time of final regulatory approval, possibly in the form of additional clinical trials or testing. This risk could be modeled and priced into the call option, or additional contingency funds could be set aside, potentially paid for by the purchaser. If difficult barriers to marketing approval remain, alliances could be formed between firms with complementary capabilities to enhance their overall competitive advantage. This would increase the chance of the drug making it through the final stages of regulatory approval as alliances have been previously shown to be more effective in drug development than single institutions" (Brogan, 2013).

Organizations, Stakeholders, And/Or Partners:

Proposed by David M Brogan of Mayo Clinic and Elias Mossialos of the London School of Economics and Political Science.

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

HEALTH IMPACT FUND

General Approach/Methods Proposed:

(PULL) Proposed pull model that would use the prize incentive as an alternative to patent protection in order to delink the price of a health product and the cost of R&D through "pay-for-performance mechanisms".

Summary:

"The Health Impact Fund (HIF) proposal is promoted by Incentives for Global Health, a non-profit organization devoted to advancing market-based solutions to global health challenges" and originated in 2003 (HIF, 2015). Via the proposed voluntary HIF "the product is supplied at a generic price and the developer is not rewarded for the R&D element until it can demonstrate that the resulting product has health value for the intended patients, i.e. the rewards would be linked explicitly to health outcomes" (Towse, 2011). A 10-year fixed payment, "the prize reward is made contingent on the product developer making all the relevant IP available to competing manufacturers as a way to secure access" (Love and Hubbard, 2007). "Underlying this proposal is the idea that the cost of R&D should be "de-linked" from the price of the product. Rather than earn monopoly rents through patents, the prize would pay the company back for any costs incurred in a single payment and the generic companies would be free to manufacture from the day the product is approved" (Towse, 2011). "In exchange for the secured payment, the firm would grant royalty-free licenses for generic production after the 10 year reward period" (HRP HIF, 2015). The HIF would operate through the establishment of a pool formed through government contribution (Botti, 2013)."While there is no "optimal" budget for the HIF, a reasonable minimum is [US]$6 billion per year, which will roughly maintain a portfolio of 20 drugs. While a substantial sum, [US]$6 billion per year is a small fraction of medical research and development spending and only represents 0.01 percent of global income" (HIF, 2015).

There has also been a proposal specifically for an antibiotics health impact fund (aHIF) "that would offer a "completely voluntary . . . alternative revenue stream of up to several billion dollars per drug over the ten-year registration period"… "The ability of the aHIF to regulate use is stronger when products are patented and the developer can arguably control use, but patent coverage is normally limited by place and time. Outterson, Pogge and Hollis propose that the control over the drug be enhanced "through an international agreement not to permit other firms to sell aHIF-rewarded antibiotics, regardless of the patent status," effectively turning the proposal into a permanent global monopoly with regulated prices and large annual subsidies" (Love, 2014).

Although it has been compared to the AMC, the HIF is generally considered to be much more comprehensive. The HIF is unique in that "it can offer incentives for R&D at an early stage because it isn't exclusive about the products that can be registered; and . . . it rewards the innovator not by subsidizing sales but on the basis of the health benefits this medicine actually brings to patients" (HIF, 2015).

Critiques/Questions Raised in the Literature:

"It is unclear if companies would respond and invest their own resources (or investors theirs in the case of biotechnology companies) against the potential promise of some or all of a prize fund, whether there would be sufficient markets to attract multiple suppliers as a way to compete the prices down, whether the prize specifications can be sufficiently detailed as to steer companies to the "right" technologies" (Wilson and Palriwala, 2010). "The promoters of the Health Impact Fund recognize, for example, that they need practical answers to the question of how health impact would be "demonstrated" in practice, and how

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

HEALTH IMPACT FUND

their model would deal with follow-on products" (Towse, 2011). "Ultimately, the HIF can become a reality only if it receives financial support from governments. Since most countries will want to participate only if others share the financial burden, a sensible approach to making progress is for countries to agree to offer financial support conditional on the participation of enough other countries" (HIF, 2015). A major criticism of the HIF, shared by KEI and others, is the lack of requirement of open licensing of drugs and its impact on generic manufacturing, which has been somewhat addressed via increased flexibility but is still an issue (KEI HIF, 2015). Challenges for an aHIF in particular include getting global agreement and deciding on which drugs meet the criteria as well as determining future value (Hollis, 2013).

Coles, et al. delineate stakeholder views on additional challenges of the HIF: **http://goo.gl/hn8DDD**

Proposed Changes/Improvements:

The HIF proposal has undergone numerous revisions and builds on previous similar proposals starting in 2003 when Michael Abramowicz "first developed a proposal for a reward system with a fixed fund, in which rewards would be based on the proportion of social value created by the innovation, as assessed after the innovation has been commercialized." Not long after, in 2003 and 2004 James Love and Tim Hubbard "proposed the creation of such a mandatory, universal fund with prizes limited to pharmaceuticals"… "suggest[ing] some of the improvements that such an approach could achieve." In 2004, Aidan Hollis "proposed that social value in such a prize mechanism be measured in QALYs or DALYs, in an approach similar to that taken by NICE, Australian PBS, etc." and also in 2004, Love "proposed that the period of prize payments could be structured over a fixed number of years, much like US Orphan Drug Act, data exclusivity, etc." In 2005, Thomas Pogge "proposed a prize system for drugs that would be voluntary, but without the proportional rewards first suggested by Abramowicz" in a paper "conceived independently of the papers of Abramowicz, Love, and Hubbard." Also in 2005, Hollis "characterized the economic properties of an optional fund for pharmaceuticals" and in 2008, Hollis and Pogge "described in much more detail a proposal for an optional fund, in which prices are regulated, but open licensing is not required." In 2009, "Talha Syed pointed out that the system need not rely on patents to qualify innovations for rewards." Most recently, over the past three years the IGH team has "attempted to explore the practical implementation of the HIF idea, and to increase the political and social awareness of the proposal. [Their] current work is focused on measuring health impact for the HIF" and, according to the HIF website, "the team's policy is to be open to suggestions and criticisms and to refine and adapt as needed" (HIF, 2015).
Currently, "Incentives for Global Health is . . . developing the health impact assessment methodology with a multidisciplinary team of experts" in order to ensure that health impact is adequately measured via Quality-Adjusted Life Years (QALYs) and other relevant metrics (HIF, 2015). There is also currently work towards implementing a pilot HIF to assess whether pharmaceutical companies respond well to the pay-for-performance mechanism (HIF, 2015). It has been suggested that antibiotics could be a realistic and useful focus of such a pilot fund to reward stewardship in tackling AMR (Outterson, 2011; Hollis, 2013).

Organizations, Stakeholders, And/Or Partners:

The HIF proposal was developed by a team of researchers including Thomas Pogge, a professor at Yale, and Aidan Hollis, a professor at the University of Calgary and is currently being developed by a team at Incentives for Global Health (HIF, 2015).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

U.K. AMR INNOVATION FUND

General Approach/Methods Proposed:

(POOL + PULL) Proposed plan to address AMR in which companies that develop a successful drug to address AMR are either bought out completely by a global body (Option 1) or, under the 'hybrid' model (Option 2), companies would maintain control of marketing but receive lower pay-outs and be subject to conditions on pricing and distribution. Additionally, pharma would support a global innovation fund for R&D.

Summary:

The Review on Antimicrobial Resistance was appointed by UK Prime Minister David Cameron in 2014 and chaired by economist Jim O'Neill and resulted in the proposal of a U.K. AMR Innovation Fund. The report advocates delinkage as a new business model for antibiotic development: "In the [delinkage] model, companies would be rewarded for R&D by other means (such as lump sums) in exchange for accepting some form of restriction on the prices they could charge for the product. The medicine could then be sold at a price close to production costs, thereby ensuring better access" (Clift, 2015). While this has been opposed because it is seen as an attack of the patent-based system and the 'free' market placing too much control in the hands of the government over allocation of funds for pharmaceutical R&D, there is some acceptance of the idea in relation to antibiotics because "in the context of resistance, most new antibiotics are unlikely to sell in large quantities initially because they should be reserved for use only when all other options have been exhausted" and "[delinkage] removes the incentive for industry to boost sales in ways which may encourage overuse or misuse in ways that accelerate the development of antibiotic resistance, and correspondingly relieves industry of the need to spend large sums on marketing" (Clift, 2015). The Review is the first influential official body to recommend solutions based on delinkage. It "proposes ways to stimulate the development of 15 new antibiotics a decade, of which four should have totally novel modes of action"… "Companies would be offered lump sum payments if they successfully develop a drug meeting specified (but yet to be defined) criteria. A 'global body', financed by as many countries as possible, would make the pay-outs" via the AMR Innovation Fund. "The cost is estimated at between [US]$15 billion (option 2) and $37 billion (option 1) over a decade" (Clift, 2015).

Additionally, the review includes a fleshed out "proposal for a global antimicrobial resistance innovation fund which it suggests should operate for five years only at a cost of [US]$2 billion", funded and supported by pharma (Clift, 2015). This global innovation fund would be used to boost funding for "blue-sky" research into drugs and diagnostics – with much of the money going to universities and small biotech companies. One promising area of research concerns so-called "resistance breakers." These are compounds that work to boost the effectiveness of existing antibiotics (Clift, 2015; Walsh, 2015). "O'Neill sees the fund as a way to kickstart early-stage antibiotic R&D at academic institutions, public health bodies and biotechs" (Taylor, 2015).

Critiques/Questions Raised in the Literature:

Critics wonder what the IP status of the drugs that would be developed thanks to the innovation fund would be as well as how a 'global body' would be constituted and financed. There are also questions concerning how the criteria for rewards would be defined and, in the favoured option, what conditions could be imposed on companies to promote conservation and access (Clift, 2015; Walsh, 2015).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

U.K. AMR INNOVATION FUND

Proposed Changes/Improvements:

The proposal is very recent. However, proponents believe that "lessons could be learnt from successful initiatives such as UNAIDS, the joint United Nations programme on HIV and AIDS, and the global vaccine initiative GAVI" (Wise, 2015). "O'Neill will spend the next year engaging with governments, non-governmental organisations, and drug companies to discuss the proposals contained in his report and will present a detailed package of actions by the summer of 2016" (Wise, 2015).

Organizations, Stakeholders, And/Or Partners:

Proposed by economist Jim O'Neill, supported by UK Prime Minister David Cameron. Proponents include John Savill, chief executive of the UK Medical Research Council, Sally Davies, chief medical adviser to the UK government, Maureen Baker, chair of the Royal College of General Practitioners, and Patrick Vallance, GlaxoSmithKline's president of pharmaceuticals research and development (Wise, 2015).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

PROPOSED WHO POOLED FUND FOR HEALTH R&D IN NEGLECTED DISEASES

(KNOWN UNDER CEWG TERMS AS TYPE III, II AND THE SPECIFIC RESEARCH NEEDS OF DEVELOPING COUNTRIES OF TYPE I DISEASES)

General Approach/Methods Proposed:

(POOL + PUSH) Proposed global inter-governmental pooled fund to finance biomedical R&D with an emphasis on neglected health needs.

Summary:

In 2014 the World Health Assembly requested the WHO Director-General with the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases to explore the possibility of using an existing mechanism to host a pooled fund for voluntary contributions towards research and development for type III and II diseases and the specific research and development needs of developing countries in relation to type I diseases. This work is ongoing and will be reported to the World Health Assembly in May 2016.

Referred to as the WHO Pooled Fund for R&D, "this [would] be the first fund that is committed to delinkage for both commercial and neglected diseases" (GHTC GF, 2014). At the 2015 World Health Assembly, "most member states . . . said they favour the establishment of a pooled fund financially managed as proposed by WHO, underlining the need for transparency and member state management . . . The European region and others said resources from the pool funding should be allocated according to evidence-based R&D needs" (Saez, 2015). "Existing multilateral funds can serve as models, such as those created to scale up delivery of treatment and prevention programmes in developing countries like the Global Fund to Fight AIDS, Tuberculosis and Malaria; Gavi, the Vaccine Alliance; and UNITAID" (DNDi, 2015b). "The priorities of the fund would be informed by the analysis of the research landscape provided by the WHO Global Observatory on Health R&D. General priority areas would be recommended by the coordination mechanism. WHO is currently examining options for such a mechanism" (KEI GF, 2014). In a recent article concerning the Proposed WHO Pooled Fund for R&D, "the authors [stress] that the proposed fund and mechanism must take an independent approach to priority-setting, monitoring, and coordination of R&D, and be based on the principles of open knowledge innovation, fair licensing, and the [delinkage] of the final price of a product from R&D costs" (DNDi, 2015b).

The complete article written by Balasegaram et al. can be accessed here: **http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001831**

DNDi outlines additional considerations for the Proposed WHO Pooled Fund for R&D here: **http://www.dndi.org/images/stories/advocacy/pilot-pooled-international-fund_web.pdf**

Critiques/Questions Raised in the Literature:

"Financial sources of the voluntary fund remain uncertain"… "the premise for the establishment of a pooled fund and the observatory depends on the availability of new funds. Several countries have pledged funds towards R&D demonstration projects and the observatory. Current donors are Brazil, France, India, Norway, Switzerland and South Africa, which announced a US1 million contribution this week" (Saez, 2015). Furthermore, "it is unclear what impact this effort on a voluntary pooled fund will have on an outstanding proposal to create a treaty or instrument for R&D" (Saez, 2015). "The fund will face some challenges including: Bringing together the political and the technical agenda and particularly making the political case for why this fund will add value; Size and sustainability of the fund; [and] Setting realistic expectations for timescales and impact of this fund, bearing in mind that this will only be one of many of a range of tools that will be necessary to sustain global health R&D" (GHTC GF, 2014).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

GLOBAL FUND FOR BIOMEDICAL R&D PROPOSAL

Proposed Changes/Improvements:

As of right now, "TDR is commissioning three studies to help to identify how to set up this new global fund for R&D and identify what is needed both financially and operationally. These studies will inform a business plan to be developed in 2016" (TDR GF, 2015). Study one is a financial modelling exercise; study two is a consultation to determine the remit of a TDR-based Scientific Working Group; and study three is a consultation on the roles of target product profiles in the neglected diseases (TDR GF, 2015). Health Action International has stated that the proposed pooled fund should be all-encompassing, covering any diseases "where there is a market failure in attracting sustainable R&D funding" and that "the pooled fund and the projects it will support should also be governed by a framework of core principles and norms as recommended by the CEWG . . . Without this, the pooled fund will be reduced to a weak mechanism that puts money into an existing system that is broken" (Saez, 2015).

Organizations, Stakeholders, And/Or Partners:

Donors so far include Brazil, France, India, Norway, Switzerland and South Africa with HAI, MSF and DNDi endorsing the proposal. Additional support for a global fund has come from "public and private research institutions, government officials, non-governmental organizations, and academic groups from Europe, China, India, and South Africa" (DNDi, 2015b). Both the US and France have opposed the proposal for a Global Fund (Carter, 2012).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

GLOBAL VACCINE DEVELOPMENT FUND

General Approach/Methods Proposed:

(POOL + PUSH) Proposed global pooled fund to finance vaccine development targeting neglected diseases and other public health threats such as MERS.

Summary:

Introduced in 2015, an "international vaccine-development fund [is believed] to be urgently needed to provide the resources and the momentum to carry vaccines from their conception in academic and government laboratories and small biotechnology firms to development and licensure by industry. Such a fund would enable basic scientists to move candidate vaccines from the laboratory through the so-called valley of death — the critical steps after good preclinical data have been obtained, comprising manufacture to Food and Drug Administration standards, a phase 1 clinical trial, and proof of concept in terms of protective immune responses. This support would permit efficacy assessment to begin" (Plotkin, 2015). This fund would promote research on vaccine development, neglected diseases, and other public health threats including "Ebola, chikungunya, Middle East respiratory syndrome coronavirus (MERS-CoV), the severe acute respiratory syndrome (SARS) virus (which is not extinct in its animal reservoir), West Nile virus, and Lyme disease . . . In addition to producing new vaccines, there is a growing need to improve old vaccines. Pertussis and influenza vaccines, for example, are currently recommended for everyone, but their effectiveness leaves much to be desired . . . External funding could permit the exploration of ideas for improving partially effective vaccines. Seed money for the proposed fund could come from governments, foundations, the pharmaceutical industry, and nontraditional sources, perhaps including the insurance and travel industries. At least [US]$2 billion would be needed at the outset. This level of funding should be achievable, even at a time when resources are scarce" (Plotkin, 2015).

"The proposed fund would invite competitive proposals from scientists, their institutions, and eligible biotech companies. Requests for support to help carry promising vaccine projects through tests in large animals, manufacturing for human use, phase 1 and 2 clinical trials, including the initial demonstration of efficacy and the production of a small stockpile, would be reviewed by an independent panel of scientists and funders. Grants would be awarded and renewed on the basis of milestones achieved and overall grant performance, which would be closely monitored by independent auditors. Institutional overhead costs would be capped. Costly phase 3 trials would have to be funded and conducted by an interested pharmaceutical partner, most likely with substantial government support or special incentives, as circumstances dictated. With initial support, however, at least a vaccine would be available for emergency use. In some cases, if phase 3 trials were impractical, results from animal or human challenge models might suffice for licensure" (Plotkin, 2015). The fund would be similar to the aforementioned proposed US$2 billion antibiotic-resistance fund (Plotkin, 2015).

Critiques/Questions Raised in the Literature:

Currently the proposed fund is not expected to cover late-stage testing although this could change. Additionally, the ownership of subsequent IP has not been specified but it has been suggested that IP rights would remain with the vaccine developers and although it could be such that the fund requests a certain percentage returned on the investment this possibility is not being stressed in the current proposal (Silverman, 2015).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Proposed by Adel Mahmoud, Professor at Princeton's Woodrow Wilson School of Public and International Affairs, Jeremy Farrar, Director of the U.K.-based Wellcome Trust, and Stanley Plotkin, emeritus professor at the University of Pennsylvania (Huber, 2015).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

THE FUND FOR RESEARCH IN NEGLECTED DISEASES (FRIND)

General Approach/Methods Proposed:

(POOL + PUSH) Proposed pooled fund and patent pool managed as a portfolio and focused on R&D for NTDs with support from PDPs emphasized.

Summary:

First introduced in 2007, "the IFPMA and Novartis . . . commissioned a feasibility study for a Fund for R&D in Neglected Diseases (FRIND) [in 2008] and estimate that US$ 6–10 billion would be needed over the coming decade to bring promising neglected disease products in the pipeline to market. FRIND would be open to applications from for-profit companies as well as from PDPs or academic institutions. As proposed, these public investments would result in intellectual property, retained by the inventing institution or company, but exclusively licensed to the fund for the particular neglected disease. Dual market opportunities, such as a secondary indication with commercial potential, would remain with the funded institution or company" (So FRIND). "FRIND [would] focus on the R&D financing of diagnostics, treatments and vaccines in late-stage clinical development (phases II and III). Consultations have shown that the need and feasibility for rigorous portfolio management is the greatest in this phase." FRIND would "use rigorous portfolio management to select the strongest compounds, and finance them in an upfront, ex-ante, basis from milestone to milestone. An independent Scientific Advisory Committee [would] be tasked to select the best compounds from the different 2 eligible entities" (WHO FRIND proposal), and would be responsible for allocating "funds based on unmet need and scientific likelihood of success, replacing individual PDP or industry portfolio management" (Health Policy Division EWG, 2009). Additionally, "FRIND proposes data sharing between projects in order speed innovation and stopping or redirecting poorly performing projects as early as possible" (HRP FRIND, 2015). "FRIND works within the existing IP framework but aims to prevent IP obstacles from obstructing neglected diseases R&D" (WHO FRIND proposal).

Critiques/Questions Raised in the Literature:

"Proposals such as FRIND raise important policy questions. Keeping the scope to neglected diseases, might this fail to address critical needs of adapting health technologies that might respond to significant sources of the burden of disease in developing countries, such as vaccines for human papillomavirus (HPV) or meningitis? Will such funding just substitute the "no profit, no loss" efforts of multinational companies with "for profit" undertakings? Would PDPs and companies be equal to the responsibility of ensuring affordable end-products for those in need? How should the funding be conditioned to ensure that resulting inventions are not just licensed back to FRIND, but registered and delivered for the intended markets in the developing world? Would PDPs and drug companies competing for the same pool of public and philanthropic monies for these projects accelerate innovation or result in less sharing and scientific exchange by companies with PDPs? How can such funding be conditioned, so that it is not business as usual, but with the objective of delivering an appropriate and affordable product for those in developing countries? How might such efforts also build capacity and engagement of scientists and firms in developing countries?" (So FRIND). Additionally, under FRIND innovators would still be granted exclusive licenses (WHO FRIND).

Proposed Changes/Improvements:

The above "questions suggest the need for a framework for rethinking the public sector's strategy behind push mechanisms of funding. Some starter

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

THE FUND FOR RESEARCH IN NEGLECTED DISEASES (FRIND)

considerations for this framework might address: targeting push mechanisms; providing value-added funding; ensuring fair returns to the public; and re-engineering the value chain of R&D" (So FRIND). Supporters of FRIND "propose a pilot phase to build a track-record, at funding levels of [US]$50-100Mn per year, financed by new, smaller, donors that have traditionally not invested in R&D for Neglected Diseases, and for whom the pooling and portfolio management are attractive features. The second phase would see an expansion of FRIND, supported by a strong track record in the first phase, and potentially attracting also the traditional R&D donors, to a funding level of [US]$100-200Mn per year" (WHO FRIND).

The Center for Global Health R&D Policy Assessment previously conducted a review on proposed pooled funds for R&D, including FRIND, IRFF, and PDP-FF (listed below): **http://goo.gl/HMxE6w**

In this evaluation, R4D stated, "a variant on the original FRIND proposal, in which the pooled fund would pay for only a limited number of efficacy trials, seems more compelling and feasible. Such a "Phase III" fund, which [it] estimate[d] might require roughly [US]$150 million annually or [US]$600 million for an initial four-year period, could provide a critical mass of financing for several drugs and vaccine candidates at an advanced stage of development, where the risks of failure are lower but the size and cost of a trial would make it hard for individual donors to back it on their own."

A **PDP+ proposal** has also been introduced that combines elements of FRIND, IRFF and PDP-FF (Herrling, 2010). It has been proposed, "The PDP+ project would demand an exclusive license to products in a field of use, in return for funding projects" (KEI PDP+, 2010). Core principles for the PDP+ fund are: "To pool investment risks and uncertainties, the Fund will support PDPs working on a range of interventions for infectious diseases disproportionately affecting the developing world. Where no PDP exists for a particular disease and/or product, other not-for-profit projects could be supported; The Fund will provide a central point to disburse funding across the multiple diseases and products covered by PDPs or other non-profit projects; The Fund will have a diverse stream of funding sources such as donor contributions, bond financing, innovative financing (e.g. taxes, voluntary donations) and revenues from sales of fund-supported products; The Fund will require pro-access policies on product pricing, intellectual property (IP) rights and licensing agreements as a condition of receiving funding to ensure maximum accessibility and affordability of fund-supported products in countries where the need is greatest; Lean, transparent and inclusive Fund governance structures will maximize resource mobilization, efficiently allocate funds to priority R&D areas and coordinate management of global health R&D portfolios; [and] The Fund will centralize information on funding and product progress across a wide range of diseases, products and groups" (Shesgreen, 2010). Critics have questioned whether "centralized decision making and large scale [will lead] to more innovation" (KEI PDP+, 2010).

Organizations, Stakeholders, And/Or Partners:

Proposed by Paul Herring, Novartis Executive, in 2011 along with the International Federation of Pharmaceutical Manufacturers & Associations.

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

THE INDUSTRY R&D FACILITATION FUND (IRFF)

General Approach/Methods Proposed:

(POOL + PUSH) Proposed pooled fund to provide secure and flexible funding to select PDPs for R&D in order to encourage industry involvement.

Summary:

The Industry R&D Facilitation Fund (IRFF), introduced in 2006, "proposes a long-term fund (supported by donors) that automatically reimburses a fixed percentage (e.g. 80%) of the funds that PDPs disburse to Western or developing country (DC) companies. [It is] designed to encourage industry partnering with public health driven PDPs, and thus provision of low or cost-price final products. [The IRFF] automatically allocates funds across all PDP drug portfolios globally, with most funding going to those who advance their portfolios most efficiently. PDPs retain portfolio management" (Health Policy Division EWG, 2009). "The funding intends to be flexible, allowing the PDPs to rely on their own expertise in managing their research portfolios" (HRP IRFF, 2015). Essentially, the IRFF "would be a long-term single central mechanism to subsidise industry input across all neglected disease drug development PPPs . . . spreading the risk of investment across projects" (UK IRFF, 2006). The estimated cost of the IRFF is "US $7 million/year per OECD country to subsidise industry input . . . with an average <$140 million/year" and with IRFF covering up to half of total PPP costs (Moran, 2006).

Critiques/Questions Raised in the Literature:

Within the IRFF proposal, "there are no concrete asks regarding intellectual property rights or pricing of products, and indeed also no details of where the money will come from, what happens when it runs out, who will manage the fund, or determine which PDPs get the 80 percent subsidy" (KEI PF, 2010). Additionally, "the proposal does not provide details of the governance structure, except for a statement that it should be "outside government or international bureaucracies," and a half a sentence on the qualifications of an advisory board" (KEI PF, 2010).

Proposed Changes/Improvements:

As aforementioned, there is now a **PDP Plus proposal** that integrates aspects of the other PDP fund proposals, including the IRFF (Herrling, 2010).

Organizations, Stakeholders, And/Or Partners:

Proposed by Mary Moran, George Institute.

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

PRODUCT DEVELOPMENT PARTNERSHIP FINANCING FACILITY (PDP-FF)

General Approach/Methods Proposed:

(POOL + PUSH) Proposed bond-financed pooled fund to provide funding to support long-term development of PDPs in R&D for NTDs.

Summary:

The Product Development Partnership Financing Facility (PDP-FF), introduced in 2009, "proposes raising funds from the sale of bonds in private capital markets to support R&D conducted by three vaccine PDPs (HIV, TB and malaria). Bond-holders are repaid from royalties on sales in high- and middle-income countries, and donor-funded premiums on sales in low-income countries. To reduce risk to bondholders and allow the PDP-FF to borrow at low interest rates, the Financing Facility would back its borrowing with guarantees from donor governments and possibly foundations" (Health Policy Division EWG, 2009).

Critiques/Questions Raised in the Literature:

According to an evaluation of multiple proposals, PDP-FF, as compared to IRFF and FRIND "has more fundamental difficulties . . . The key problem lies with its inclusion of HIV, TB and malaria vaccines, since it is unlikely that a sufficiently effective HIV or malaria vaccine will be available in the next 10 years to provide the planned 7-10% royalty-based revenue streams from Western markets. As a result, TB vaccine revenues may need to cross-subsidize other areas. Alternatively, developing country markets will be squeezed for margins on less commercially successful vaccines (e.g. initial lower efficacy malaria and HIV vaccines). Since poor countries may not be able to pay higher prices (or only at the cost of reduced patient access), donors will likely need to pay the price premium on their behalf (their willingness to do so being a moot point). Bond purchasers, looking at these figures and delivery timelines, may also be disinclined to risk their funds" (Health Policy Division EWG, 2009). Essentially "the proposal links, rather than [delinks], prices and R&D costs" (KEI PF, 2010).

Proposed Changes/Improvements:

"The proposal acknowledges that the royalties and fees to repay the bonds increase prices for vaccines. The PDPFF may have a positive impact on affordability if it lowers the costs of capital and increases the leverage of the PDPs to negotiate lower prices" (KEI PF, 2010). "If restricted to more commercially attractive Type II vaccines that are already in development (e.g. TB, pneumonia, meningitis), the PDP-FF would likely perform substantially better" (Health Policy Division EWG, 2009).

As of 2010, and as aforementioned, negotiations were being held to develop **the Product Development Partnership Plus (PDP+) Fund** with ideas incorporated from, FRIND, IRFF and PDP-FF for "a single, joint mechanism to fund Product Development Partnerships" (Herrling, 2010). However, few details are currently available pertaining to this proposal beyond those discussed above.

Organizations, Stakeholders, And/Or Partners:

Proposed by IAVI and "developed in conjunction with Aeras Global TB Vaccine Foundation and PATH-Malaria Vaccine Initiative" (KEI PF, 2010).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

REVOLVING FUND TO FINANCE R&D FOR NEGLECTED TROPICAL DISEASES

General Approach/Methods Proposed:

(POOL + PUSH) Proposed revolving fund specific to NTD R&D, wherein the initial investment is reimbursed out of resources generated by the projects that were financed.

Summary:

"With the intention of building local research capacity and providing sustainable financing for research, Costa Rica proposed a revolving fund for R&D in neglected disease[s]" in 2009. "The fund would support type I, II and III diseases, and invest in both projects with market potential and those that could lower government health spending by addressing a significant health challenge. If the fund supports a project with commercial market opportunities, then the developer would have to reimburse the fund upon the successful development of the health technology. Costa Rica proposes an endowment of [US]$100,000 to $1 million for the initial fund" (HRP RF, 2015) towards "financing research, technical development and innovation projects under two headings: (a) Projects leading to innovations which, thanks to their commercial potential, could generate income enabling the resources originally invested from the fund to be reimbursed either wholly or in part; [and] (b) Projects whose pay-off involves focusing on the improvement of public health and thereby translates into lower health costs" (WHO RF proposal).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Proposed by Dr Luis Tacsan Chen Director, Department of Scientific and Technical Development for Health Ministry of Health of Costa Rica. Supporters and potential partners include "National Council for Research in Science and Technology, Costa Rican Social Security Fund, public and private-sector universities, and research institutes" (WHO RF proposal).

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

PILOT POOLED INTERNATIONAL FUND
(ALTHOUGH THE NAME OF THE FUND IS NOT FINALIZED, IT IS COMMONLY REFERRED TO IN THIS WAY)

General Approach/Methods Proposed:

(POOL + PUSH) Proposed pilot pooled international fund to finance selected demonstration projects for both neglected and commerical diseases.

Summary:

The pilot Pooled International Fund, which is referenced by some literature as the pPIF, proposed in 2014 via a Resolution at the 67th World Health Assembly, was developed with support from DNDi and member countries by the WHO CEWG and could be realized as soon as 2016 if enough funds are procured (Moon 2014; GHTC GF, 2014). The pilot Pooled International Fund would potentially be a pilot for the proposed Global Fund for Biomedical R&D and it would be managed by the WHO TDR and the Global R&D Observatory in order to finance coordinated open knowledge innovation and implementation for global biomedical R&D through voluntary contributions, delinking the cost of R&D from the price of subsequent products for both neglected and commercial diseases (Moon, 2014; Grepstad, 2014; GHTC GF, 2014), beginning with four currently selected demonstration projects.

If effective, the pilot Pooled International Fund would "[s]trengthen coordination of global R&D efforts; [m]atch global priority-setting to resources; [and act as a] [v]ehicle to implement and evaluate open-knowledge innovation approaches" (Moon, 2014). In its current form, the pool will function as follows: "1) resource mobilization, 2) priority-translation > call for proposals, 3) proposal selection, 4) resource deployment, and 4) monitoring, evaluation and learning" (Moon, 2014). "Estimates suggest that the four Demonstration Projects would cost about 60 million USD over five years." The CEWG has recommended "that contributions should be proportional to a country's share of global GDP" (Grepstad, 2014). "The fund will not only support R&D projects, but will also support a process for selecting priorities through a global health R&D observatory, which would monitor the R&D funding landscape globally" (GHTC GF, 2014).

Critiques/Questions Raised in the Literature:

"If potential new funders prefer not to pool (i.e. bilateral approaches), adequate new funds will not be raised through a pPIF" (Moon, 2014). In terms of funds raised versus the estimated amount needed, "the current gap is over US$76 million, according to WHO" (Saez, 2015). Challenges for the pilot fund, as with the proposed Global Fund, include: "Bringing together the political and the technical agenda and particularly making the political case for why this fund will add value; Size and sustainability of the fund; [and] Setting realistic expectations for timescales and impact of this fund, bearing in mind that this will only be one of many of a range of tools that will be necessary to sustain global health R&D" (GHTC GF, 2014). "Such a pilot should provide evidence on at least three key questions: 1. How effective and feasible are open knowledge innovation approaches?; 2. How feasible are new forms of coordination among R&D actors?; and 3. How will Member States mobilize new funding to support innovative R&D models?" (Moon, 2014). MSF argues, "More funding and subsidies combined with fewer regulatory requirements is not the solution. They called for a Global Biomedical R&D Fund and Mechanism for Innovations of Public Health Importance" (Saez, 2014).

Proposed Changes/Improvements:

If the pilot Pooled International Fundwere effective, the next step would be the formation of a more permanent, larger Pooled International Fund, for example the proposed WHO Pooled Fund for R&D

B2 DRUG DISCOVERY INCENTIVES
C. INNOVATION FUND/PLATFORM

PILOT POOLED INTERNATIONAL FUND (PPIF)

(Moon, 2014). For now, "leading governments should form a Core Working Group to demonstrate political support for such a fund, design an interim governance structure, and agree upon minimum starting levels of financing to justify operating costs. While risk and uncertainty are greatest at this relatively early-phase, governments willing to take leadership will also benefit from first-mover advantage – the small group of countries who commit today will have the advantage of shaping the governance structures, policies and principles on which the fund will operate" (Moon, 2014). TDR is planning to conduct three studies: a financial modeling exercise, "a consultation to determine the mandate of a TDR-based scientific working group", and "a consultation on the role of target product profiles in the neglected diseases" although some of this will be more related to the observatory rather than the fund (Saez, 2014). HAI stresses that the fund must have "norms that ensure needs-driven R&D and affordable access to medical products from the start of the innovation process through applying the principle of [delinkage]" (Saez, 2014).

Organizations, Stakeholders, And/Or Partners:

While DNDi and Suerie Moon of Harvard University were involved in the proposal, "the WHO Joint Coordinating Board of the Special Programme for Research and Training in Tropical Diseases (TDR) will be responsible for the oversight of the funding mechanism . . . Several countries have pledged funds towards R&D demonstration projects and the observatory. Current donors are Brazil, France, India, Norway, Switzerland and South Africa" (Saez, 2015).

B3 DRUG LICENSING: DRUG PATENT POOLS AND RELATED INITIATIVES

ESSENTIAL MEDICAL INVENTIONS LICENSING AGENCY (EMILA)

General Approach/Methods Proposed:

(POOL) Non-profit entity created to manage patent pools for medical inventions in order to enable generic competition.

Summary:

Proposed in 2006, "The Essential Medical Inventions Licensing Agency (EMILA) [would] be established as a nonprofit organization that manages patent pools or licensing programs that increase access to patented medical products and vaccines in developing countries. The fundamental idea behind EMILA is to provide a professional platform to facilitate collective management of intellectual property rights and more efficient, reasonable and non-discriminatory licensing strategies to enable generic competition to supply developing country markets with more affordable medical technologies" (KEI EMILA, 2007). EMILA would "be funded initially by donations and grants, but [would] seek to develop a sustainable source of funding from fees drawn from licensing royalties . . . EMILA [would] assist various national, regional or multilateral third parties (partners) to create and manage patent pools. The partners [would] determine the policy objectives for each pool, including, for example, the geographic coverage, targeted diseases or conditions, and the specific licensing terms for patent holders and patent users" along with assistance from the Scientific Advisory Board . . . On behalf of such pools, EMILA [would] seek voluntary licenses from owners of relevant patents and other intellectual property rights. To the maximum extent practicable, EMILA [would] strive to standardize licensing terms for each pool, in order to facilitate sub-licensing" (KEI EMILA, 2007). EMILA "would require a grant-back or back-license of patentable improvements made by a generic producer that manufactures the medicine so that other generic manufacturers and the original licensor could benefit from the improvement . . . The EMILA model also deals with regulatory issues by including an additional "Authorization to Reference or Rely upon Health Registration Data" to aid in medicine registration and standards for acceptable manufacturers to ensure the safety of products" (Crager, 2009).

Model in-licenses and out-licenses as well as expected benefits of EMILA: **http://www.keionline.org/misc-docs/emila.pdf**

Critiques/Questions Raised in the Literature:

"Beyond mechanisms for creating low-cost developing country access, which are better understood for small-molecule drugs, new mechanisms would need to be developed for the required sharing of know-how and materials" (Crager, 2009). There is also concern about creating a stand-alone organization for the sole purpose of then creating pools, which is complicated enough in itself, rather than housing the pool[s] under a pre-existing organization (Sae-Lim, 2010). EMILA's "mission suggests that the proposal focuses primarily on delivery phase pooling, although it is difficult to state with certainty that this is its intention" (Nicol, 2010).

Proposed Changes/Improvements:

"An optional feature of EMILA that could encourage voluntary licensing of patents is the possibility that licensing patents to a pool would be a requirement to qualify for innovation prizes. The possibility of rewarding innovators with prizes or monetary rewards has been advocated by several economists and health experts" (KEI EMILA, 2007). Crager et al. (2009) proposes a "patent, materials and know-how (PMK) pool" that adds mechanisms for information sharing to the EMILA proposal.

Organizations, Stakeholders, And/Or Partners:

Proposed by KEI and other public health and industry experts.

B4 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT
PARTNERSHIPS CHALLENGING CURRENT R&D SYSTEM

DEVELOPMENT OF CLASS D CPG ODN (D35) AS AN ADJUNCT TO CHEMOTHERAPY FOR CUTANEOUS LEISHMANIASIS AND POST KALA- AZAR DERMAL LEISHMANIASIS (PKDL)

General Approach/Methods Proposed:

(COLLABORATIVE + POOL + PUSH) Coordinated and collaborative approach via pooled funding to develop D35 for treatment of Leishmaniasis.

Summary:

"The proposed [Drug Development] project aims to combine the use of antimonials with a novel innate immune modulator that activates the immune cells embedded in the skin. The project has 4 phases: 1) Production and characterization of GMP-grade D35; 2) Pre-clinical studies in 2 species (rat and primates) to assess potential toxicities; 3) Proof of concept clinical trials for D 35 and the combination of D35 with antimonials establishing safety profile and optimal dose, and 4) Establishing efficacy across L. major species and licensing" (WHO Class D, 2015). The "US-FDA owns the family of patents for D type ODN including the patents for D35" (Verthelyi 2, 2014). "The purpose of treatment in cutaneous leishmaniasis is to accelerate healing, reduce scarring, and prevent relapses. The proposed strategy is to combine the use of proven chemotherapy to accelerate the elimination of the parasite with an enhancer of the effector immune response to improve the immune response to the parasite and accelerate healing. D35 is a synthetic oligonucleotide designed to activate the innate immune system and enhance the T cell effector mechanism to control Leishmania infection. Synthetic oligonucleotide D35 could meet the requirements of a target product profile for a disease such as CL/PKDL in terms of being field-friendly, affordable, and expected to be safe; as well as in leading to accelerated healing, with reduced incidence of mucocutaneous complications" (Verthelyi, 2014).

According to the project proposal, "the US-FDA licensing arrangement allows sublicensing and the WHO coordinating consortium would be responsible for selecting and overseeing these agreements in a way to ensure that maximizes access to an affordable, safe, quality and effective product. The funds that sustain the cost of implementing the necessary R&D to develop the product could come from pooling monies within the global health community. Thus, the R&D costs and the price of the product will be fully delinked under this proposal" (Verthelyi 2, 2014). "This project will allow [for] demonstrating the effective use of delinking of the price of R&D and the price of the product though equitable or humanitarian licensing for global access, which ensures a low price of the final product given that the US-FDA has no [interest in] recovering the investment in R&D as part of the Agency's mission"… "Development will require pooled funding from member countries. The time from manufacture to license is estimated at 7-8 years. But a new coordinated and collaborative approach with involvement of target countries' National Health authorities, National Regulatory Authorities, donors and other relevant international and national stakeholders will foster a more efficient and faster process for making this medicine available and affordable to populations in need in target countries" (Verthelyi, 2014).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

This project has been merged with the VL Global R&D Initiative (Nakatani, 2014).

Organizations, Stakeholders, And/Or Partners:

Proposed by U.S. FDA and partners including Osaka University (WHO Class D, 2015). A joint letter was sent by "DNDI, Ken Ishii and Daniela Verthelyi to a Japanese funding agency to finance the manufacture and preclinical testing of the ODN. In addition, Daniela Verthelyi has approached scientists at the Center for Human Immunology at the US-NIH to provide scientific support in the characterization of the immune response of the patients" (Verthelyi, 2014). The project is now receiving funding from the Department for International Development (DFID), UK and DNDi has partnered with the FDA and Osaka University to continue the development of D35 (DNDi, 2015a).

B4 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT
PARTNERSHIPS CHALLENGING CURRENT R&D SYSTEM

CHAGAS R&D ACCELERATOR INITIATIVE: A COORDINATION MECHANISM FOR ACCELERATING THE DEVELOPMENT OF NEW HEALTH TOOLS FOR CHAGAS DISEASE

General Approach/Methods Proposed:

(COLLABORATIVE + PULL + OPEN) Creation of a coordinated and collaborative Chagas Disease R&D Initiative focused on new biomarkers for testing therapeutic efficacy, a biobank portal, and development of drug candidates.

Summary:

"This proposal recommends as a Candidate Demonstration Project the creation of a coordinating mechanism based on open knowledge and innovation principles to accelerate the development and delivery of new tools to treat and control Chagas disease"… "The Coordination Initiative would be composed of representatives of the scientific community, key Latin American governments, PAHO/WHO, TDR, DNDi, treatment providers, and the International Federation of People Affected by Chagas Disease (FINDECHAGAS), supported by a secretariat housed in an existing institution. The Secretariat will need to be committed to minimizing overhead costs and achieving value for money"… "The responsibilities of the Initiative would be to: Review and validate R&D priorities for Chagas disease; Define priority treatment candidates and biomarker projects; Oversee development of a Chagas disease biobank portal; Develop and implement an equitable access policy; Review and validate funding needs; Identify potential funding mechanisms at country, regional, and international levels; Review and validate proposals for innovative incentive mechanisms such as prizes; Review and propose regulatory, financial, and procurement policies to facilitate access to final products; Monitor project implementation and results; Review and validate financial reports; Facilitate information sharing with national programs and regional initiatives; [and] Appoint and have oversight of delegated activities of the Secretariat" (DNDi, 2014a).

"The goal of this Coordination Initiative would be to accelerate R&D for Chagas disease, in order to deliver and support the scale-up of new treatment options (shorter treatment regimens, combinations of existing drugs, and brand-new drug therapies), as well as a new field-friendly PCR diagnostic kit and new qualified biomarkers for assessing treatment response, within 5 years" (DNDi, 2014a). "A mix of incentives will be the best way to achieve this objective. Push mechanisms (through grants) and a pull mechanism such as [a] milestone prize could be considered" (WHO Chagas template). "The guiding principles of the Initiative are defined as: Open knowledge and innovation: institutions, companies and researchers from different Platforms and networks . . . would sign a formal agreement ensuring open knowledge sharing; Sustainable funding: members of the committee, principally governments, would commit to secure the necessary funding for the identified priorities through different mechanisms; [and] Equitable access: development of an access policy for funded projects requiring that new therapeutic and diagnostic tools be developed as public goods and ultimately available at affordable prices"… "Collaboration and open and equitable access policies would be incentivized by the availability of funding and access to the in-kind resources provided by members of the coordinating committee, such as expertise and facilities. This funding and use of resources would be tied to agreement by the recipients to the open innovation and access policies. The Initiative would also explore the use of specific awards or prizes to researchers and engineers who openly publish and share their research contributing to Chagas R&D"… "An estimate of total funding needs is [US]$53.58 million over 5 years, with $2.1 million for the Chagas R&D Accelerator Initiative and a virtual fund of $51.48 million to support priority R&D projects" (DNDi, 2014a).

B4 DRUG DEVELOPMENT
A. DISEASE-SPECIFIC PRODUCT DEVELOPMENT PARTNERSHIPS CHALLENGING CURRENT R&D SYSTEM

CHAGAS R&D ACCELERATOR INITIATIVE: A COORDINATION MECHANISM FOR ACCELERATING THE DEVELOPMENT OF NEW HEALTH TOOLS FOR CHAGAS DISEASE

Critiques/Questions Raised in the Literature:

"Critical problems that would need to be solved to ensure proper product access: Poor demand quantification at country level, and poor aggregation of demand at regional and international levels; Weak procurement practices; Uncertain routes to market for new products or suppliers (e.g. lack of clear regulatory pathways); Reliance on single suppliers where alternatives are possible, raising concerns about price and supply security; [and] Lack of operational and human resources to deliver treatments in the field to ensure treatment scale-up" (DNDi, 2014a).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Proposed by DNDi in partnership with PAHO/WHO, TDR, and the International Federation of People Affected by Chagas Disease. Potential partners include the "Chagas Clinical Research Platform [CCRP], Nuevas Herramientas para el Diagnóstico y la Evaluación de Pacientes con Enfermedad de Chagas [NHEPACHA Network], and Integrated Chagas Disease Program [PIDC]" (DNDi, 2014a).

B4 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS WORKING ACROSS DISEASES

DEVELOPMENT FOR EASY TO USE AND AFFORDABLE BIOMARKERS AS DIAGNOSTICS FOR TYPES II AND III DISEASES

General Approach/Methods Proposed:

(COLLABORATIVE) Use of a high-throughput biomarker screening platform for diagnostic development focused on NTDs.

Summary:

"This project will leverage a well-established high-throughput screening platform based on [genomics, proteomics and transcriptomics] (OMICS) technologies developed by China NDI (China Tropical Diseases Drugs and Diagnostics Innovation Network) research group, which will be applied to discover novel biomarkers and process them to development. For better understanding of humoral immunity to clinical schistosomiasis, echinococcosis, vivax malaria and sleeping sickness as well as comprehensive analysis of humoral immuno-epidemiology, [ANDI and China NDI] will screen biomarkers of the four different parasitic diseases with genome-wide scales of 8000-10,000 proteins, using the samples from 2,000-4,000 human subjects. The biomarkers associated with these parasite infections will be identified as well. The diagnostic kits identified by high-throughput platform will be translated into field and population based use"… "Specific aims of the project [are], 1) [To develop] protein microarrays containing 8000-10,000 selected antigens for individual diseases; 2) [To] probe well-characterized infected human sera from China and Africa and identify serodiagnostic antigens; 3) [To] develop, evaluate, validate and optimize field deployable tests for each agent applicable to each region; [and] 4) [To] seek regulatory approval and promote use of products in endemic area" (WHO Biomarker, 2015). To begin with, the project will focus on Malaria Vivax, Trypanosomiasis, Leishmaniasis, and Schistosomiasis (Nwaka 2, 2014). "The overall budget for 2014-2019 is USD 19 million . . . ANDI and China NDI have spent approximately USD 250,000 secured with USD 50,000 pledged for biomarker discovery in the first year by China NDI" (WHO R&D, 2015). "This project describes an innovative inter-and intra-regional cooperative approach for South-South cooperation. Analysis of the pan African Centres of Excellence undertaken by ANDI… show that there is little or no South South collaboration for R&D and local production for neglected diseases including in the area of financing. The project emphasis capacity building, open source and knowledge sharing approaches in all elements of its implementation. A critical component of the project is the implementation of common platforms and protocols for all data evaluation and standardization. Shared databases will be used for data management but final results and conclusions will be made accessible." For all biomarkers, "IP will reside by any institutions that produces or owns them but the project network through China NDI and ANDI will seek a license (exclusive or nonexclusive in nature) to facilitate access to final product in developing countries" and "the network will ensure that any product that results from the project will be publicly available under preferential pricing terms. This will be included in specific manufacturing agreements with companies" (Nwaka, 2014).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Proposed by ANDI. "The roles played by ANDI, ANDI Centres of Excellence as well as China NDI and other partners have been clearly identified in relation to each activity, with additional room available to bring in more partners . . . Implementing partners include five ANDI centres of excellence, 4 Chinese research institutions associated with China NDI plus other partners such as EASE-Medtrend" (WHO R&D, 2015), the National institute for Parasitic Diseases (NIPD), CDC China, Fudan University, Second Military Medical University, Kenya Medical Research Institute (KEMRI), University of Lagos, National Institutes for Food and Drug Control, PATH, SD diagnostics South Korea, and the WHO (Nwaka 2, 2014). "ANDI is presently supported by WHO, TDR, European Union, Nigeria government, African Development Bank through Korean and Brasil Trust Funds. China NDI has been supported by WHO/TDR and Chinese government. All efforts will be made to generate funds from china for this project" (Nwaka, 2014).

B4 DRUG DEVELOPMENT
B. PRODUCT DEVELOPMENT PARTNERSHIPS WORKING ACROSS DISEASES

MULTIPLEXED POINT-OF-CARE TEST FOR ACUTE FEBRILE ILLNESS (MPOCT)

General Approach/Methods Proposed:

(COLLABORATIVE + OPEN) Creation of a consortium to develop a Multiplexed Point-of-Care test for acute febrile illness via an open platform.

Summary:

According to the mPOCT proposal, the project would "use simple field deployable lateral flow formats, which with some innovation, can be used for the generation of multiplex test for at least 5-6 major high-burden pathogens responsible for AFI in tropical and subtropical regions of the world especially SEARO region. Based on literature search, infectious diseases which cause major burden of AFI and also amenable to multiplexing include Malaria, Dengue, Typhoid/ Paratyphoid, Chikungunya, Leptospirosis and Scrub Typhus [1-3, 5, 9]. These are the diseases that are proposed to be targeted by multiplex POCT." The proposal includes "generat[ing] high quality diagnostic intermediates/reagents for each pathogen" and an "affordable handheld mobile phone based test reader which will improve both the sensitivity and specificity of the test . . . The strategy will involve parallel/ simultaneous detection of IgM antibodies against particular pathogen and pathogen specific antigen in whole blood or serum" (mPOCT proposal, 2013).

"Open platform: The lateral flow platform is being proposed for the development of a multiplexed POCT for six pathogens. The major advantage of this format is that it is available in the public domain and is free from IP issues. Importantly, the tests in this format can be manufactured by companies from developing countries" (WHO mPOCT template).

"Product Development Partnerships: For the present project, the public players such as WHO TDR, DBT could be partnered in consortium mode with BMGF and various NGOs for various stages of product development. In the initial discussions, some of the agencies mentioned have already shown interest in the concept along with ministry of health, Govt. of India" (WHO mPOCT template).

"[Delinking] the cost of R&D from the product price: [Delinkage] eliminates monopolies on final products and permits a much more decentralized system of manufacturing, distributing and marketing. In the proposed project, the [delinkage] component is already in-built to large extent, since this will essentially be a public-funded project" (WHO mPOCT template).

"Field testing and validation: This will be carried out by a consortium of stakeholders including hospitals/ clinicians from SEARO countries… These will essentially be the partners who engage in creation of a well-defined sera panel for this purpose. This activity will be coordinated from THSTI with support from WHO TDR and FIND" (WHO mPOCT template).

Additionally, "since the final product is being targeted to public health system, the Governments will be in a position to give assurance, in the form of an advance market commitment (AMC) that a certain volume of product will be utilized by the public sector. Therefore, the company who will manufacture the product without having to worry about the sustainability of its product, since a large bulk will be procured by the public sector. The AMC will ensure a robust supply chain . . . The estimated cost of this project would be around 20 million USD" (WHO mPOCT template).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Translational Health Science and Technology Institute "(THSTI), India will play the role of coordinator (nodal point) for this project" and it was submitted by SEARO through THSTI (mPOCT proposal, 2013).

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

MSF 3P PROJECT

General Approach/Methods Proposed:

(COLLABORATIVE + PUSH + PULL + POOL) Open collaborative platform with pooling of IP and push and pull incentive-based mechanisms to foster development of new drug regimens for TB, and particularly MDR-TB, with an emphasis on delinkage.

Summary:

Previously a CEWG Demonstration Project, "the 3P Project is a new approach to developing affordable, effective new drug regimens to treat tuberculosis." It "uses an open collaborative approach to conduct drug research and development (R&D), and uses novel approaches to finance and coordinate the process" (MSF 3P, 2015):

- push funding to finance R&D activities upfront (i.e. through grants);
- pull funding to incentivise R&D activities through the promise of financial rewards on the achievement of certain R&D objectives (i.e. through milestone prizes); and
- pooling of intellectual property (IP) to ensure open collaborative research and fair licensing for competitive production of the final products.
-

"These well-targeted incentives aim to bring new researchers and developers to the problem, re-engage traditional investors in TB drug development, ensure a healthy drug development pipeline, and ensure that several drug candidates are developed in parallel as combination regimens" (MSF 3P, 2015). "A central feature of [the 3P] proposal is to incentivize the pooling of the relevant IP at the earliest stages to ensure that open, collaborative approaches to R&D are facilitated, and to ensure that the IP for the final product(s) is made widely available to ensure equitable access" (MSF Access, 2014). "The total estimated cost of the project ranges from [US]$83 million to $250 million" (MSF Access, 2014).

"The 3P project is broken down into the following steps: Step 1: Incentive Collaborative early-stage research; Step 2: Fortify and accelerate preclinical development; Step 3: Accelerate regimen-based clinical development; Step 4: Secure public financing for phase III trials; [and] Step 5: Ensure multiple suppliers" (MSF Access, 2014).

The project has a proposed virtual organization structure including (1) a Scientific/Technical Advisory Committee (STAC), (2) Incentive Management Body covering financing and disbursement, (3) open collaborative platform, and (3) patent pooling mechanism (MSF Access, 2014).

While it is still in its early stages, it is argued that "the 3P Project proposal offers benefits over the current TB drug R&D framework by: Reducing duplication of research efforts, thereby saving time and money; Reducing the risks associated with developing potential combinations early in the R&D process; Accelerating the development of all-new drug regimens; Reducing the risk of resistance to new compounds by ensuring their use as part of regimens; Coordinating disparate sources of funding and linking financial rewards to an obligation to share scientific and clinical data and IPR; Separating ('delinking') R&D costs from the final price of the new TB combination regimen" (3P proposal, 2014).

Critiques/Questions Raised in the Literature:

Concerns have been raised about how to deal with regulatory barriers although MSF has countered that 3P is not equated with deregulation but rather the strengthening of regulation at country level (New, 2015).

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

MSF 3P PROJECT

Proposed Changes/Improvements:

MPP has suggested itself as a potential partner for the 3P project. "While th[e] proposal has been widely circulated in the TB community, as of yet, there has been little firm commitment from stakeholders (pharma or donors) wanting to be involved. The MPP could seed that interest and commitment with early involvement . . . The MPP could lead and house the project or the MPP could focus on coordinating IP licensing and pooling aspects" (Gardiner, 2015).

Organizations, Stakeholders, And/Or Partners:

MSF proposed the 3P project and believes the STAC could include members from the WHO, CPTR, TB Alliance, biotechs, and the pharmaceutical industry and other stakeholders in the TB field.

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

THE VISCERAL LEISHMANIASIS (VL) GLOBAL R&D & ACCESS INITIATIVE

General Approach/Methods Proposed:

(COLLABORATIVE + PULL + PUSH + POOL + OPEN) Creation of a coordinated and collaborative Visceral Leishmaniasis Initiative focused on financing R&D with development of a diagnostic tool and chemotherapy tools as primary objectives.

Summary:

The VL Global R&D Access Initiative proposes combining all "groups already working on chemotherapy [for VL] into a single organization" (Ready, 2014). "The VL Global Initiative's aim is to demonstrate that health R&D can be incentivized and optimized through: innovative incentive mechanisms… to fill R&D gaps, such as the NTDs Drug Booster, to finance R&D notably through pool funding, to increase knowledge, decrease the risk of failure, raise the resources needed, capitalize on existing resources, and develop affordable drugs applying the principle of [delinkage]; [and] strengthening cross-regional coordination with multidisciplinary partners, and key role of endemic countries" (WHO VL, 2014). This project "would seek to develop durable oral drugs that do not require cold storage or intravenous delivery" (Hayden, 2014) and would require a budget of 32,000,000 EUR, "of which 9,187,500 EUR is secured and a further 6,100,000 EUR is pledged" (WHO R&D, 2015).

"To address identified VL R&D gaps… the VL Global Initiative (hereafter 'Initiative') requires innovative incentive mechanisms that [delink] R&D costs from product price"… "[Delinkage] is ensured through: (1) DNDi's intellectual property (IP) policy adopted in 2004"…; "(2) Contractual provisions with pharmaceutical partners"…; and "(3) PDPs as push mechanisms"… "To develop a diagnostic tool based on quantitative PCR (qPCR) (Objective 2) a milestone or small end-stage prize is a suitable incentive for partners to better evaluate VL transmission via asymptomatic carriers and PKDL patients"… "The VL prize would notably reward a group already invested in qPCR and stimulate developing countries' research orientations and researchers, thus strengthening capacities. A small prize, up to EUR 500 thousand would attract small organizations, and shift some costs of failure to the prize-funder rather than researchers"… "The Initiative steering committee and scientific advisory committee will define the design and rules for the prize following key principles of [delinkage] (i.e. availability and affordable access) and compliance with the initiative's IP and licensing rules (including open source publication of findings)"… "The Drug Accelerator Consortium… proposed, based on current DNDi negotiations with several pharmaceutical companies, will be launched in 2014. It transcends existing approaches of bilateral agreements, and will pool resources, compounds, and expertise across companies, expediting identification and selection of candidates for promising new chemical entities from lead optimization to pre-clinical research"… "The Accelerator would collectively adhere to the licensing practices described above, and reduce costs and time of the discovery phase of R&D. Outcomes would be placed into the public domain (e.g. through the EU Open PHACTS Discovery Platform) to catalyse further research"… "The Initiative will secure innovative licensing terms (see Question 1) to make research outputs global public goods" and "will apply an equitable access policy to all new therapeutic and diagnostic tools, based on agreed-upon principles that ensure affordable pricing, sustainable production, and [delinkage]" (WHO VL template).

"The Initiative aims to demonstrate that R&D projects can be effective while strengthening coordination among multidisciplinary partners and through innovative R&D financing and coordination mechanisms" (WHO VL 2, 2014).

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

THE VISCERAL LEISHMANIASIS (VL) GLOBAL R&D & ACCESS INITIATIVE

Incentives and innovative mechanisms will include "grant funding with access clauses; collaborative coordination with EDCTP and the consortiums and platforms in endemic countries; milestone prizes; development of a shared, open-access database; [delinkage] of R&D costs from final product prices; regulatory, financial, and procurement policies with involvement of endemic countries regulators in the platform to accelerate the registration; [and] pull[ing] public and private funding into a fund" (WHO VL template).

Critiques/Questions Raised in the Literature:

"One of the issues to scale up treatment is the need for more operational resources to deliver treatments in the field" (WHO VL template).

Proposed Changes/Improvements:

This project has been merged with the Development of Class D Cpg Odn (D35) project (Nakatani, 2014).

Organizations, Stakeholders, And/Or Partners:

Proposed by DNDi and submitted via AFRO and EMRO. "Current funders include The Bill and Melinda Gates Foundation, Médecins Sans Frontières, DFID (UK), Ministry of Health, France and the French Development Agency, GHIT and Wellcome Trust. Discussions with a variety of other potential donors are underway" (WHO R&D, 2015). "The Initiative will partner with the LEAP clinical platform in Africa, EDCTP, IMI, CSIR and OSDD, in addition to DNDi's pharmaceutical and academic partners" (WHO VL 2, 2014). The proposal was "initially supported by Sudan, France, Switzerland, Spain" (Pecoul, 2014).

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

THE OPEN SOURCE MULTIPLEX POC FEVER DIAGNOSTIC PROJECT

General Approach/Methods Proposed:

(COLLABORATIVE + PUSH + PULL + OPEN) Creation of a new ecosystem for financing the development of an open source, multiplex, point of care (POC) diagnostic test via push and pull incentive-based mechanisms.

Summary:

"The aim of 'open source fever project' is to create a new ecosystem [via multi-government collaboration] for financing the development of an open source, multiplex, point of care (POC) diagnostic test for the differential diagnosis of fever or sepsis. This project incorporates novel approaches to financing in order to accelerate innovation and provide more equitable access to better diagnostic tools"… "The proposal uses 'push' funding to finance R&D activities upfront, 'pull' funding to incentivise R&D activities through the promise of financial rewards on the achievement of specific objectives and does so in a way that fully separates or "delinks" the cost of the R&D from the price of the resulting diagnostic device so that access and affordability are ensured. All funded technologies will be fully disclosed and available for use and license to third parties . . . This project is designed to create multiple mechanisms to finance development of open source multiplex point of care (POC) diagnostic tests for the differential diagnosis of fever/sepsis. Each of the mechanisms, grants and research contracts, milestone prizes, best progress prizes, end product prizes and the open source dividend, have strong points, but also gaps and weaknesses" but by combining them their potential will be maximized. "The cost of the project is expected to be between US $70-$200 million, depending on the level of donor support. Governance of the project would include a Donor Committee, responsible for setting high-level policies and facilitating contracts with one or more entities to manage a portfolio of grants and innovation prizes (for example, the Special Program for Research and Training in Tropical Diseases (TDR), UNITAID, or the World Bank)" (MSF proposal, 2013).

The steps for the project would be as follows: "Step 1: Encourage research and development of key objectives toward achieving fever diagnostic through grants and milestone prizes; Step 2: Accelerate progress through additional grants and prizes; Step 3: Ensure open access and licensing of intellectual property rights, data and know-how for follow-on innovation; [and] Step 4: Secure production of the device and encourage competition from multiple manufacturers through open licensing of intellectual property and transfer of know-how" (MSF proposal, 2013).

Critiques/Questions Raised in the Literature:

"One important barrier in developing an open platform is the management of various intellectual property (IP) assets related to developing a multiplex POC platform. Manufacturers have either found a way around the existing patents by having their own proprietary assays or nucleic acid amplification technique or have waited for IPs to expire. Other issues that have been raised in opening up IP to other manufacturers include the control of quality-assurance of the devices. There are several risks to this project. One is that the solution, while assumed to be feasible, will not be known within the project's life. The risk of not solving the end points is greater when the end product prizes are smaller, and lower when the end product prizes are higher. Another risk is the potential for products to be manufactured that do not meet quality standards and prove unreliable in the field . . . There is a risk that a third party will patent a possible useful technology and not agree to the open licensing incentives." However, the proposal discusses ways to mitigate these risks (WHO OS template).

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

THE OPEN SOURCE MULTIPLEX POC FEVER DIAGNOSTIC PROJECT

Proposed Changes/Improvements:

"This proposal builds upon but also has some differences with earlier proposals to use prizes to stimulate the development of point of care diagnostics, including in particular the ideas from the April 2008 MSF expert meeting on IGWG and R&D for tuberculosis, the 2009 proposal by Bangladesh, Barbados, Bolivia, and Suriname for a Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis to the WHO Expert Working Group on R&D financing and coordination, the work beginning in 2009 on a proposed TB Diagnostics XPrize, the 2011 Bio Ventures for Global Health (BVGH) proposal for the Global Health Innovation Quotient Prize: A Milestone-Based Prize to Stimulate R&D for Point-of-Care Fever Diagnostics, submitted to the WHO Consultative Expert Working Group (CEWG) on R&D" (WHO OS template).

Organizations, Stakeholders, And/Or Partners:

Proposed by MSF.

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

ANDI AS THE REGIONAL COORDINATION MECHANISM FOR DEMONSTRATION PROJECTS AND PRODUCT R&D IN AFRICA

General Approach/Methods Proposed:

(COLLABORATION + POOL + PUSH + OPEN) Leveraging of the existing ANDI structure and creation of an innovation hub to pool funds and provide grants in order to develop and promote access to medicines, diagnostic tests, medical devices, and other technologies primarily for type II and III diseases.

Summary:

"The proposal seeks to leverage existing ANDI structure to develop and promote access to medicines, diagnostic tests, medical devices, and other technologies for type II, III and special needs of developing countries in type I diseases, where there is a gap, need and opportunity. In addition, ANDI will use its global network of partners to implement essential technology platforms for R&D, such as the development and access to novel classes of compound library based on traditional medicines and natural products, technology evaluation platforms, open source databases and access to critical R&D facilities and equipment etc. ANDI have relevant experience and track record in R&D program coordination, pre-competitive project identification, selection and financing in Africa. It has established a broad network of African and international institutions (public and private), exemplified by the 38 pan African Centres of Excellence implemented by ANDI as well as South South and North South partnerships in various R&D and manufacturing areas . . . "This innovative and sustainable approach will: i) manage and oversee the implementation of demonstration and other R&D projects that meet the needs of developing countries, ii) fundraise and disburse funds for projects, iii) implement call for proposal, as required, to ensure optimal portfolio balance and delivery of milestones, iv) develop and utilize open source and technology platforms in support of projects, and access to critical equipment, v) coordinate the establishment of local and global partnerships, networks, technology transfer and capacity building in support of demonstration projects . . . ANDI will proactively identify additional partners to support projects and ensure that project milestones are met and projects are successfully transitioned from one phase to another.

An important part of this project will be the development of ANDI KnowledgeBase to support the management of demonstration projects and promote information sharing, in manner that adds value and supports open innovation . . . Another example of an innovative and much needed technology platform that will be implemented and made available by ANDI is an annotated compound library of traditional medicines and natural products from African biodiversity that can support screening campaigns and reverse pharmacological evaluations . . . ANDI has established a mechanism to promote the [delinkage] of the cost of R&D from product price . . . As part of the development of the strategic business plan for ANDI, a proposal was made to establish an African Innovation Fund (AIF) at the African Development Bank (AfDB) to support health R&D and access in Africa.

Although the AIF has not been implemented, the concept is very relevant to the current discussion on options for financing R&D for diseases that disproportionately affect developing countries. Such fund can house a pooled or special fund from taxes for health R&D and access, from which demonstration and future health R&D projects can be financed . . . Such [a] fund can be managed as a self-sustaining Social Venture Fund that can be divided into two parts: i) a grant making part that could fund R&D and product registration, e.g. WHO pre-qualification, and ii) a second portion with modest loaning modality to support the manufacture and large scale production of products emanating from these projects (WHO ANDI template). "This proposal is not focusing on a

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

ANDI AS THE REGIONAL COORDINATION MECHANISM FOR DEMONSTRATION PROJECTS AND PRODUCT R&D IN AFRICA

specific candidate molecule or technology, but it is seeking to manage and coordinate the development of a pipeline of relevant products and technologies that emanate from Africa, including approved demonstration projects and to make these technologies more likely to deliver agreed products. This approach also supports the development of a diversified portfolio that provides opportunity for cross learning from multiple projects, diseases and implementing partners" (WHO ANDI template).

For additional info about the African Network for Drugs and Diagnostics Innovation refer to the section on ANDI under existing initiatives.

Critiques/Questions Raised in the Literature:

Potential risks for this project include: 1) "Human capacity and funding to support the coordination and funding of demonstration projects; 2) "Lack of partners to support selected demonstration projects"; [and] "Regulatory challenges in Africa" but the proposal includes suggestions for mitigating these risks (WHO ANDI template).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

ANDI will be the main stakeholder and will work with a "network or consortium of partners including public and private agencies, PDPs or individual with expertise in the various parts of the product R&D value chain, working together to implement the project . . . The work of ANDI is presently supported with funding from the European Union, WHO/TDR, Nigeria, the African Development Bank including through Trust Funds from South Korea and Brasil" (WHO ANDI template).

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

ANTIBIOTICS INNOVATION FUNDING MECHANISM (AIFM)

General Approach/Methods Proposed:

(POOL + PUSH + PULL + OPEN) Creation of an innovation fund to address antibiotic resistance along with economic incentives to encourage open data and knowledge.

Summary:

The AIFM "proposal focuses on addressing antibiotic resistance." It "would test a new open innovation business model for the development of antibiotic drugs. The project would have two stages of implementation. The first stage would involve the creation of a new governance structure, initial funding commitments, and the adoption of initial policies and norms, and the use of grants and innovation inducement prizes to stimulate innovation. The second stage would involve the implementation of a new fee or tax on the use of antibiotic drugs, with the revenue from the fee or tax used to partly or completely fund the grants and innovation inducement prizes, and to discourage low value uses of antibiotic drugs that generate significant negative externalities. Taken together, the project would replace the current system of temporary monopolies as the reward for the development of new drugs, with a new system with the following features: The creation of new financial innovation incentives that are delinked from drug prices; The elimination of perverse incentives for drug developers to promote inappropriate or low value use of drugs, particularly where there are significant negative impacts on the conservation of the antibiotic resources; The creation of economic incentives to induce the open sharing of knowledge, data, materials, and technology relevant to the development of new products; The competitive production of generic supplies of products at affordable prices; The transfer of technology to drug manufacturers in developing countries; Opportunities for researchers, institutions and both small and large businesses to participate as suppliers of innovations, in both developed in developing countries; [and] A sustainable system of financing for open source development of new antibiotics . . . In Stage 1, the AIFM provides a combination of grants and innovation inducement prizes . . . Among the innovation inducement prizes are (1) end product prizes, (2) interim results prizes, and (3) open source dividend prizes that reward the open sharing of knowledge, data, materials, and technology relevant to the development of new antibiotic drugs.

The AIFM would operate under policies that condition grant and prize money to the licensing of rights in inventions, data, and other intellectual property. These rights would be managed according to policies set out by the public sector entities providing funding for the grants and prizes. In Stage 2, the AIFM would be engaged in the development of multilateral norm setting as regards the levels of funding for the innovation grants and prizes, the implementation of a system of fees or taxes on the use of antibiotic drugs, and the norms and objectives as regards the conservation of antibiotic drugs . . . All funds allocated for grants or cash prizes would be conditioned upon licenses to use all patents, knowhow, data and other intellectual property rights, in the field of use of antibiotics for humans and animals . . . The AIFM would provide a role for decentralized decision making and management, including through the use of Competitive Intermediaries to manage grants and interim results prizes" (WHO AIFM template). Essentially, "The AIFM is a combination of patent buy-outs prize funds… and a fee on antibiotic use" (Outterson, 2014).

Critiques/Questions Raised in the Literature:

"The current system of mechanisms to fund R&D for new drugs is mature and receives extensive support from intellectual property and drug reimbursement regimes. The development of national and global norms and mechanisms to fund innovation as a public good is less mature, and that presents challenges" (WHO AIFM template).

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Proposed by KEI.

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

COMBATING TUBERCULOSIS IN THE REGION BY DEVELOPMENT OF DIAGNOSTICS & DRUGS

General Approach/Methods Proposed:

(COLLABORATIVE + PUSH + PULL + POOL) Creation of a collaborative platform for development of TB diagnostics and drugs with pooling of resources and push and pull incentives implemented.

Summary:

"The proposal is to set up a drug development platform for TB in the countries with disease burden in collaboration with competent institutions in public and private sector in such countries" (WHO TB Platform template). "The project proposes to put in place a translational platform for neglected diseases as a pre-competitive collaborative space which can be used by industry or other research organization to develop drugs for neglected diseases. The above approach is demonstrated through the conduct of the proposed trial of a novel combination for TB." This project aims to: "Develop a standardized 3 drug regimen that is both more efficacious and safe; Shorten the duration of therapy; [and] Eventually aim for a single regimen for both DS and MDR TB . . . The proposed project has a promising lead as a need for novel diagnostics development and/or delivery to be catered for the most dreaded disease for the poor which needs immediate action. The technology will be fulfilling the ASSURED criteria existing for the diagnostics and will be better than the existing ones. This will be supported by pooled funding" (WHO TB Template).

Some of the following coordination of R&D would be demonstrated:
"**Consortium:** Creation of a consortium of like-minded partners including developers, Foundation of Innovative Diagnostics (FIND), UNITAID, StopTB partnership, WHO and Ministry of Health (MoH) from partnering countries from the very beginning;
Open access repositories: can be made in different partner regional countries which will include validated sera panel and the diagnostic and drug candidate can be validated in the respective set up which will be real value addition;
Computational resources: Will be initiated in the regional partner countries;
Open Screening facilities: will be initiated in the regional partner countries for drug screening; [and]
Inter-country Governmental Pooled funding: the partnering countries will be negotiated and brought together for pooled funding of their R&D finding resources to strengthen the work development" (WHO TB template).
"The financing mechanism for health research and development will be a novel approach like:
Product Development Partnerships: the public players such as Department of Biotechnology (DBT), Indian Council of Medical Research (ICMR) and Ministry of Health could be partnered with the facilitatory support by WHO, with Bill and Melinda Gate Foundation (BMGF), FIND, the Program for Appropriate Technology in Health (PATH), The Infectious Diseases Research Institute and US National Institute of Health consortia for point of Care diagnostics development of the product at the various stages of the product development pipeline. The donors work with diagnostic companies to develop PoC diagnostic tests for TB. The Grand Challenges Canada by Canadian Government has initiated provide support for call for proposals for the POC test development. WHO can facilitate in leveraging funds from several conventional and unconventional donors and country governments for supporting the development of the diagnostics;
[Delinking] the cost of R&D from the product price: [Delinkage] of the R&D cost from the product price will eliminate monopolies on final products which will permit a much more decentralized system of manufacturing, distributing and marketing. In the proposed project, the [delinkage] component will already be in-built;

B5 INITIATIVES ADDRESSING 4 OR MORE INNOVATIVE R&D MECHANISMS

COMBATING TUBERCULOSIS IN THE REGION BY DEVELOPMENT OF DIAGNOSTICS & DRUGS

Prizes to incentivize and reward diverse diagnostics and drug discovery efforts[,] which will promote open sharing of innovations from the researchers with others and license the relevant IP to a patent pool. The milestone prizes can be introduced for rapid development of the technology; [and]
Grants to support clinical trial: Public financing need to be made available to push the promising compounds through clinical trials" (WHO TB template).

For the first TB drug expected to complete development, "OSDD treats the drug development as an IP neutral, pre-competitive activity. OSDD is not expecting return on investment and will not charge any royalty from the manufacturers and will license the drug non-exclusively to facilitate generic manufacture and competition in the marketplace which will make the drugs affordable and accessible" (WHO TB template).

Critiques/Questions Raised in the Literature:

None found.

Proposed Changes/Improvements:

None found.

Organizations, Stakeholders, And/Or Partners:

Submitted by the Translational Health Science and Technology Institute (THSTI); Biotechnology Industry Research Advisory Council (BIRAC), India. and the Open Source Drug Discovery (OSDD) programme of the Council of Scientific & Industrial Research (CSIR), India (WHO TB Platform template). " In India, partners could be: NIRT, AIIMS, JALMA, Lala Ram Swarup Institute of Tuberculosis and Respiratory Diseases, New Delhi; Bigtec Lab, Bangalore, Tulip group, Goa and THSTI" (WHO TB template).

07

ACRONYMS

AfDB: African Development Bank
aHIF: Antibiotics Health Impact Fund
AIF: African Innovation Fund
AIFM: Antibiotics Innovation Funding Mechanism
ALS: amyotrophic lateral sclerosis
AMC: advanced market commitment
AMR: Antimicrobial Resistance
ANDi: the African Network for Drugs and Diagnostics Innovation
ARV: antiretroviral
ASEAN: Association of South East Asian Nations
BBBS: Bangladesh, Barbados, Bolivia, and Suriname
BIO: Biotechnology Industry Organization
BiOS: Biological Open Source
BMGF: Bill & Melinda Gates Foundation
BrIDGs: the Bridging Interventional Development Gaps programme
BTD: blood transfer device
BVGH: BIO Ventures for Global Health
CDD: Collaborative Drug Discovery
CDIPD: Center for Discovery & Innovation in Parasitic Diseases
CEWG: Consultative Expert Working Group
CFFT: Cystic Fibrosis Foundation Therapeutics
China NDI/ CNDI: China Tropical Diseases Drugs and Diagnostics Innovation Network
CHOVI: Cholera Vaccine Initiative
CPTR: Critical Path to TB Drug Regimens
CRO: contract research organization
DC: developing country
DECs: Disease Endemic Countries
DNDi: Drugs for Neglected Diseases initiative
DOMI: Diseases of the Most Impoverished
DREAM: Dialogue for Reverse Engineering Assessment and Methods
DVI: Dengue Vaccine Initiative
EDCTP: European Developing Countries Clinical Trials Partnerships
EMILA: Essential Medical Inventions Licensing Agency
EU: European Union
EVI: European Vaccine Initiative
EVRI: European Vaccine Research Development Infrastructure
FDA: Food and Drug Administration
FIND: Foundation for Innovative New Diagnostics
FINDECHAGAS: the International Federation of People Affected by Chagas Disease
FP7: European Commission's (EC) 7th Framework Programme
FRIND: The Fund for Research in Neglected Diseases
GAVI: Global Alliance for Vaccines and Immunizations
GHIF: Global Health Investment Fund
GHIT: Global Health Innovative Technology Fund
HAND: Humanitarian Assistance for Neglected Diseases
HAT: Human African Trypanosomiasis
HHI: Human Hookworm Initiative (Sabin)
HIF: Health Impact Fund
HITs: health information technologies
HPV: Human Papilloma Virus
IAVI: International AIDS Vaccine Initiative
IC: InnoCentive
ICMR: Indian Council of Medical Research
ICTs: Information and Communication Technologies
IDRI: Infectious Disease Research Institute
IFFIm: International Finance Facility for Immunisation
IMI: Innovative Medicines Initiative
INAT: Introducing new approaches and tools
IOI: Initiative for Open Innovation
IOWH: Institute for OneWorld Health

07

ACRONYMS

IP: intellectual property
IPM: International Partnership For Microbicides
IRFF: Industry R&D Facilitation Fund
IVI: International Vaccine Initiative
LEAP: Leishmaniasis East Africa Program
LMICs: low- and middle-income countries
LP: Longitude Prize
MDGH: Medicines Development for Global Health
MDR-TB: multidrug-resistant tuberculosis
MERS: Middle East Respiratory Syndrome
MIPF: Medicine Innovation Prize Fund
MMV: Medicines for Malaria Venture
MoU: Memorandum of Understanding
mPOCT: Multiplexed Point-of-Care test
MPP: Medicines Patent Pool
MSF: Médecins Sans Frontières/ Doctors Without Borders
MVI: Malaria Vaccine Initiative (PATH)
MVP: Meningitis Vaccine Project (PATH)
NCEs: New Chemical Entities
NGO: Non-Governmental Organization
NID: neglected infectious disease
NTD: neglected tropical disease
ODA: Orphan Drug Act
OMA: Options Market for Antibiotics
OMICS: genomics, proteomics and transcriptomics
OSDD: Indian Open Source Drug Discovery
P4L: Prize4Life
PAHO: Pan American Health Organization
PBD: Protein Data Bank
PDP: product development partnership
PDP-FF: PDP Financing Facility
PDP+: Product Development Partnership Plus Proposal
PDVI: Pediatric Dengue Vaccine Initiative
PFH: Patents for Humanity
PMK: patent materials and know-how
PMTCT: prevention of maternal to child transmission
POC: point of care
POINT: Pool for Open Innovation against NTDs
pPIF: pilot Pooled International Fund
PPM: Public-private mix
PPP: Public-private partnership
PRO-ACT: Pooled Resource Open-Access Clinical Trials Database
PRV: Priority Review Voucher
QALY: Quality-Adjusted Life Years
R&D: research and development
RDSTG: Rapid Drug Susceptibility Testing Group
RDTs: rapid diagnostic tests
RF: Revolving Fund
RFP: request for proposal
RPD: rare pediatric disease
S4S: Support for Success Platform
SARS: Severe Acute Respiratory Syndrome
SGC: Structural Genomics Consortium
SIVAC: Supporting National Independent Immunization and Vaccine Advisory Committees
SMEs: small and medium-sized enterprises
SOPs: standard operating procedures
SSI: Sustainable Sciences Institute
STAC: Scientific and Technical Advisory Committee
STIs: sexually transmitted infections
STTR: Small Business Technology Transfer
SVI: Schistosomiasis Vaccine Initiative (Sabin)
TB: Tuberculosis
TBVI: Tuberculosis Vaccine Initiative
TDP: Therapeutics Development Program
TDR: Tropical Diseases Research
TDRU: Tropical Disease Research Unit
THSTI: Translational Health Science and Technology Institute
TPP: Target Product Profile

07

ACRONYMS

TSAP: Typhoid Fever Surveillance in sub-Saharan Africa Program
TSL: The Synaptic Leap
UNOPS: United Nations Office for Project Services
VIVA: Vi-based Vaccines for Asia
VL: Visceral Leishmaniasis
VRR: Vaccines Research Relief
WAP: weighted average price
WHO: World Health Organization
WIPO: World Intellectual Property Organization

08

GLOSSARY

Existing Initiatives
Any current initiatives that have clearly delineated projects and are receiving funding to address and aim to ameliorate at least one inadequate aspect of the current research and development (R&D) system.

Proposed Initiatives
Any initiatives that have been discussed in the literature or presented publicly eg at a conference and are expected to address and ameliorate at least one inadequate aspect of the current R&D system but are not yet being funded and/or implemented.

Delinkage
The separation of the cost of R&D for a drug from the ultimate product price.

Push Mechanism
Direct funding for R&D, often in the form of a grant, as well as indirect incentives, such as tax breaks and in-kind contributions, that help finance R&D upfront and thus mitigate the R&D investment required; they are given independently of the results of such research.

Pull Mechanism
Mechanisms to incentivize R&D activities through the promise of financial rewards once specified objectives or milestones have been met, creating viable market demand. It includes prizes, priority review vouchers (PRVs), advanced market commitments (AMCs), and cash payments.

Pooling Mechanism
Pooling of funds that are aggregated and managed jointly by an established entity, typically a board or committee, to be allocated based on priority setting in order to distribute risk and finance biomedical R&D. The goal of pooled funding is to address inefficient flow and volatility of funds as well as poor allocation of and lack of sufficient resources (Grace, 2011).

Additionally, pooling of intellectual property (IP): typically via a patent pool, an agreement between two or more patent owners to pool their patent rights and license the rights to use these patents together to one another as well as third parties often with the requirement of royalties being paid. The goal of patent pools is typically to enable access to biomedical discoveries and encourage downstream competition by simplifying and improving voluntary and cooperative licensing negotiations (Bartels et al., 2013).
These two distinct types of pooling can occur independently or jointly.

Collaborative Initiative
An R&D initiative that involves a network, consortium, or partnership between two or more of any academic or research institutions, non-profit organizations, NGOs, governments, government entities, or members of the private sector including biotech and pharmaceutical companies. Exchange of information and data pooling is often regulated via Material Transfer Agreements and restricted to within the involved entities unless the initiative is also open.

Open Initiative
R&D initiatives that apply open source, open access, open data, or open knowledge principles. Interested parties are able to contribute knowledge or know-how, data, technology, etc. to be shared in the public domain and, in the case of open source, in coordination with patent-free research. Open initiatives provide literature and/or other information such as biomedical data, typically digital or online, often without any fee or cost and without any copyright and licensing restrictions such as royalties, in order to encourage further access to and reuse of this information and facilitate open collaboration and exchange in biomedical R&D (Creative Commons, 2011). Open access typically pertains to making publications freely available;

08 GLOSSARY

open source typically pertains to making licenses or IP freely available; and open data typically refers to making data, methods, and/or tools freely available.

Crowdsourcing

"The practice of obtaining needed services, ideas, or content by soliciting contributions from a large group of people and especially from the online community rather than from traditional employees or suppliers," (Merriam-Webster, n.d.) often used in online competitions to encourage R&D and ultimately further drug discovery.

Neglected Tropical Diseases (NTDs)

According to the WHO (2015), "a diverse group of diseases with distinct characteristics that thrive mainly among the poorest populations. The 17 NTDs prioritized by WHO are endemic in 149 countries and affect more than 1.4 billion people, costing developing economies billions of dollars every year" and "result[ing] from four different causative pathogens: Protozoa, Helminth[s], Bacteria, [and] Virus[es]."

Rare Paediatric Diseases (RPDs)

Rare diseases that are "serious, often chronic and progressive," including all genetic diseases, autoimmune diseases, and rare cancers, "which affect a small number of people compared to the general population and [for which] specific issues are raised in relation to their rarity" such as lack of scientific knowledge and of available or affordable vaccines, diagnostics, and/or treatments (Orphanet, 2012). "In Europe, a disease is considered to be rare when it affects 1 person per 2000" although this definition varies by region and is different within U.S. (Orphanet, 2012). Additionally, "a disease can be rare in one region, but common in another" because of differences in prevalence. "There are also many common diseases whose variants are rare"... "To date, six to seven thousand rare diseases have been discovered and new diseases are regularly described in medical literature. The number of rare diseases also depends on the degree of specificity used when classifying the different entities/disorders"... "For many rare diseases, signs may be observed at birth or in childhood"... "However, over 50% of rare diseases appear during adulthood, such as Huntington['s] diseases, Crohn disease, Charcot-Marie-Tooth disease, amyotrophic lateral sclerosis, Kaposi's sarcoma or thyroid cancer" (Orphanet, 2012).

Type I Diseases

Diseases that are incident in low, middle, and high-income countries, with large numbers of vulnerable populations in each eg diabetes mellitus

Type II Diseases

Diseases that are incident in low, middle, and high-income countries, but with a substantial proportion of the cases in impoverished countries eg TB, HIV

Type III Diseases

Diseases that are overwhelmingly or exclusively incident in low- and middle-income countries eg river blindness, chagas

Drug discovery and data-sharing platforms

Drug discovery incentives

End Product Prizes

Also known as Final Product Prizes, End Product Prizes "reward developers for a specific product that meets the technical specifications declared on the onset of the competition. These pull mechanisms remove some of the risk from funding entities since they only pay the full amount of the prize upon the delivery of a viable product. At the same time, developers are guaranteed funding that would recoup their R&D costs and provide a sufficient return on investment" (Results for Development Institute, 2015a).

08 GLOSSARY

Milestone Prizes

"Pull incentives that reward innovation for incremental achievements along the product development path. These prizes [are typically] smaller in size than a final [or end] product prize and [can] be awarded for an R&D milestone that falls short of actually registering a product. The spectrum of potential milestone prizes is large" as they be given at any point in the pipeline" (Results for Development Institute, 2015b).

Open Source Dividend

The open source dividend approach provides an incentive for openness and knowledge, data, materials, and technology sharing (Love, 2009). The approach is typically adopted by prize funds via the sharing of a percentage of end product or interim prize money as a reward for those who open source knowledge and other resources either by placing it in the public domain or implementing open, non-remunerated licenses. For example, "the prize proposals submitted by Barbados and Bolivia contained systems for rewards of interim research results that were only available to entities that offered royalty free open licenses inventions, data, materials, and know-how"... "The winning entrant would get 90 percent of the prize money; the remaining 10 percent of the prize money would be given to unaffiliated and uncompensated (by the winning entrant) scientists and engineers that openly published and shared research, data materials and technology, on the basis of who provided the most useful external contributions to achieving the end result" (Love, 2009).

Tax Incentives

R&D tax credits or enhanced tax deductions offered by the government to companies as a reward for pursuing R&D that addresses a specified disease or area of health, for example, rare paediatric diseases (Pringle, 2015).

Innovation Fund/Platform

While an innovation fund solely pools and then provides monetary and/or in-kind resources to finance selected drug R&D, a platform additionally directly facilitates translational research, "providing expertise and performing required studies." Both innovation funds and platforms often also facilitate resource-sharing and collaboration for drug R&D (IOM, 2010).

Venture Philanthropy for Drug Discovery and Development

A mechanism wherein nonprofit organizations and others invest in drug discovery and development using methods appropriated from the venture capital field with money invested up front typically paid back in part or in full in the form of royalties given success.

Patent Pool

"An agreement between two or more patent owners to license one or more of their patents to one another or to third parties. Often, patent pools are associated with complex technologies that require complementary patents in order to provide efficient technical solutions" (WIPO, 2014).

Public-Private Partnership (PPP)

The World Bank (2014) Definition for a PPP is "a long-term contract between a private party and a government entity, for providing a public asset or service, in which the private party bears significant risk and management responsibility, and remuneration is linked to performance."

08 GLOSSARY

Larger PPPs or Organizations that House Multiple Innovative R&D Initiatives
Public-Private Partnerships or organizations without ongoing public engagement that house any combination of two or more of the delineated innovative drug R&D initiatives, for example a PDP and an innovation fund.

Product Development Partnership (PDP)
"A not-for-profit organization that builds partnerships between the public, private, academic, and/or philanthropic sectors to drive the development of new products for underserved markets. Through their unique, collaborative efforts, PDPs are able to access a variety of funding sources and apply a wide range of tools and knowledge to their programs. PDPs retain direct management and oversight of their projects, though much of the laboratory and clinical work is done through external research facilities and contractors. In the global health arena, PDPs were established to accelerate the development of new technologies to fight TB, AIDS, malaria, and a wide range of neglected diseases. Currently, there are more than 140 neglected disease drug, diagnostic, and vaccine projects in the combined PDP portfolio. PDPs are created for the public good; their products are made affordable to all those who need them" (UAEM, 2015).

There are currently several WHO Expert Working Group on R&D Financing endorsed proposals for a pooled fund financed by governments and donors to provide long-term and reliable funding to PDPs via grants "with limited interference with the licensing of intellectual property rights or the pricing of products" and the capacity "to automate or centralize funding decisions across [PDP] portfolios to a lesser or greater degree" depending on need (KEI PF, 2010).

09

BIBLIOGRAPHY

Aeras. (2015). Advancing Tuberculosis Vaccines for the world. *AERAS*. Retrieved from **http://www.aeras.org/**

African Network for Drugs and Diagnostics Innovation (ANDI). (n.d.a). ANDI as the regional coordination mechanism for demonstration projects and product R&D in Africa. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/1.pdf**

African Network for Drugs and Diagnostics Innovation (ANDI). (n.d.b). Regional Network for Drugs and Diagnostics Innovation. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/documents/RegionalandnationalnetworksAfrican.pdf**

African Network for Drugs and Diagnostics Innovation (ANDI), China Tropical Diseases Drugs and Diagnostics Innovation Network (China NDI), et al. (2015). Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/demo_project_andi_ndi/en/**

African Network for Drugs and Diagnostics Innovation (ANDi), China Tropical Diseases Drugs and Diagnostics Innovation Network (China NDI), et al. (2014). Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/ANDI_ChinaNDI_documents.pdf?ua=1**

Anderson, G. F. (2009). Spurring New Research For Neglected Diseases. *Health Affairs*, 28(6), 1750-1759. doi: 10.1377/hlthaff.28.6.1750.

ANDi. (2014). ANDi Health Innovation for Development. *the African Network for Drugs and Diagnostics Innovation*. Retrieved from ANDi website: **http://www.andi-africa.org/**

Årdal, C., & Røttingen, J. A. (2012). Open Source Drug Discovery in Practice: A Case Study. *PLoS Neglected Tropical Diseases, 6*(9), e1827. doi:10.1371/journal.pntd.0001827

Asian Scientist Newsroom. (2015 June 15). Removing Early Barriers To Drugs For Neglected Diseases. *Asian Scientist*. Retrieved from website: **http://www.asianscientist.com/2015/06/pharma/removing-early-barriers-drugs-neglected-diseases/**

Balasubramaniam, T. (2014, December 22). EB136: WHO outlines contours of a Pooled Fund for Global Health Research and Development. Blog. *Knowledge Ecology International*. Retrieved from KEI website: **http://keionline.org/node/2157**

Balasubramaniam, T. (2008, June 27). WIPO patent committee embarks on positive agenda. Blog. *Knowledge Ecology International*. Retrieved from KEI website: **http://keionline.org/node/75**

Balesagaram, M. (2013, May 16). DNDi at ten: past success, future challenges. *Médecins Sans Frontières (MSF)*. Retrieved from MSF website: **http://www.msf.org/article/dndi-ten-past-success-future-challenges**

Bangladesh, Barbados, Bolivia and Suriname (BBBS). (2008). Proposal 4: Cancer Medicines and Vaccines in Developing Countries Prizes as a Reward Mechanism for New Cancer Treatments. Working Document. Retrieved from KEI website: **http://keionline.org/misc-docs/b_b_igwg/prop4_cancer_prizes.pdf**

BBBS. (2015, September 4). Proposal by Barbados, Bolivia, Suriname and Bangladesh: A Prize Fund to Support Innovation and Access for Donor Supported Markets. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_DonorPrize.pdf**

09

BIBLIOGRAPHY

Bartels, H.G., Beyer P., Kampf R., Krattiger, A, Mirza, Z., et al. (2013, February). INTELLECTUAL PROPERTY: WHO-WIPO-WTO BOOK. Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade. *World Trade Organization*. Retrieved from WTO website: **https://www.wto.org/english/tratop_e/trips_e/trilatweb_e/ack_trilat_web_13_e.htm**

BBBS. (2009, September). Submission by the Governments of Barbados, Bolivia and Suriname. *World Health Organization*. Retrieved from WHO website: **http://www.who.int/phi/public_hearings/second/contributions/BangladeshBarbadosSurinamandBolivia.pdf**

BiOS. (2015). Retrieved from the Biological Innovation for Open Society Initiative website: **http://www.bios.net/daisy/bios/bios.html**

BioWorld Insight. (2008, February 25). Neglected Disease Efforts Require Delicate Balance. *BioWorld*. Retrieved from website: **http://www.bioworld.com/content/neglected-disease-efforts-require-delicate-balance**

Botros, S., & Nwaka, S. (2009). Overview of the African Network for Drugs and Diagnostics Innovation (ANDI). *ANDi Health Innovation for Development*. Retrieved from the WIPO website: **http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_res_dev_ge_09/wipo_res_dev_ge_09_www_130163.pdf**

Botti, D. (2013, March). Binding Market and Mission: Pharmaceuticals for the World's Poor. *Solutions, 4*(1). Retrieved from website: **http://www.thesolutionsjournal.org/node/2241**

Bradley, P. D. J. (2007, November 13). Criticism of the X Prize Foundation. Blog. *Over the Counter Culture*. Retrieved from website: **http://www.overthecounterculture.com/2007/criticism-of-the-x-prize-foundation/**

BrIDGs. (2015, March 23). Bridging Interventional Development Gaps. National Center for Advancing Translational Sciences (NCATS). Retrieved from the NIH website: **http://www.ncats.nih.gov/bridgs**

Brogan, D. M., & Mossialos, E. (2013). Incentives for new antibiotics: the Options Market for Antibiotics (OMA) model. *Globalization and Health*, 9, 58, doi: 10.1186/1744-8603-9-58

BSR Healthcare Working Group. (2014). GHIT Fund (Global Health Innovative Technology Fund), Astellas Pharma Inc. *Guiding Principles on Access to Healthcare: A Project of the BSR Healthcare Working Group*. Retrieved from website: **http://gpah.bsr.org/en/case-studies/view/ghit-fund-global-health-innovative-technology-fund**

BSR Healthcare Working Group (BSR HWG). (n.d.) An Open Approach to Tackling Diseases of the Developing World, GlaxoSmithKline. *Guiding Principles on Access to Healthcare: A Project of the BSR Healthcare Working Group*. Retrieved from website: **http://gpah.bsr.org/en/case-studies/view/an-open-approach-to-tackling-diseases-of-the-developing-world**

Business Wire. (2015, June 23). Prize4Life, Sage Bionetworks and DREAM Launch an Open Science Challenge to Find Clues to Understanding Heterogeneity in Patients with Amyotrophic Lateral Sclerosis (ALS). Business Wire. Retrieved from website: **http://www.businesswire.com/news/home/20150623006278/en - .VZWiZ01Vikr**

09

BIBLIOGRAPHY

BVGH. (2015). Impacting global health through multi-stakeholder initiatives, high impact partnering, and alliance management. *BIO Ventures for Global Health*. Retrieved from BVGH website: **http://www.bvgh.org/**

BVGH. (2006, October). Tuberculosis Vaccines: The Case for Investment. Retrieved from the BVGH website: **http://www.bvgh.org/Portals/0/Reports/2006_10_tb_vaccines,_the_case_for_investment.pdf**

Carter, Z. (2012, May 25). Obama Administration Blocks Global Health Fund To Fight Disease In Developing Nations. *Huffington Post*. Retrieved from website: **http://www.huffingtonpost.com/2012/05/25/global-health-fund-obama-administration_n_1544399.html**

Castle-Clarke, S. (2014, March 25). A New Model for Open Innovation: The Structural Genomics Consortium. *EuroScientist*. Retrieved from website: **http://www.euroscientist.com/a-new-model-for-open-innovation-the-structural-genomics-consortium/**

Cecil, A. (2005). Institute for OneWorld Health Receives Grant To Lay Foundation for Next Steps in Control of Deadly Infectious Disease. *The Gates Foundation Press Room*. Retrieved from website:**http://www.gatesfoundation.org/Media-Center/Press-Releases/2005/04/Institute-for-OneWorld-Health-Receives-Grant**

CDD. (2015). The Drug Discovery informatics platform your Project Team will embrace. *Collaborative Drug Discovery, Inc*. Retrieved from CDD website: **https://www.collaborativedrug.com/pages/company**

CDD. (2013, March 12). Top 10 ways CDD has democratized informatics technologies for drug discovery researchers. *Collaborative Drug Discovery*. Retrieved from website: **https://www.collaborativedrug.com/buzz/2013/03/12/top-10-ways-cdd-has-democratized-informatics-technologies-for-drug-discovery-researchers/**

CDD. (2008, November 17). Collaborative Drug Discovery Receives Gates Foundation Grant to Support the Development of a Database to Accelerate Discovery of New Therapies Against Tuberculosis. *Collaborative Drug Discovery*. Retrieved from website: **https://www.collaborativedrug.com/buzz/2008/11/17/collaborative-drug-discovery-receives-gates-foundation-grant-to-support-the-development-of-a-database-to-accelerate-discovery-of-new-therapies-against-tuberculosis/**

CDIPD. (2015). The Center for Discovery and Innovation in Parasitic Diseases. Retrieved from CDIPD website: **http://www.cdipd.org/index.php/about-us**

CFFT. (2015). Cystic Fibrosis Foundation Therapeutics. Retrieved from CFF website: **https://www.cff.org/Our-Research/Cystic-Fibrosis-Foundation-Therapeutics/**

CGDEV AMC Working Group. (2005, April). Advance Market Commitment. CGDEV Global Health Policy Research Network AMC Working Group. Retrieved from CGDEV website: **http://www.cgdev.org/page/advance-market-commitment**

Cimoli, M., Dosi, G., Maskus, K. E., Okediji, R. L., & Reichman, J. H. (2014). *Intellectual Property Rights: Legal and Economic Challenges for Development* [Google Books Version]. OUP Oxford. Retrieved from **http://books.google.com/books**

09

BIBLIOGRAPHY

Clift, C. (2015, May 14). De-linkage: A Way Forward for Antimicrobial Drugs. *Chatham House*. Retrieved from **http://www.chathamhouse.org/expert/comment/17659**

Cohen, D., & Rafferty, J. (2014). Paying twice: questions over high cost of cystic fibrosis drug developed with charitable funding. Biomedical Journal of Medicine, 348:g1445. Retrieved from the BMG website: **http://www.bmj.com/content/348/bmj.g1445**

Coloma, J., & Harris, E. (2009). From Construction Workers to Architects: Developing Scientific Research Capacity in Low-Income Countries. *PLoS Biol, 7*(7), e1000156. doi: 10.1371/journal.pbio.1000156

CPTR. (2015a). CPTR Progress. *Critical Path Institute*. Retrieved from C-Path website: **http://c-path.org/programs/cptr/ - section-6001**

CPTR. (2015b). Critical Path to TB Drug Regimens. Retrieved from CPTR website: **http://www.cptrinitiative.org/**

Crager, S. E., Guillen, E., & Price, M. (2009). University Contributions to the HPV Vaccine and Implications for Access to Vaccines in Developing Countries: Addressing Materials and Know-How in University Technology Transfer Policy. *American Journal of Law & Medicine*, 35(2), 253-279. Retrieved from website: **http://www.med4all.org/fileadmin/med/pdf/2_Crager_Formatted_June3_HPV-Impfung.pdf**

Creative Commons. (2011, March 2). Creative Commons and Open Access. Retrieved from webiste: **https://wiki.creativecommons.org/wiki/Creative_Commons_and_Open_Access**

crowdsourcing. (n.d.). *Merriam-Webster Online*. In Merriam-Webster. Retrieved from website: **http://www.merriam-webster.com/dictionary/crowdsourcing**

Dengue Vaccine Initiative (DVI). (2015). Retrieved from **http://www.denguevaccines.org/**

DeRoeck, D., Bawazir, S. A., Carrasco, P., Kaddar, M., Brooks A., & Fitzsimmons, J. (2005). Regional group purchasing of vaccines: Review of the Pan American Health Organization EPI revolving fund and the Gulf Cooperation Council group purchasing program. *International Journal of Health Planning & Management, 21*(1), 23-43. doi: 10.1002/hpm.822

DNDi. (2015a, August). CpG-D35. Drugs for Neglected Diseases initiative. Retrieved from website: **http://www.dndi.org/diseases-projects/portfolio/cpg-d35.html**

DNDi (2015b, May) MSF and DNDi Join Call for a Biomedical Research and Development Fund and Mechanism to Meet Pressing Global Health Needs. Press Release. Retrieved from website: **http://www.dndi.org/media-centre/press-releases/2136-pr-msf-dndi-randd-fund.html**

DNDi. (2015c). Drugs for Neglected Diseases Initiative. Retrieved from DNDi website: **http://www.dndi.org/**

DNDi. (2014a). Chagas R&D Accelerator Initiative: a coordination mechanism for accelerating the development of new health tools for Chagas disease. Drugs for Neglected Diseases initiative Proposal. Retrieved from WHO website: **http://www.who.int/phi/implementation/chagas_R_D_accelerator_initiative.pdf**

DNDi. (2014b). The Visceral Leishmaniasis (VI) Global R&D & Access Initiative. Drugs for Neglected Diseases initiative proposal addendum. *World Health Organization*. Retrieved from WHO website: **http://www.who.int/phi/implementation/demo_project_dnd_i/en/**

09

BIBLIOGRAPHY

DSW. (n.d.). Product Development Partnerships (PDPs). *Deutsche Stiftung Weltbevoelkerung*. Retrieved from DSW website: **http://www.dsw.org/uploads/tx_aedswpublication/1408_PDP_UK_A4_web.pdf**

Drugs for Neglected Diseases initiative (DNDi). (n.d.a). Chagas R&D Accelerator Initiative: a coordination mechanism for accelerating the development of new health tools for Chagas disease. *World Health Organization*. Retrieved from WHO website: **http://www.who.int/phi/implementation/4.pdf**

DNDi. (n.d.b). The Visceral Leishmaniasis (VI) Global R&D & Access Initiative. Drugs for Neglected Diseases initiative proposal. *World Health Organization*. Retrieved from WHO website: **http://www.who.int/phi/implementation/5.pdf**

EDCTP. (2015). European & Developing Countries Clinical Trials Partnership. Retrieved from EDCTP website: **http://www.edctp.org/**

EDCTP. (2013, October 18). STRATEGIC BUSINESS PLAN for the second phase of the European & Developing Countries Clinical Trials Partnership programme (EDCTP2, 2014-2023) undertaken by several Member States under Article 185 of the Treaty on the Functioning of the European Union (EU). Version 22.1. European & Developing Countries Clinical Trials Partnership. Retrieved from website: **http://www.edctp.org/web/app/uploads/2015/03/EDCTP_Strategic_Business_Plan_EDCTP2.pdf**

EFPIA. (2013, July 10). IMI2 Launch to Further Innovative Medicines Initiative Success: Right Prevention and Treatment at the Right Time. European Federation of Pharmaceutical Industries and Associations. Retrieved from EFPIA website: **http://www.efpia.eu/mediaroom/112/43/IMI2-Launch-to-Further-Innovative-Medicines-Initiative-Success-Right-Prevention-and-Treatment-at-the-Right-Time**

Ekins, S., & Bunin, B. A. (2013). The Collaborative Drug Discovery (CDD) database. *Methods Mol Bio, 993*, 139-54. doi: 10.1007/978-1-62703-342-8_10

Elmer, C., Grossenbacher, T., Gruhnwald, S., & Schäfer, M. (2015, April 1). The People Pay, Corporations Cash In: Problems Plague EU Medical Research Initiative. *Spiegel Online International*. Retrieved from website: **http://www.spiegel.de/international/europe/imi-in-eu-project-citizens-count-corporations-cash-in-a-1025550.html**

European Commission. (2015a, May 5). A big booster for vaccine development. European Commission: Horizon 2020. Retrieved from website: **http://ec.europa.eu/programmes/horizon2020/en/news/big-booster-vaccine-development**

European Commission. (2015b, March 6). EU inducement prize reaps rewards for European vaccine development SME. European Commission: Research & Innovation News Alerts. Received from website: **http://ec.europa.eu/research/index.cfm?pg=newsalert&year=2015&na=na-060315**

European Commission. (2014). German company has won the EU's € 2 million vaccine prize. Retrieved from EC website: **http://ec.europa.eu/research/health/vaccine-prize_en.html**

European Commission. (2003, April 22). United Kingdom Vaccines Research Relief: Introduction of a new scheme and modification of State aid. *Center for Global Health R&D Policy Assessment*. Retrieved from wesbite: **http://healthresearchpolicy.org/sites/healthresearchpolicy.org/files/EU Commission-Vaccine research relief.pdf**

09

BIBLIOGRAPHY

European Vaccine Initiative (2015). EVI. *Universitäts Klinikum Heidelberg*. Retrieved from website: **http://www.euvaccine.eu/**

EVI. (2015). European Vaccine Initiative. *TRANSVAC*. Retrieved from website: **http://www.transvac.org/partners/evi**

Fauber, J. (2013, May 19). Cystic Fibrosis: Charity and Industry Partner for Profit. *Sentinel/MedPage Today*. Retrieved from website: **http://www.medpagetoday.com/Pulmonology/CysticFibrosis/39217**

FDA. (2015). For Industry: Developing Products for Rare Diseases & Conditions. U.S. Department of Health & Human Services. Retrieved from FDA website: **http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm2005525.htm**

FIND. (2015). Foundation for Innovative New Diagnostics. Retrieved from FIND website: **http://www.finddiagnostics.org/**

FSG. (2015). Medicines for Malaria Venture Charts a Path toward Malaria Eradication. Retrieved from FSG website: **http://www.fsg.org/projects/medicines-malaria-venture-charts-path-toward-malaria-eradication**

Gaffney, A., & Mezher, M. (2015, August 20). Regulatory Explainer: Everything You Need to Know About FDA's Priority Review Vouchers. *Regulatory Affairs Professionals Society*. Retrieved from website: **http://www.raps.org/Regulatory-Focus/News/2015/05/28/21722/Regulatory-Explainer-Everything-You-Need-to-Know-About-FDA%E2%80%99s-Priority-Review-Vouchers/**

Gardiner, E., & Trinity Partners, LLC. (2015, April). TB Strategic Expansion Assessment [Report]. Retrieved from MPP website: **http://www.medicinespatentpool.org/wp-content/uploads/MPP-Intervention-in-TB-Trinity-Partners-.pdf**

GAVI The Vaccine Alliance (2015). How the pneumococcal AMC works. *GAVI The Vaccine Alliance*. Retrieved from website: **http://www.gavi.org/funding/pneumococcal-amc/how-the-pneumococcal-amc-works/**

Geels, M. J., Imoukhuede, E. B., Imbault, N., van Schooten, H., McWade, T., et al. (2011). European Vaccine Initiative: lessons from developing malaria vaccines. *Expert Rev. Vaccines, 10*(12), 1697-1708. doi: 10.1586/erv.11.158

Genzyme Corp. (2006). Genzyme Launches Initiative to Assist the Development of Treatments for Neglected Diseases: Partners with Leading Institutions on First Two Projects. *PR Newswire*. Retrieved from website: **http://www.prnewswire.com/news-releases/genzyme-launches-initiative-to-assist-the-development-of-treatments-for-neglected-diseases-56183387.html**

Gerhardsen, T. I. S. (2006, May). Meeting the need for treatment: the initiatives. Bulletin of the World Health Organization, 8(5), 337-424. Retrieved from WHO website: **http://www.who.int/bulletin/volumes/84/5/news30506/en/**

GHIF. (2015). Global Health Investment Fund. Retrieved from GHIF website: **http://www.ghif.com/**

Ginsberg, A. (2011). The TB Alliance: overcoming challenges to chart the future course of TB drug development. *Future Med. Chem., 3*(10), 1247–1252. Retrieved from website: **http://50.56.29.53/newscenter/research_papers/(2011) FMC - Overcoming challenges to chart the future course of TB drug development.11.pdf**

GlaxoSmithKline. (2015). Open Innovation. Retrieved from GSK website: **http://uk.gsk.com/en-gb/research/sharing-our-research/open-innovation/**

09

BIBLIOGRAPHY

Global Health Innovative Technology Fund (GHIT). (n.d.). In Wikipedia. Retrieved from website: **https://en.wikipedia.org/wiki/Global_Health_Innovative_Technology_Fund_(GHIT)**

Global Health Progress. (2012) Infectious Disease Research Institute (IDRI). Retrieved from GHP website: **http://www.globalhealthprogress.org/programs/infectious-disease-research-institute-idri**

Global Health Policy Research Network. (2005). Advance Market Commitment. *Center for Global Development*. Retrieved from website: **http://www.cgdev.org/page/advance-market-commitment**

Global Health Technologies Coalition (GHT). (n.d.a). Assistance for Neglected Diseases: A Time for Partnership [Report]. Retrieved from GHT Coalition website: **http://www.ghtcoalition.org/files/Assistance_for_ND_Summary.pdf**

Global Health Technologies Coalition (GHT). (n.d.b). Neglected Diseases Tax Credit. Fact Sheet. Retrieved from GHT Coalition website: **http://www.ghtcoalition.org/files/Neglected_Disease_Tax_Credit_One_Pager.pdf**

Godony, K. (2015, January 26). Transforming Healthcare Technology in Africa: 50 Health Experts Gather in Addis Ababa to Prioritize Mechanisms That Will Enable Sustained Health Innovation in Africa. *UNICEF*. Retrieved from website: **http://www.unicefstories.org/2015/01/26/transforming-healthcare-technology-in-africa/**

Goetz, T. (2013, April 12). How Kaggle is Changing How We Work. *The Atlantic*. Retrieved from **http://www.theatlantic.com/technology/archive/2013/04/how-kaggle-is-changing-how-we-work/274908/**

Goldman, M. (2012). The Innovative Medicines Initiative: A European Response to the Innovation Challenge. *Clinical Pharmacology & Therapeutics, 91*(3), 418–425. doi: 10.1038/clpt.2011.32

Gothefors, L., Troye-Blomberg, M., & Persson, L. (2009). The Relevance and Future Role of the International Vaccine Institute (IVI) 2000–2006. SIDA Evaluation. Department for Research Cooperation. Retrieved from website: **http://www.sida.se/contentassets/9173f760cbb14b80b515606abbeb4e32/0709-the-relevance-and-future-role-of-the-international-vaccine-institute-ivi_2000.pdf**

Grabowski, H. (2003). Increasing R&D Incentives for Neglected Diseases-The Lessons Learned from the Orphan Drug Act. *Duke Economics Working Paper*. Retrieved from website: **http://public.econ.duke.edu/Papers//Other/Grabowski/Orphan_Drug.pdf**

Grace, C., Pearson, M., & Lazdins J. (2011). Pooled Funds: Assessing New Models for Financing Global Health R&D. Technical Background Paper. *Results for Development Institute*. Retrieved from website: **http://healthresearchpolicy.org/sites/healthresearchpolicy.org/files/assessments/files/Pooled Funding Technical Background Paper.pdf**

Grepstad, M., Moon, S., & Røttingen, J. (2014, September 5). Who Should Contribute to Funding of Global Health R&D and How Much? *PLoS Community Blog*. Retrieved from website:**http://blogs.plos.org/speakingofmedicine/2014/09/05/contribute-funding-global-health-rd-much/**

Hale, V. (2005, January 10). Oxymoron no more: nonprofits can deliver medicines for the poor of the world [Presentation]. *Institute for OneWorld Health*. Retrieved from website: **http://www.grady.uga.edu/knighthealth/voices/2006.hale/2006.Hale.ppt.pdf**

Hayden, E. C. (2014, January 7). Projects set to tackle neglected diseases: But they do little to alter the process of drug development. *Nature*, 505, 142. doi: 10.1038/505142a

09

BIBLIOGRAPHY

Health Impact Fund (HIF). (n.d.). In Wikipedia. Retrieved from website: **https://en.wikipedia.org/wiki/Health_Impact_Fund**

Health Policy Division EWG (2009, December). Comparative Review of Innovative Financing Proposals for R&D. *George Institute for International Health: Health Policy Division Expert Working Group*. Retrieved from WHO website: **http://www.who.int/phi/CompreviewEWGDec09.doc**

Herman, L. (2008, June 30). International Partnership for Microbicides Evaluation Report. The Evaluation Management Group of the IPM Donors. Retrieved from IPM website: **http://www.ipmglobal.org/sites/default/files/IPM-Evaluation-Report.pdf**

Herrling, P. L. (2010, August 5). Funding neglected disease R&D: The next hurdle. Corporate Citizenship at Novartis. *Knowledge Ecology International*. Retrieved from website: **http://keionline.org/sites/default/files/2010-08-05_Herrling.pdf**

HIF. (2015). Health Impact Fund. *Incentives for Global Health*. Retrieved from HIF website: **http://healthimpactfund.org/**

HM Revenue & Customs. (2008, August 1). Changes to the Research & Development (R&D) and Vaccine Research Relief (VRR) tax relief rules. *The National Archives*. Retrieved from **http://webarchive.nationalarchives.gov.uk/+/http://www.hmrc.gov.uk/research/vrr-tax-relief-rules.htm**

Hollis, A., & Pogge, T. (2008). *The Health Impact Fund, Making New Medicines Accessible for All, A Report of Incentives for Global Health*. Book Excerpt, 105-106. Retrieved from website: **http://keionline.org/blogs/2008/11/18/hif-on-sanders-prize-fund**

Hollis, A. (2013, February 27). Antibiotic Health Impact Fund [Presentation]. University of Calgary & Incentives for Global Health. Retrieved from website: **http://www.brookings.edu/~/media/events/2013/2/27-bcadd-meeting/presentation.pdf**

Hotz, R. L. (2009, May 8). The Science Prize: Innovation or Stealth Advertising? *The Wall Street Journal: Science Journal*. Retrieved from website: **http://www.wsj.com/articles/SB124173078482897809**

Hu, R. (2011, April 6). Recommendations to the UNITAID Patent Pool Initiative: A "Square" Model. *University of Michigan*. Retrieved from website: **https://ctools.umich.edu/access/content/user/huran/Public Portfolio Files/Recommendations to the UNITAID Patent Pool Initiative.pdf**

Huber, B. R. (2015, August 3). Global Vaccine-Development Fund Could Save Thousands of Lives, Billions of Dollars. *Woodrow Wilson School*. Retrieved from website: **http://wws.princeton.edu/globalvaccinedevelopmentfund**

Hunter, J. (2011). Challenges for pharmaceutical industry: new partnerships for sustainable human health. *Phil. Trans. R. Soc.*, 369, 1817-1825. doi: 10.1098/rsta.2010.0377

Hunter, J. (2010). Is open innovation the way forward for big pharma? *Nature Reviews Drug Discovery* 9, 87-88. doi: 10.1038/nrd3099

Ioset, J., & Chang, S. (2011). Drugs for Neglected Diseases initiative model of drug development for neglected diseases: current status and future challenges. Special Report. *Drugs for Neglected Diseases Initiative*. Retrieved from DNDi website: **http://www.dndi.org/images/stories/pdf_scientific_pub/2011/Chang%2CIoset_FutureScience.pdf**

09

BIBLIOGRAPHY

IAVI. (2015). International AIDS Vaccine Initiative. Retrieved from IAVI website: **http://www.iavi.org/**

IAVI. (n.d.). IAVI's Innovation Fund To Bring Novel Early-Stage Technologies to AIDS Vaccine Research. International AIDS Vaccine Initiative: Info Sheet. Retrieved from website: **http://healthresearchpolicy.org/sites/healthresearchpolicy.org/files/IAVI_Innovation_Fund.pdf**

IAVI Report. (2015). The Publication on AIDS Vaccine Research. *International AIDS Vaccine Initiative*. Retrieved from website: **http://www.iavireport.org/Pages/default.aspx**

IDRI. (2015). Infectious Disease Research Institute. Retrieved from IDRI website: **http://www.idri.org/**

IFPMA & Novartis (n.d.). Fund for Research and Development of Neglected Diseases. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/news/phi_20_cewg_frind_en.pdf**

IMI. (2010). Innovative Medicines Initiative. Retrieved from IMI website: **http://www.imi.europa.eu/**

Initiative for Open Innovation (IOI). (2015). *Cambia*. Retrieved from website: **http://www.bios.net/daisy/ioi/about.html**

InnoCentive. (2009). The Rockefeller Foundation and InnoCentive Renew Partnership Linking Non-Profit Organizations to World-Class Scientific Thinkers. *InnoCentive Press Release*. Retrieved from website: **http://www.innocentive.com/rockefeller-foundation-and-innocentive-renew-partnership-linking-non-profit-organizations-world-clas**

Innovative Medicines Initiative (IMI). (n.d.). In Wikipedia. Retrieved from website:**https://en.wikipedia.org/wiki/Innovative_Medicines_Initiative**

Institute for OneWorld Health. (n.d.). In Wikipedia. Retrieved from website: **https://en.wikipedia.org/wiki/Institute_for_OneWorld_Health**

Institute of Medicine (IOM) Forum on Drug Discovery, Development, and Translation (2011). *Breakthrough Business Models: Drug Development for Rare and Neglected Diseases and Individualized Therapies: Workshop Summary*. 3, The Food and Drug Administration's Orphan Drug Programs. Book Excerpt. Washington (DC): National Academies Press (US). Current Model for Financing Drug Development: From Concept Through Approval. Retrieved from website: **http://www.ncbi.nlm.nih.gov**

A prize purpose. (2014, June 16). Editorial. *Nature Reviews Microbiology*, 12, 457. doi: 10.1038/nrmicro3306

Institute of Medicine (IOM) Committee on Accelerating Rare Diseases Research and Orphan Product Development. (2010). Field M. J., Boat T. F., editors. *Rare Diseases and Orphan Products: Accelerating Research and Development*. 5, Development of New Therapeutic Drugs and Biologics for Rare Diseases. Book Excerpt. Washington (DC): National Academies Press (US); 2010. 4, Discovery Research for Rare Diseases and Orphan Product Development. Retrieved from website: **http://www.ncbi.nlm.nih.gov/books/NBK56191/?report=reader**

International AIDS Vaccine Initiative (IAVI). (n.d.). In Wikipedia. Retrieved from website: **https://en.wikipedia.org/wiki/International_AIDS_Vaccine_Initiative**

IPM. (2011). International Partnership For Microbicides. Retrieved from IPM website: **http://www.ipmglobal.org/**

IVI. (2012). International Vaccines Institute. Retrieved from IVI website: **http://www.ivi.int/web/www/01_02_01**

09

BIBLIOGRAPHY

Jahn, A. (2014). The Report of the Consultative Expert Working Group on Research and Development (CEWG): Financing and Coordination. South Centre/ UNDP Workshop, 31 March – 2 April, Geneva. Retrieved from website: **http://www.southcentre.int/wp-content/uploads/2014/03/Ev_140331_A-Jahn-CEWG-Report.pdf**

Jakobsen P. H., Wang M.-W., & Nwaka, S. (2011). Innovative Partnerships for Drug Discovery against Neglected Diseases. PLoS Neglected Tropical Diseases, 5(9), e1221. doi:10.1371/journal.pntd.0001221

Jarvis, L. (2010, May 6). Open Innovation: A Panacea for Neglected Diseases? Chemical & Engineering News: Archived Blogs. Retrieved from website: **http://cenblog.org/the-haystack/2010/05/open-innovation-a-panacea-for-neglected-diseases/**

Jones, M. M., Castle-Clarke, S., Brooker, D., Nason, E., Huzair, F., & Chataway, J. (2014). The Structural Genomics Consortium A knowledge platform for drug discovery [Report]. RAND Europe with the Institute on Governance. Retrieved from website: **http://www.rand.org/content/dam/rand/pubs/research_reports/RR500/RR512/RAND_RR512.pdf**

Kaggle. (2015). Kaggle: The Home of Data Science. Retrieved from website: **https://www.kaggle.com/**

Kaiser, J. (2013, August 26). XPrize Pulls Plug on $10 Million Genomics Competition. American Association for the Advancement of Science. *Science Insider*. Retrieved from website: **http://news.sciencemag.org/biology/2013/08/xprize-pulls-plug-10-million-genomics-competition**

Karst, K. R. (2015, February 15). The 2014 Numbers Are In: FDA's Orphan Drug Program Shatters Records. FDA: Law Blog. Retrieved from website: **http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2015/02/the-2014-numbers-are-in-fdas-orphan-drug-program-shatters-records.html**

Katz, R. (2008, March 20). Reminder: Piramal Prize – $25k for Healthcare Innovations. *Next Billion*. Retrieved from website: **http://nextbillion.net/blogpost.aspx?blogid=981**

Kellen, M. J. (2014, February 18). DREAM Challenges Advancing our understanding of human disease through data-centric competitions. [Presentation]. Sage Bionetworks. Retrieved from website: **https://catalyst.uw.edu/workspace/file/download/8395822c61e4c99a79add189b14c3300a80ea87532f14e646b357504a9b018b7**

Kemppainen-Bertram, K. (2013, September 23). Can a new Global Health Investment Fund save more lives? Blog. ONE. Retrieved from website: **http://www.one.org/us/2013/09/23/can-a-new-global-health-investment-fund-save-more-lives/**

Kepler, T.B., Marti-Renom, M. A., Maurer, S. M., Rai, A. K., Taylor, G., & Todd, M. H. (2006). Open Source Research — the Power of Us. Aust. J. Chem. 59(5), 291. Retrieved from website: **http://www.publish.csiro.au/view/journals/dsp_journal_fulltext.cfm?nid=51&f=CH06095**

Kesselheim, A. (2008). Drug Development for Neglected Diseases — The Trouble with FDA Review Vouchers. New England Journal of Medicine, 359, 1981-1983. doi: 10.1056/NEJMp0806684

King, T. (2014, June 19). Can open science help patients and save pharma? Retrieved from Opensource.com website: **http://opensource.com/health/14/6/can-open-science-help-patients-and-save-pharma**

09

BIBLIOGRAPHY

Knowledge Ecology International (KEI). (2013). Antibiotics Innovation Funding Mechanism (AIFM). *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/7.pdf**

Knowledge Ecology International (KEI). (2011a, June 22). Knowledge Ecology International submission to the World Health Organization Consultative Expert Working Group on R&D Financing: Innovation Inducement Prizes. Retrieved from website: **http://www.who.int/phi/news/phi_2_kei_prizes_cewg_22june2011_en.pdf**

Knowledge Ecology International (KEI). (2011b). The Health Impact Fund Proposal. Knowledge Ecology International. Retrieved from KEI website: **http://keionline.org/hif**

Knowledge Ecology International (KEI). (2007, June 1). The Essentials Medical Inventions Licensing Agency Working Plan. Knowledge Ecology International. Retrieved from KEI website: **http://www.keionline.org/misc-docs/emila.pdf**.

Kotz, J. (2007). Sustainable Sciences Institute. *Nature Chemical Biology*, 3, 751. doi: 10.1038/nchembio.2007.500

Laneur. (2015). WHO takes up the baton on dementia. Editorial. *The Lancet Neurology*, 14(5), 455. doi: http://dx.doi.org/10.1016/S1474-4422(15)00022-8

Leahy, P., & Grassley, C. (2015, May 20). Leahy & Grassley Introduce Bipartisan Legislation To Encourage The Humanitarian Work Of American Innovators. Press Release. U.S. Senator Patrick Leahy of Vermont. Retrieved from website: **http://www.leahy.senate.gov/press/leahy-and-grassley-introduce-bipartisan-legislation_to-encourage-the-humanitarian-work-of-american-innovators**

Lehrer, J. (2008, February 20). InnoCentive. *Scienceblogs*. Retrieved from website: **http://scienceblogs.com/cortex/2008/02/20/innocentive/**

Light, D. W. (2009, March). Advanced Market Commitments Current Realities and Alternate Approaches. Paper Series. *Health Action International (HAI) Europe & Medico International*. Retrieved from website: **http://www.haiweb.org/31032009/27%20Mar%202009%20AMC%20Current%20Realities%20&%20Alternate%20Approaches%20FINAL.pdf**

Love, J. P. (2014, September 19). Alternatives to the Patent System that are used to Support R&D Efforts, Including both Push and Pull Mechanisms, with a Special Focus on Innovation-Inducement Prizes and Open Source Development Models. *Knowledge Ecology International & WIPO*. Retrieved from KEI website: **http://keionline.org/sites/default/files/wipo_cdip_14_inf_12_alternatives_to_patents.pdf**

Love, J. (2013, October 23). PAHO recommends 4-7 R&D projects for consideration in December WHO meeting. Blog. *Knowledge Ecology International*. Retrieved from KEI website: **http://keionline.org/node/1819**

Love, J. (2011, May 27). Senator Sanders introduces two medical innovation prize bills in U.S. Senate to de-link R&D costs from drug prices. Blog. *Knowledge Ecology International*. Retrieved from KEI website: **http://keionline.org/node/1147**

Love, J. (2010a, May 17). PDP+ presented at WHA to skeptical audience. *Knowledge Ecology International*. Retrieved from KEI website: **http://keionline.org/node/843**

Love, J. (2010b, May 23). Why is there resistance to prize funds? Blog. *Knowledge Ecology International*. Retrieved from KEI website: **http://keionline.org/node/848**

09

BIBLIOGRAPHY

Love, J. (2009, June 23). Designing Prizes [Presentation]. Meeting of the Columbia University Initiative for Policy Dialogue; Task Force on Intellectual Property and Development. The University of Manchester & Brooks World Poverty Institute. *Knowledge Ecology International*. Retrieved from KEI website: **http://policydialogue.org/files/events/Love_Designing_Prizes.pdf**

Love, J. & Hubbard, T. (2009). Prizes for Innovation of New Medicines and Vaccines. *Annals of Health Law, 18*(2), 155-186. Retrieved from website: **http://lawecommons.luc.edu/cgi/viewcontent.cgi?article=1111&context=annals**

Magariños, M. P., Carmona, S. J., Crowther, G. J., Ralph, S. A., Roos, D. S., Shanmugam, D., et al (2012). TDR Targets: a chemogenomics resource for neglected diseases. *Nucleic Acids Research, 40*(Database issue), D1118–D1127. doi:10.1093/nar/gkr1053

Marine, M. W. (2014, April 30). Celebrating 20 years of public health advancements: Sabin Vaccine Institute's Scientific Symposium. *Global Health Technologies Coalition Blog*. Retrieved from Sabin website: **http://www.sabin.org/updates/blog/celebrating-20-years-public-health-advancements-sabin-vaccine-institute%E2%80%99s-scientific**

Masum, H., Schroeder, K., Khan, M., & Daar, A. (2011). Open Source Biotechnology Platforms for Global Health and Development: Two Case Studies [Research Report]. Annenberg School for Communication & Journalism. *Information Technologies & International Development, 7*(1), 61-69. Retrieved from website: **http://itidjournal.org/itid/article/viewFile/697/295**

Matee, M. I., Manyando, C., Ndumbe, P. M., Corrah, T., & Jaoko, W. G. (2009). European and Developing Countries Clinical Trials Partnership (EDCTP): the path towards a true partnership. *BMC Public Health*, 9,249. doi: 10.1186/1471-2458-9-249

McCarthy, N. (2014, January 14). Exploiting the Pathogen Box: an international open source collaboration to accelerate drug development in addressing diseases of poverty. WHO Proposal. Retrieved from WHO website: **http://www.who.int/phi/implementation/MMV_documents.pdf**

McConaghle, A. (2015, March 17). Big pharma signs up to $100m Dementia Discovery Fund. *Pharmaphorum*. Retrieved from website: **http://www.pharmaphorum.com/news/big-pharma-signs-up-to-100m-dementia-discovery-fund**

McKerrow, J. (2015). Meeting the Challenge of Developing Drugs for Ebola and Other Neglected Tropical Diseases [Presentation]. *Center for Discovery and Innovation in Parasitic Diseases, UCSF*. Retrieved from website: **http://pharmacy.ucsd.edu/faculty/media/McKerrow_Ebola_Presentation.pdf**

McMillan, R. (2015, February 9). Data-science Darling Kaggle Cuts a Third of Its Staff. *Wired*. Retrieved from website: **http://www.wired.com/2015/02/data-science-darling-kaggle-cuts-one-third-staff/**

MDGH. (2015). Medicines Development for Global Health. *Medicines Development Limited*. Retrieved from MDGH website:**http://www.medicinesdevelopment.com/**

Medicines for Malaria Venture (MMV). (2015). Exploiting the Pathogen Box: An International Open Source Collaboration to Accelerate Drug Development in Addressing Diseases of Poverty. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/demo_project_mmw/en/**

09

BIBLIOGRAPHY

Medicines for Malaria Venture (MMV). (2013, July 7). Exploiting the Pathogen Box: an International Open Source Collaboration to Accelerate Drug Development in Addressing Diseases of Poverty. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/11.pdf**

Medicines Patent Pool (MPP). (2015). MPP. *UNITAID*. Retrieved from website: **http://www.medicinespatentpool.org/?lang=es**

Medicines Patent Pool (MPP). (2011). The Medicines Patent Pool [Factsheet]. Retrieved from WIPO website: **http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_gc_lic_ge_12/wipo_gc_lic_ge_12_ref_factsheet.pdf**

Médecins Sans Frontières (MSF). (n.d.). Ecosystem for financing development of an open source multiplex point of care (POC) diagnostic device for the differential diagnosis of fever or sepsis. Henceforwards, this will be referred to as the Open Source Fever Diagnostic Project. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/9.pdf**

Mehta, P., Earl, C. D., Taylor, W., Bock, K., & Nilekani, P. (2009). Global Health Innovators: A Collection of Case Studies. *BIO Ventures for Global Health*. Retrieved from BVGH website: **http://www.bvgh.org/LinkClick.aspx?fileticket=867bPGw-kYo%3D&tabid=79**

Ministry of Health of Costa Rica. (n.d.). Development of innovative sources of financing for health research and technical development in Costa Rica. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/CostaRica_En.pdf**

MMV. (2015). Medicines for Malaria Venture. Retrieved from MMV website: **http://www.mmv.org/**

Moon, S. (2014, July). Demonstrating Financing: Considerations for The New International Fund for R&D. Discussion Paper. *Drugs for Neglected Diseases Initiative*. Retrieved from DNDi website: **http://www.dndi.org/images/stories/advocacy/pilot-pooled-international-fund_web.pdf**

Moran, M. (2006, March). Funding neglected disease drug R&D: The Industry R&D Facilitation Fund (IRFF). [Presentation]. *The George Institute for International Health*. Retrieved from website: **http://slidegur.com/doc/3449506/draw-down-fund--the-concept**

Mostert, B. (2015), March 31). Evaluation of the European & Developing Countries Clinical Trials Partnership. *Technopolis Group*. Retrieved from website: **http://www.technopolis-group.com/evaluation-of-the-european-developing-countries-clinical-trials-partnership/**

Mostert, B, de Jongh, T., Nooijen, A., & Ploeg, M. (2014, November 18). Review of the Product Development Partnerships Fund 2011-2014: Final report to the Dutch Ministry of Foreign Affairs. *Technopolis Group*. Retrieved from website: **http://www.rijksoverheid.nl/bestanden/documenten-en-publicaties/rapporten/2014/11/18/review-of-the-product-development-partnerships-fund-2011-2014/review-of-the-product-development-partnerships-fund-2011-2014.pdf**

MSF Access. (2015). PUSH, PULL, POOL: Accelerating Innovation and Access to Medicines for Tuberculosis. *MSF Access Campaign*. Retrieved from website: **http://www.msfaccess.org/3Ps-project**

09

BIBLIOGRAPHY

MSF Access. (2014, February). The '3P Project': An overview of the 3P proposal to accelerate innovation and access for new treatment regimens for TB. *Médecins Sans Frontières (MSF)*. Retrieved from MSF Access website: **http://www.msfaccess.org/sites/default/files/TB demo project extended version For Web_12032014.pdf**

MSF Access. (2013, November 25). Proposal for a CEWG Demonstration Project by Médecins Sans Frontières (MSF) – November 2013: The Open Source Fever Diagnostic Project. *World Health Organization*. Retrieved from MSF Access website: **http://www.msfaccess.org/content/proposal-cewg-demonstration-project-m%C3%A9decins-sans-fronti%C3%A8res-msf-november-2013**

MSF Access. (n.d.). What is a Patent Pool and why do we need one? MSF Access Campaign. Retrieved from MSF Access website: **http://www.msfaccess.org/spotlight-on/patent-pool**

Mueller-Langer, F. (2013). Neglected infectious diseases: Are push and pull incentive mechanisms suitable for promoting drug development research? *Health Economics, Policy, and Law, 8*(2), 185–208. doi: 10.1017/S1744133112000321

Multinational Monitor (2009). Eyes on the Prize: Incentivizing Drug Innovation without Monopolies. Interview with Jamie Love. *MM, 30*(3). Retrieved from website: **http://www.multinationalmonitor.org/mm2009/052009/interview-love.html**

Nagarajan, R. (2014, April 1). Funds dry up for drug discovery project. The Times of India. Retrieved from website: **http://timesofindia.indiatimes.com/india/Funds-dry-up-for-drug-discovery-project/articleshow/33048063.cms**

Nakatani, K. (2014, September 30). Towards implementation of the WHA Strategic Workplan: Financing and Coordination of Health R&D. Ambassadors' meeting [Presentation]. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/Presentation_ADGs_Kieny_Nakatani_30Sep2014_AmbassadorsMeeting.pdf**

Neglected Tropical Diseases (NTDs). (2015). *World Health Organization*. Retrieved from website: **http://www.who.int/neglected_diseases/diseases/en/**

Neill, U. S. (2007). The Gotham Prize: a beacon for cancer researchers. *Journal of Clinical Investigation, 117*(8), 2016. doi: 10.1172/JCI33097

Nesta (2014, July). Longitude Prize 2014. Paper for Open Review. Retrieved from website: **https://www.nesta.org.uk/sites/default/files/longitude-paper-antibiotics-open-review.pdf**

New, W. (2015, May 25). WHA 68: Experts discuss delinking drug R&D costs from pricing to make them affordable. European AIDS Treatment Group (EATG). Retrieved from website: **http://www.eatg.org/news/172323/WHA_68%3A_Experts_discuss_delinking_drug_R%26D_costs_from_pricing_to_make_them_affordable**

New, W., & Suarez, C. (2015, February 20). WIPO Re:Search Celebrates 3 Years, Looks To The Future. Intellectual Property Watch. Retrieved from website: **http://www.ip-watch.org/2015/01/20/wipo-research-programme-celebrates-3-years-and-looks-to-the-future/**

News Medical. (2015, May 22). GHIT Fund expands investments in leishmaniasis, diagnostic tests. *AZO Network*. Retrieved from website: **http://www.news-medical.net/news/20150522/GHIT-Fund-expands-investments-in-leishmaniasis-diagnostic-tests.aspx**

09

BIBLIOGRAPHY

Nicol, D, & Nielsen, J. (2010). Ed. By Pogge, T., Rimmer, M., & Rubenstein, K. *Incentives for Global Public Health: Patent Law ad Access to Essential Medicines*. Opening the dam: patent pools, innovation and access to essential medicines. Book Excerpt, 235-252. Cambridge University Press, NY. Retrieved from website: **http://s1.downloadmienphi.net/file/downloadfile4/206/1390316.pdf**

Nwaka (2014, May 10). Stakeholders Meeting on ANDI Demonstration Project: Development of Easy to Use & Affordable Diagnostics for Types II & III Diseases [Presentation]. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/demo_project_technical_overview_innovative_aspects_implementation_next_steps.pdf?ua=1**

O'Neill, J. (2015, May). Securing New Drugs for Future Generations: The Pipeline of Antibiotics. The Review on Antimicrobial Resistance. Retrieved from website: **http://amr-review.org/sites/default/files/SECURING NEW DRUGS FOR FUTURE GENERATIONS FINAL WEB_0.pdf**

Open Source Drug Discovery (OSDD). (n.d.). An Open Collaborative Drug Discovery Model for Tuberculosis. Proposal Submitted before WHO Expert Working Group on R&D Financing. *World Health Organization*. Retrieved from website: **http://healthresearchpolicy.org/sites/healthresearchpolicy.org/files/Open source drug discovery-TB.pdf**

Orphanet. (2012, October 25). About Rare Diseases. Retrieved from website: **http://www.orpha.net/consor/cgi-bin/Education_AboutRareDiseases.php?lng=EN**

OSDD. (n.d.). Open Source Drug Discovery. *CSIR India*. Retrieved from OSDD website: **http://www.osdd.net/about-us/What-is-OSDD**

Outterson, K. (2014). New Business Models for Sustainable Antibiotics. Working Group on Antimicrobial Resistance: Paper 1. Retrieved from website: **http://petrieflom.law.harvard.edu/assets/publications/Outterson_Health_Law_Workshop_paper.pdf**

Outterson, K., Pogge, T., & Hollis, A. (2011). Combating Antibiotic Resistance Through the Health Impact Fund. Boston Univ. School of Law, Law and Economics Research Paper No. 11-30. Retrieved from website: **http://ssrn.com/abstract=1866768**

Pagliusi, S., Jain, R., Suri, R. J., & the DCVMN Executive Committee Group. (2015). Vaccines, our shared responsibility. *Vaccines, 33*(19), 2197–2202. doi: 10.1016/j.vaccine.2015.02.065 **http://dx.doi.org/10.1016/j.vaccine.2015.02.065**

PAHO. (2014, October 14). About PAHO Revolving Fund. Pan American Health Organization. Retrieved from website: **http://www.paho.org/hq/index.php?option=com_content&view=article&id=9562:about-paho-revolving-fund&Itemid=40717&lang=en**

PATH. (2015). Driving Transformative Innovations to Save Lives. Retrieved from website: **http://www.path.org/**

PATH. (2011, December 16). OneWorld Health to become an affiliate of PATH. Press Release. Retrieved from website: **http://www.path.org/news/press-room/203/**

PATH (global health organization). (n.d.). In Wikipedia. Retrieved from website: **https://en.wikipedia.org/wiki/PATH_(global_health_organization)**

09

BIBLIOGRAPHY

Pearson, M., Clarke, J., Ward, L., Grace, C., Harris, D., & Cooper, M. (2011, June) Evaluation of the International Finance Facility for Immunisation (IFFIm). *HLSP*. Retrieved from website: **http://www.iffim.org/library/documents/evaluations/**

Pecoul, B. (2014, March 31). Opportunities & Challenges in the Landscape of R&D for NTDs [Presentation]. Drugs for Neglected Diseases initiative. *South Centre*. Retrieved from website: **http://www.southcentre.int/wp-content/uploads/2014/03/Ev_140331_Bernard-Pecoul.pdf**

Philippidis, A. (2011, October 10). Big Pharma's Open Innovation Initiatives Zoom In on Discovery. *Genetic Engineering & Biotechnology News*. Retrieved from website: **http://www.genengnews.com/insight-and-intelligenceand153/big-pharma-s-open-innovation-initiatives-zoom-in-on-discovery/77899468/**

Plotkin, S. A., Mahmoud, A. F., & Farrar, J. (2015). N Engl J Med, 373, 297-300. doi: 10.1056/NEJMp1506820

Porcher, D., & Kerouedan, D. (2011). Health Financing: Evolving Context, Evolving Methods. A Review on Innovative Financing for Health [Draft Report]. French Ministry of Foreign and European Affairs. Retrieved from website: **http://www.leadinggroup.org/IMG/pdf/4-_engReview_on_innovative_financing_for_health_final.pdf**

Portilla, L. M. (2012, October 9). Catalyzing Innovation: NIH National Center for Advancing Translational Sciences [Presentation]. *National Center for Advancing Translational Sciences. GUIRR Meeting*. Retrieved from website: **http://sites.nationalacademies.org/cs/groups/pgasite/documents/webpage/pga_072891.pdf**

Pringle, E. (2015). Pharmaceutical R&D tax incentives. *Ernst & Young Global Limited*. Retrieved from website: **http://www.ey.com/GL/en/Industries/Life-Sciences/EY-pharmaceutical-r-d-tax-incentives**

Prize4Life. (2014). About Prize4Life (P4L). Retrieved from P4L website: **http://www.prize4life.org/page/about**

Ramamoorthi, R., Graef, K. M., & Dent, J. (2014). WIPO Re:Search: Accelerating anthelmintic development through cross-sector partnerships. Invited Review. *International Journal for Parasitology: Drugs and Drug Resistance*. 4(3), 220-225. doi:10.1016/j.ijpddr.2014.09.002

Rao. (2011). R&D Tax Credits A Tool to Advance Global Health Technologies? Research for Development Institute: *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/sites/healthresearchpolicy.org/files/assessments/files/R4D%20-%20RD%20Tax%20Credits%20-%20A%20Tool%20to%20Advance%20Global%20Health%20Technologies.pdf**

Reddy, D. (2015). Introduction from MMV [Presentation]. *Medicines for Malaria Venture*. Retrieved from WHO website: **http://www.who.int/phi/implementation/introduction_mmv_opensource_davidreddy_.pdf?ua=1**

Renwich, M., Brogan, D., & Mossialos E. (2014). A Critical Assessment of Incentive Strategies for Development of Novel Antibiotics [Report]. *LSE Health, London School of Economics and Political Science*. Retrieved from website: **http://www.esrc.ac.uk/files/news-events-and-publications/news/2015/a-critical-assessment-of-incentive-strategies-for-development-of-novel-antibiotics/**

09

BIBLIOGRAPHY

Research For Development (R4D). (2014a). Foundation for Innovative New Diagnostics (FIND) 2009-2014. *Department for International Development*. UKAID. Retrieved from website: **http://r4d.dfid.gov.uk/Project/60703/**

Research For Development (R4D). (2014b). Institute for OneWorld Health (iOWH). *Department for International Development*. UKAID. Retrieved from website: **http://r4d.dfid.gov.uk/Project/60704/**

Results for Development Institute (RDI). (2015a). Bio Ventures for Global Health (BVGH) Business Cases. *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/bio-ventures-global-health-bvgh-business-cases**

Results for Development Institute (RDI). (2015b). Chagas Disease Prize Fund for the Development of New Treatments, Diagnostics and Vaccines. *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/chagas-disease-prize-fund-development-new-treatments-diagnostics-and-vaccines**

Results for Development Institute (RDI). (2015c). Discovery or Milestone Prizes. *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/discovery-or-milestone-prizes**

Results for Development Institute (RDI). (2015d). Fund for R&D in Neglected Diseases (FRIND). *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/fund-rd-neglected-diseases-frind**

Results for Development Institute (RDI). (2015e). Health Impact Fund (HIF). *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/health-impact-fund-hif**

Results for Development Institute (RDI). (2015f). Industry R&D Facilitation Fund (IRFF). *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/industry-rd-facilitation-fund-irff**

Results for Development Institute (RDI). (2015g). Open Source Dividend for Prizes. *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/open-source-dividend-prizes**

Results for Development Institute (RDI). (2015h). Product-Specific Final Product Prizes. *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/product-specific-final-product-prizes**

Results for Development Institute (RDI). (2015i). Revolving Fund to Finance R&D for Neglected Tropical Diseases. *Center for Global Health R&D Policy Assessment*. Retrieved from **http://healthresearchpolicy.org/node/124**

Results for Development Institute (RDI). (2015k). The Synaptic Leap (TSL). *Center for Global Health R&D Policy Assessment*. Retrieved from website: **http://healthresearchpolicy.org/content/synaptic-leap-tsl**

Ridley, R.G., & Gutteridge, W.E. (1999). Medicines for Malaria Venture (MMV). *World Health Organization*. Retrieved from website: **http://www.who.int/phi/documents/medicines_for_malaria_venture.pdf**

Rimmer, M. (2012). Patents for Humanity. *The World Intellectual Property Organization WIPO Journal, 3*(2), 196-221. Retrieved from website: **http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2173096**

09

BIBLIOGRAPHY

Romero, K. (2014, September 5). Critical Path to TB Drug Regimens [Presentation]. 7th International Workshop on Clinical Pharmacology of Tuberculosis Drugs. Retrieved from website: http://regist2.virology-education.com/2014/7th_TB_PK/5_Romero.pdf

Rosenberg, Z. (2008, August 4). What The Future Holds For Next Generation Microbicides What The Future Holds For Next Generation Microbicides And Partnerships With Industry [Presentation]. Industry Liaison Forum Industry Liaison Forum, Mexico City. Retrieved from website: http://www.iasociety.org/Web/WebContent/File/MOSAT2702.pdf

RossMartin. (2015, August 18). Research & Development Relief. Ross Martin Tax Consultancy. Retrieved from website: http://www.rossmartin.co.uk/companies/running-the-business/394-research-a-development-relief

SABIN Vaccine Institute. (2015). SABIN. Retrieved from website: http://www.sabin.org/

Sae-Lim, C. (2010). Pharmaceutical Patent Pools: A Solution to Innovation and Consumers' Access? [Report]. Retrieved from website: http://www.law.kyushu-u.ac.jp/programsinenglish/conference2010/draft11.pdf

Saez, C., & New, W. (2015, May 24). WHO Advances R&D Financing Effort; Global R&D Observatory To Launch In January. *Intellectual Property Watch*. Retrieved from website: http://www.ip-watch.org/2015/05/24/who-advances-r-global-rd-observatory-to-launch-in-january/

Saieed, A. [n.d.]. Open Source Space Exploration. [Presentation]. *UNISEC*. Retrieved from http://www.unisec-global.org/pdf/1/Group5_Open-Source Space Exploration.pdf

Sasinowski, F., Panico, E. B., & Valentine, J. E. (2015). Quantum of Effectiveness Evidence in FDA's Approval of Orphan Drugs: Update, July 2010 to June 2014. Therapeutic Innovation & Regulatory Science 1-18. doi: 10.1177/2168479015580383

SGC. (2015). Structural Genomics Consortium (SGC). Retrieved from website: http://www.thesgc.org/

Shesgreen, D. (2010). The PDP+ Fund: Accelerating R&D in New Products for Diseases of Poverty. Center for Global Health Policy. Science Speaks: HIV and TB News. Retrieved from website: http://sciencespeaksblog.org/2010/05/17/the-pdp-fund-accelerating-rd-in-new-products-for-diseases-of-poverty/

Shetty, P. (2011, February 16). Biomed Analysis: Public–private health R&D can't stall. *SciDevNet*. Retrieved from website: http://www.scidev.net/global/health/analysis-blog/biomed-analysis-public-private-health-r-d-can-t-stall.html

Silverman, E. (2015, July 28). We Need a Vaccine Development Fund for 'Death Valley:' Mahmoud Explains. *The Wall Street Journal Pharmalot Blog*. Retrieved from WSJ website: http://blogs.wsj.com/pharmalot/2015/07/28/we-need-a-vaccine-development-fund-for-death-valley-mahmoud-explains/

Silverman, E. (2014, December 3). Congress Should fix the Priority Review Voucher Program: MSF's Rius Explains. *The Wall Street Journal Pharmalot Blog*. Retrieved from WSJ website: http://blogs.wsj.com/pharmalot/2014/12/03/congress-should-fix-the-priority-review-voucher-program-msfs-ruis-explains/

09

BIBLIOGRAPHY

Silverman, R., Fan, V., & Glassman, A. (2013, April). Background paper prepared for the Working Group on Value for Money: An Agenda for Global Health Funding Agencies. *Center for Global Development* [Report]. Retrieved from CGDEV website: **http://www.cgdev.org/doc/Silverman_UNITAID_Background.pdf**

Singh, S. (2008). India Takes an Open Source Approach to Drug Discovery. *Cell, 133*(2), 201-203. doi: 10.1016/j.cell.2008.04.003

Skingle, M. (2010, May 28). Open Innovation in the Pharmaceutical Industry. [Presentation]. ASTP 10th Anniversary, Paris. *GlaxoSmithKline*. Retrieved from website: **http://www.kmtp.lt/uploads/Renginiai/ASTP%20konferencija/Malcolm%20Skingle.pdf**

Skoll Foundation. (2015). Institute for OneWorld Health (iOWH). Retrieved from website: **http://www.skollfoundation.org/entrepreneur/victoria-hale/**

Slingsby, B. T., & Kurokawa, K. (2013). The Global Health Innovative Technology (GHIT) Fund: financing medical innovations for neglected populations. *The Lancet Global Health Blog*, 1(4), e184–e185. doi: **http://dx.doi.org/10.1016/S2214-109X(13)70055-X**

Smith, L., Reilly, K. M. A., & Benkler, Y. (2014). Open Development: Networked Innovations in International Development. MIT Press. [Google Books Version]. Retrieved from website: **http://books.google.com/books**

So, A. D. (2009). Between pull and pools, where's the "push" for global health R&D? Innovating for the Health of All. *Council on Health Research for Development*, Geneva, Switzerland. Global Forum Update on Research for Health, 6, 119-122. Retrieved from website: **http://www.isn.ethz.ch/Digital-Library/Publications/Detail/?lang=en&id=112343**

So, A. D., & Shah, T. A. (2014). New business models for antibiotic innovation. *Upsala Journal of Medical Sciences*, 119, 176–180. doi: 10.3109/03009734.2014.898717

So, A. D., & Ruiz-Esparza, Q. (2012). Technology innovation for infectious diseases in the developing world. *Infectious Diseases of Poverty, 1*(2), Retrieved from website: **http://www.biomedcentral.com/content/pdf/2049-9957-1-2.pdf**

Sornarajah, S. (2015, May 28). Data Science and Kaggle. Blog. *Sornars*. Retrieved from website: **http://www.sornars.com/data-science-and-kaggle.html**

Spulber, D. F. (2014). Prices versus Prizes: Patents, Public Policy, and the Market for Inventions. *Northwestern Law & Econ Research Paper No. 14-15*. Retrieved from website: **http://www.law.northwestern.edu/research-faculty/searlecenter/innovationeconomics/documents/Spulber_Prices_versus_Prizes.pdf**

SSI. (2015). Sustainable Sciences Institute. Retrieved from website: **http://sustainablesciences.org/**

Sullivan, M. (2014). Drug developers with moxi. *Medicines Development for Global Health*. Retrieved from website: **http://www.internationalinnovation.com/build/wp-content/uploads/2014/12/Mark_Sullivan_Intl_Innovation_165_Research_Media.pdf**

TACD. (2011, June). Resolution on Innovation and Access to Medical Technologies. *Trans Atlantic Consumer Dialogue (TACD)*. DOC No. IP 14-11. Retrieved from website: **http://test.tacd.org/wp-content/uploads/2013/09/TACD-IP-14-11-Innovation-and-Access-to-Medical-Technologies.pdf**

09 BIBLIOGRAPHY

Taylor, N. P. (2015, February 5). U.K. panel calls for innovation fund to break antibiotic discovery dam. *EuroBiotech Report*. Retrieved from website: **http://www.fiercebiotech.com/story/uk-panel-calls-innovation-fund-break-antibiotic-discovery-dam/2015-02-05**

TB Alliance. (2015). Putting science to work for a faster TB cure. Retrieved from TBA website: **http://www.tballiance.org/**

TBVI. (2015). Tuberculosis Vaccine Initiative (TBVI). Retrieved from website: **http://www.tbvi.eu/**

TDR Targets. (2015). The TDR Drug Targets Network. Retrieved from website: **http://tdrtargets.org/**

TDR Targets. (2008, June 23). The TDR Targets Database: An Introduction [Presentation]. Retrieved from website: **http://www.slideshare.net/tdrtargets/introduction-to-tdr-targets**

Terry, R. (2015, 15 May). Proposed pooled R&D fund under discussion at World Health Assembly. TDR News Item. Retrieved from WHO website: **http://www.who.int/tdr/news/2015/pooled_r-d_fund_wha/en/**

The Global Health Network. (2014). GHTC Webinar: Pooled Funding Mechanisms for Global Health R&D Summary Document. *Global Health Trials*. Retrieved from TGHN website:**https://globalhealthtrials.tghn.org/site_media/media/articles/PooledFundingWebinarSummaryReportUpdated_20150114.pdf**

The George Institute for International Health. (2006, April). Memorandum submitted by The George Institute for International Health, London Unit. Retrieved from website: **http://www.publications.parliament.uk/pa/cm200506/cmselect/cmintdev/921/921m49.htm**

The Independent Evaluation Group (IEG). (2007). The Medicines for Malaria Venture. *The World Bank: Global Program Review, 1*(2). Retrieved from website: **http://ieg.worldbank.org/Data/reports/gpr_mmv.pdf**

The Seattle Foundation. (n.d.). Infectious Disease Research Institute (IDRI). Retrieved from website: **http://www.seattlefoundation.org/npos/Pages/InfectiousDiseaseResearchInstitute.aspx**

The World Bank. (2014). Public-Private Partnerships Reference Guide: Version 2.0. International Bank for Reconstruction and Development. Retrieved from website: **http://www.scribd.com/doc/236899332/PPP-Reference-Guide**

Towse, A., Keuffel, E., Kettler, H. E., & Ridley, D. B. (2011, May 21). Drugs and Vaccines for Developing Countries. Occasional Paper 11/04. Office of Health Economics. *The Oxford Handbook of the Economics of the Biopharmaceutical Industry*, 302. Retrieved from website: **https://faculty.fuqua.duke.edu/~dbr1/research/developing-Oxford.pdf**

Translational Health Science and Technology Institute (THSTI). (2013). Multiplexed Point-of-Care test for acute febrile illness (mPOCT) proposal. *World Health Organization*. Retrieved from WHO website: **http://www.who.int/phi/implementation/19_summary_EN.pdf**

Translation Health Science and Technology Institute (THSTI). (n.d.). Multiplexed Point-of-Care test for acute febrile illness (mPOCT). *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/19.pdf**

TRANSVAC. (2015). European Network of Vaccine Research and Development. Retrieved from website: **http://www.transvac.org/roadmap**

09

BIBLIOGRAPHY

UAEM. (2015, January 17). Document on De-linkage. Universities Allied for Essential Medicines. Unpublished Research.

United States Patent and Trademark Office (USPTO). (2015, July 1). Patents for Humanity Program Info. Office of Policy and International Affairs. Retrieved from website: **http://www.uspto.gov/patent/initiatives/patents-humanity/patents-humanity-program-info**

Uniting to Combat Neglected Tropical Diseases (UCNTD). (2015). *GlaxoSmithKline*. Retrieved from website: **http://unitingtocombatntds.org/endorsement/glaxosmithkline**

Villa, S., Compagni, A., & Reich, M. R. (2009). Orphan drug legislation: lessons for neglected tropical diseases. *The International journal of health planning and management, 24*(1), 27-42. doi: 10.1002/hpm.930

Velzen, W., Kamal, R., Meda, N., Nippert, I., Piot, P., & Sauer, F. (2009, December 14). Independent External Evaluation Report of the European and Developing Countries, Clinical Trials Partnership (EDCTP programme) [Report]. Retrieved from website: **http://cordis.europa.eu/fp7/art185/docs/20100419-review-report-2-by-w-van-velzen-as-sent-to-ep-council.pdf**

Vertex Pharmaceuticals (2015, February 13). Annual Report. 10-K. Retrieved from website: **http://investors.vrtx.com/secfiling.cfm?filingID=875320-15-12&CIK=875320**

Verthelyi, D. (2014). Development of Class D Cpg Odn (D35) as an Adjunct to Chemotherapy for Cutaneous Leishmaniasis and Post Kala-Azar Dermal Leishmaniasis (Pkdl). *U.S. Food and Drug Administration*. Retrieved from WHO website: **http://www.who.int/phi/implementation/USFDA_Osaka_documents.pdf?ua=1**

Walsh, F. (2015, May 14). Call for $2bn global antibiotic research fun. *BBC News*. Retrieved from website: **http://www.bbc.com/news/health-32701896**

Wei, M. (2007). Should prizes replace patents? A critique of the Medical Innovation Prize Act of 2005 [Working Paper]. *Boston University Journal of Science & Technology Law*. Retrieved from **https://www.bu.edu/law/central/jd/organizations/journals/scitech/volume131/documents/Wei_WEB.pdf**

WHO CEWG. (2015). CEWG Demonstration Projects: Background and Process [Timeline]. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/cewg_background_process/en/**

Williams, H. (2012). Innovation Inducement Prizes: Connecting Research to Policy. *Journal of Policy Analysis and Management, 00*(0), 1-25. doi: 10.1002/pam.21638

Wilson, P. (2010, April). Giving developing countries the best shot: An overview of vaccine access and R&D [Report]. *MSF Access*. Retrieved from MSF website: **http://www.msf.org.uk/sites/uk/files/Vaccine_Report_201005111518.pdf**

WIPO. (2015). World Intellectual Property Organization. Retrieved from WIPO website: **http://www.wipo.int/research/en/**

WIPO. (2014, March). Patent Pools and Antitrust – A Comparative Analysis. *World Intellectual Property Organization*. Retrieved from WIPO website: **http://www.wipo.int/export/sites/www/ip-competition/en/studies/patent_pools_report.pdf**

09

BIBLIOGRAPHY

Wizemann, T., Robinson S., & Giffin, R. (2008). Breakthrough Business Models: Drug Development for Rare and Neglected Diseases and Individualized Therapies: Workshop Summary. National Academy of Sciences. *National Academies Press*. Retrieved from website: **http://www.nap.edu/openbook.php?record_id=12219&page=2**

Woo, K. (n.d.) Partnering for Global Health [Presentation]. *Institute for OneWorld Health (iOWH)*. Retrieved from website: **http://www.bvgh.org/LinkClick**.

Woods, D. (2009, September 29). The Myth of Crowdsourcing. Forbes. Retrieved from website: **http://www.forbes.com/2009/09/28/crowdsourcing-enterprise-innovation-technology-cio-network-jargonspy.html**

World Health Organization (WHO). (2015). Selected Health R&D Demonstration Projects: Indicators for Measuring Success. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/DemoProjects_Indicators_to_Measure_Success_analysis_secretariatMarch2015.pdf?ua=1**

World Health Organization (WHO). (2011, July 12). Medicines Patent Pool Signs Licence Agreement with Gilead to Increase Access to HIV/AIDS Medicines. *UNITAID*. Retrieved from website: **http://www.unitaid.eu/en/resources/news/348-medicines-patent-pool-signs-licence-agreement-with-gilead-to-increase-access-to-hivaids-medicines**

World Health Organization (WHO). (2006, July 19). Advanced Market Commitments for vaccines. Retrieved from WHO website: **http://www.who.int/immunization/newsroom/amcs/en/**

World Technology Network. (2005). Institute for OneWorld Health. Retrieved from The World Technology Network website: **http://www.wtn.net/2004/bio196.html**

XPrize. (2015). XPrize is an innovation engine. Retrieved from website: **http://www.xprize.org**

Ylä-Jääski, J. (2015, March 16). Nomination period for the 2016 Millennium Technology Prize begins. Aalto University. Retrieved from website: **http://www.aalto.fi/en/current/news/2015-03-16-005/**

Zakaib, G. (2015, March 20). *Alzforum*. Retrieved from website: **http://www.alzforum.org/news/community-news/100-million-dementia-discovery-fund-stimulate-drug-research**

Zenois, S., Denend, L., & McCutcheon, S. (2012). IDRI: Neglected Disease R&D with a Nonprofit Model [Academic Case Study]. *Stanford Graduate School of Business Center for Social Innovation*. Retrieved from website: **http://csi.gsb.stanford.edu/idri-neglected-disease-rd-nonprofit-model**

Zorzet, A., & So, A.D. (n.d.b). Establishing a Drug Discovery Platform for Sourcing Novel Classes of Antibiotics as Public Goods. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/16.pdf**

Zorzet, A., & So, A. D. (n.d.a) Building a Diagnostic Innovation Platform to Address Antibiotic Resistance. *World Health Organization*. Retrieved from website: **http://www.who.int/phi/implementation/15.PDF**

10

APPENDIX 1

List of internally shared documents that were reviewed and either written by or discussed among UAEM members and allies.

UAEM *Publications and Works in Progress*

- Intellectual Property & Cultural Rights
- Alternative R&D Mechanisms
- Alternative R&D Models Bibliography
- Delinkage

Documents found via the Knowledge Ecology International *(KEI) Website*

- Prizes to Stimulate Innovation
- Annotated Bibliography of Articles and Books on Innovation Prizes
- Prizes for Innovation of New Medicines and Vaccines
- Selected Innovation Prizes and Reward Programs
- The role of prizes in stimulating R&D: Comment to WHO IGWG
- Collective Management of IPR & Patent Pools
- Survey of Patent Pools Demonstrates Variety of Purposes and Management Structures
- WHO Expert Working Group on R&D Financing (EWG)

Documents found via the Doctors Without Borders *(MSF) and* MSF Access *Websites*

- Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases
- Medical Innovation for Neglected Patients
- Medical Innovation: The Issues
- Putting Patients' Needs First: New Directions in Medical Innovation
- Financing Medical Innovation Through Alternative Mechanisms: How to boost R&D for a low-cost, point-of-care rapid diagnostic test and better drugs for tuberculosis
- Giving developing countries the best shot: An overview of vaccine access and R&D
- Addressing the Crisis in Research and Development for Neglected Diseases

Documents from WIPO & WHO CEWG & TDR

- Promoting Access to Medical Technologies and Innovation Intersections between public health, intellectual property and trade
- Alternatives to the Patent System that are Used to Support R&D Efforts, Including Both Push and Pull Mechanisms, With a Special Focus on Innovation-Inducement Prizes and Open Source Development Models
- Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination
- Follow-up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination
- Selected Demonstration Projects: Examination of Innovative Aspects – Original Results

Additional Publications and Websites Shared by UAEM Members

- Two Ideas To Increase Innovation And Reduce Pharmaceutical Costs and Prices
- Alternative Incentive Models Delinking R&D Costs from Pharmaceutical Product Price
- Medicine for Tomorrow: Some Alternative Proposals to Promote Socially Beneficial Research and Development in Pharmaceuticals
- New Approaches to Rewarding Pharmaceutical Innovation
- Innovative Financing for Global Health R&D
- PIJIP List of Alternative Models of Financing Medical Innovation
- Global Health Technologies Coalition Resources
- Articles on Innovative Financing Mechanisms
- Prizes for Global Health Technologies
- Open Source for Neglected Diseases Magic Bullet or Mirage?
- Innovative Financing Mechanisms for Global Health: Overview and Considerations for U.S. Government Participation

10

APPENDIX 1

- Time for the EU to lead on innovation: EU policy opportunities in biomedical innovation and the promotion of public knowledge goods
- The Structural Genomics Consortium: A knowledge platform for drug discovery
- New Business Models for Sustainable Antibiotics
- A Global Biomedical R&D Fun and Mechanism for Innovations of Public Health Importance
- 3Rs for innovating novel antibiotics: sharing resources, risks, and rewards