CENTER FOR GLOBAL HEALTH R&D POLICY ASSESSMENT

Pooled Funds to Fight Neglected Diseases

Assessing New Models to Finance Global Health R&D

Executive Summary and Main Findings

RESULTS FOR DEVELOPMENT INSTITUTE

The Results for Development Institute (R4D) is a nonprofit organization dedicated to accelerating social and economic progress in low and middle income countries. We provide policy analysis, critical information, decision-making tools, and policy advice to governments, civil society organizations, and international funders in order to stimulate positive change. With expertise in many areas—including specialties in economics and finance, health policy, education, and governance—R4D works with leaders, globally and at the country level, to design and test solutions to some of the world's biggest development challenges.

R4D's **Center for Global Health R&D Policy Assessment** provides objective and rigorous assessments of new ideas to advance research and development for global health. Launched in late 2009 with support from the Bill & Melinda Gates Foundation, the Center evaluates proposed policy innovations aimed at accelerating R&D for global health technologies including drugs, vaccines, and diagnostics. The Center convenes funders, policy makers, product developers, and advocacy organizations to discuss its findings and stimulate action. For more information, visit **www.healthresearchpolicy.org**.

This document comprises an executive summary and main findings from the Center's technical background report "Pooled Funds: Assessing New Models for Financing Global Health R&D" by Cheri Grace, Mark Pearson, and Janis Lazdins. To read the report, please visit www.healthresearchpolicy.org.

Results for Development Institute
1875 Connecticut Avenue, Suite 1210, Washington, DC 20009

For additional information, please contact policyassessment@resultsfordevelopment.org.

TABLE OF CONTENTS

Acknowledgments

The Center for Global Health R&D Policy Assessment would like to thank the stakeholders who agreed to be interviewed for this report. In order to maintain confidentiality, in “Institutions Interviewed” we have listed the institutions but not the individual names of those interviewed.

We are grateful to the members of the Expert Group for their valuable guidance and feedback throughout the assessment process: Adrian Towse, Ok Pannenborg, Rachel Nugent, Saul Walker, and Richard Skolnik.

The Center also wishes to thank the proponents of the three pooled funding proposals for their openness in sharing information and for reviewing the early findings and the consultation draft of the report.

Finally, the Center acknowledges the following individuals for their feedback on the consultation draft: Jonas Ahlén, Kevin Callahan, Wouter Deedler, Chris Dippel, Marja Esveld, Heather Ignatius, Nancy Katz, Rachel Lenington, Josh Michaud, Zafar Mirza, Carol Nacy, Leonor Pacheco, Anne-Marie Sevcsik, Peter Small, Wendy Taylor, and Regine Webster.

Introduction

There is growing interest in innovative tools and policies to accelerate the development of drugs, vaccines, and diagnostics for neglected diseases, including the list of World Health Organization (WHO) tropical diseases and other major infectious diseases, like HIV/AIDS, tuberculosis (TB), and malaria. Product development partnerships (PDPs), nonprofit research institutes, and private sector groups are working individually and in collaborations to conduct research and development (R&D) on these new global health technologies. However, some argue that their efforts are disjointed and that funding flows inefficiently to individual research projects, resulting in inadequate resources, funding volatility, and poor resource allocation. In response, several mechanisms for pooling funds for neglected-disease R&D have been proposed to address what proponents see as the key problems in the current system.

Three pooled funding proposals in particular have attracted considerable notice: the Product Development Partnership-Financing Facility (PDP-FF) put forward by the International AIDS Vaccine Initiative (IAVI), the Industry R&D Facilitation Fund (IRFF) originally proposed by the George Institute, and the Fund for Research in Neglected Diseases (FRIND) advanced by Novartis.

This paper assesses whether these three proposed mechanisms would help to accelerate R&D for neglected diseases, focusing on how the proposals are likely to perform against two central criteria: their ability to *raise additional money* for neglected-disease R&D and their capacity to *make the allocation of those funds more efficient*.

Proposals to Pool R&D Funding for Global Health

What IRFF, FRIND, and PDP-FF share in common is that they would draw on contributions from multiple public sector and private funders to establish an R&D fund. This pool of money would then be distributed across a range of R&D projects at different stages of the product development continuum.

All three proposals would require some sort of governance structure—a board or committee—to deliberate on and approve resource allocation decisions.

A more detailed description of the proposals is provided in the box below and in the second part of this paper.

While they have common features, there are important differences across PDP-FF, IRFF, and FRIND:

- ***How funds would be raised***—In the IRFF and FRIND, governments, foundations, and private funders would contribute grants to the common pool. With PDP-FF, government funders would offer guarantees that would allow a third party—possibly the World Bank or a regional development bank—the authority to issue bonds in capital markets. PDP-FF would repay bondholders through revenues generated from royalties from the sale of vaccines, drugs, and diagnostics in developed country markets and "premiums" paid by the same or other donors on future product sales in low-income settings.
- ***How money would be allocated to R&D projects***—In the IRFF, participating PDPs would be reimbursed for a fixed percentage of their expenditures incurred in collaboration with industry partners, based on agreed-upon milestones. With the PDP-FF, specific PDPs would receive predetermined shares of the pool, which they could

Figure 1: Proposal Overview

PDP-FF. The rationale for the PDP-FF is to draw on the future value of PDP products for funding today. The PDP-FF would provide stable funding to PDPs through a bond-financed pooled fund with designated shares allocated to PDPs. This guaranteed funding would allow PDPs to focus their energies on long-term product development. Once products are developed, PDP-FF would draw on two sources of revenue to repay bondholders: royalties on sales in developed countries and premiums on sales in developing countries. For donors who choose to support the mechanism by committing to pay premiums, and thereby increase the return on product sales to the fund, PDP-FF would offer the advantage of requiring payment only for success. PDP-FF would require a small staff and a board to approve bond issuances and assignment of proceeds to the product development organizations, but administrative costs would be low because most portfolio management activities would be carried out by the individual PDPs.

IRFF. The IRFF would provide predictable medium-term funding for participating PDPs so that they could operate confidently and flexibly, reducing the amount of time they would have to spend on fundraising. PDPs would be partially reimbursed for R&D expenditures that are aligned with approved business plans. In the original proposal, only expenditures for industry partnerships would qualify, but the proponents have discussed revising this provision. Donors would thus invest in a portfolio of PDPs and would not have to carry out due diligence on individual R&D organizations.

FRIND. FRIND would apply to neglected-disease research the portfolio management techniques used by private pharmaceutical firms. FRIND proposes that available funding be pooled and then allocated by a board that represents developing countries, major funders, and other international health stakeholders. As a project meets milestone targets, additional payments would be released from the fund. PDPs, university-based research institutes, and biopharma companies could submit proposals to FRIND. Participating organizations would agree to donate the intellectual property (IP) for successful products to the fund's license pool, although the proponents are reconsidering the IP requirements for the fund.

draw down over a period of many years, thus giving the PDPs a stable and predictable source of funds. In the FRIND, PDPs and private drug (and possibly vaccine) developers would compete for the available pooled funds, with a "portfolio management committee" composed of independent experts making allocation decisions for specific projects on a performance/milestone basis.

- ***Eligibility for the Fund***—PDP-FF and IRFF would extend funding only to PDPs (although IRFF would reimburse spending through partnerships with industry); FRIND, on the other hand, would be open to all product developers, including industry. IRFF and PDP-FF both aim to fund a diverse portfolio of projects ranging from early- to late-stage development. PDP-FF might have a bias in favor of products with more lucrative markets and larger revenue streams in order to improve the chances for bond repayment. The scope of FRIND has yet to be finalized, but recent discussions suggest two potential approaches. In the first, FRIND would cover a wide range of early- and late-stage products, requiring several billions of dollars to achieve critical mass and operate effectively. In the second model, FRIND would focus on late-stage clinical trials. This would increase the cost per project (since efficacy trials are inherently expensive), but lower the overall financial requirement for the fund to several hundred million dollars while improving the chances of success.

Assessment Methodology and Approach

This report assesses the potential of the three pooled funding proposals against dimensions of the two main criteria described above—new resource generation and more efficient resource allocation. The generic expected "causal pathway" hypothesized for each pooled funding proposal to achieve health gains for the poor is shown in Figure 2. The key questions we posed for each proposal are as follows:

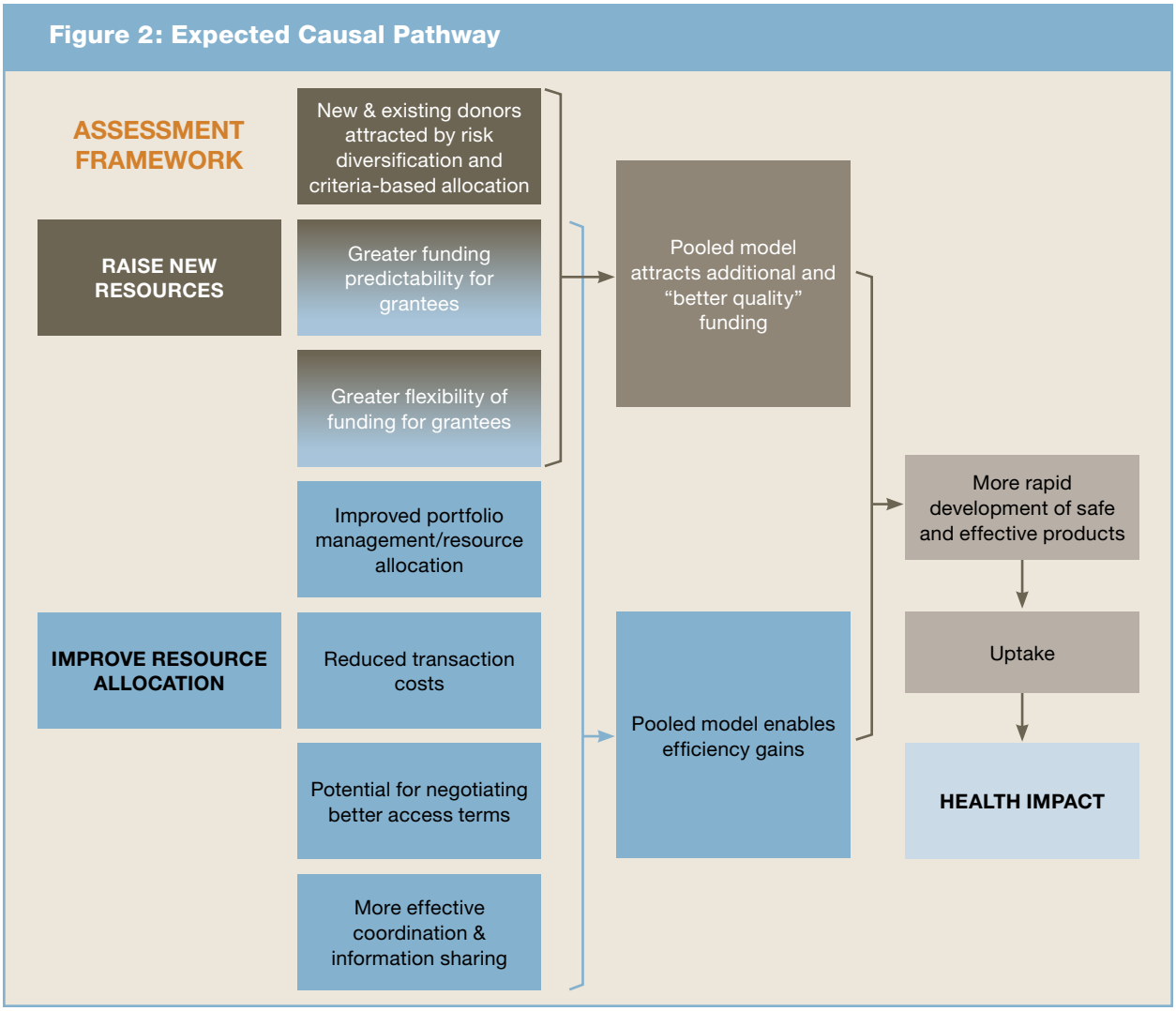
- ***Resource Mobilization:*** Is the pooled fund likely to draw *more resources* into neglected-disease R&D from existing or new donors, or from other sources such as capital markets?
- ***Predictability:*** Would the fund create a more *secure and predictable* stream of financing, both for neglected-disease R&D as a whole and for individual PDPs?

- ***Flexibility:*** Would the fund give PDPs more *flexibility* to spend their budgets, with fewer restrictions and earmarks than at present?
- ***Transaction and Operating Costs:*** How large would the initial *setup and ongoing administrative costs* of the fund be?
- ***Portfolio Management:*** Would the fund improve *resource allocation* across neglected-disease R&D so that only the most promising projects are supported?
- ***Intellectual Property Policies:*** Do the fund's policies on IP strike the right balance between *fostering access* to the technologies it supports and giving product developers incentives to invest in neglected-disease R&D?
- ***Improving Coordination and Information Sharing:*** Would the fund improve *coordination* and *information sharing* among product developers?

The proposals assume that there is some underlying obstacle or inefficiency along one or more of these dimensions in the current R&D system. We examine the extent of the problems in each area and the potential of the proposed pooled fund to address them. The "Main Findings" section of this document provides a more detailed analysis.

Our work was based on a review of existing literature, a mapping of current opportunities and obstacles in global health R&D, interviews with over 50 experts in the field, and modelling of the estimated size of the different pooled funds.

Figure 2: Expected Causal Pathway



Key Results

New Resource Generation

All three pooled funding proponents claim that these mechanisms raise new financial resources, both from new funders and from current donors who wish to increase their contributions to global health R&D. While the scope of this assessment did not permit us to conduct a systematic survey of donors, we did speak with a large number of public sector donors, private foundations, and the major research institutes in emerging economies and the United States Although we did hear positive responses from a few organizations, including certain private foundations interested in entering the global health arena, the majority of donors who already support neglected-disease R&D showed limited interest in pooled funding proposals and expressed scepticism regarding the added value of such a mechanism.

When probed more deeply, it turned out that some donors were hesitant to back pooled funding arrangements because they feared the loss of control that they currently enjoy with their direct bilateral financial support to PDPs. Others liked the pooling concept but were not convinced that it would solve existing problems with portfolio management, security, and predictability of financing, etc. Indeed, several donors were not even sure that the key constraints in the current neglected-disease R&D space had been well defined, so it was hard for them to judge if the new mechanisms would be able to make a difference. Still other donors said that their budgets were already fully committed and were not growing, so they did not see how they could make a contribution to a pooled fund at this stage even if they wished to do so.

Among the three proposals that we analyzed, interviewees acknowledged that the PDP-FF had the potential to leverage fresh funding for R&D via loan guarantees, offered donors a choice of "backloading" their financing through guarantees or future premiums on product sales, and could potentially attract new and existing donors who are interested in innovative financing options. At the same time, some donors said that the PDP-FF created some presentational issues—it could appear that the funders who agree to pay the premiums are simply covering the liabilities of other donors who provide the loan guarantees. Donors also expressed concern that the design of the PDP-FF could raise suspicions among their politicians and electorates, especially given that the recent global financial crisis was caused in part by exotic financial engineering.

While PDP-FF is particularly suited to public sector donors able to offer financial guarantees, FRIND and IRFF could be backed by a wider range of funders, including those philanthropic organizations interested in supporting R&D on new drugs and vaccines for neglected diseases but lacking expertise to conduct their own due diligence. Several people from private banks that either operate their own foundations or advise clients who practice philanthropy said that FRIND and IRFF might be mechanisms they could back, but it was difficult to tell whether these groups could offer enough money to justify setting up a new fund. It could be worth exploring further whether there is sufficient appetite among these potential donors to achieve a minimum size—IRFF's proponents suggest that $100-200 million per year over five years, or a half billion to a billion dollars, would be adequate to establish the fund as per the original proposal.

Improved Predictability and Efficiency

Our interviews and independent assessment of the three pooled funding proposals suggested that each idea has important strengths but also significant questionable features regarding their ability to improve efficiency and quality of R&D.

On the positive side, the ***PDP-FF*** model would provide more predictable long-term funding to individual PDPs. It would frontload financing, alleviating cash flow difficulties for PDPs over the next few years. It would also offer the possibility of self-financing through revenue streams from royalties and premiums (if drugs and vaccines are successfully developed), thus enabling donors to recoup their investments and avoid actual calls on their loan guarantees.

On the negative side, the design of PDP-FF locks donors into a pattern of resource allocation to the PDPs that is largely agreed upon at the outset—if certain PDPs perform poorly, it would be difficult to move financing away from them to other drug and vaccine development efforts. The existing portfolio management systems of the individual PDPs would determine how PDP-FF resources are spent, with a limited role for the Financing Facility's board. In addition, given the high scientific risks associated with new vaccines for AIDS, TB, and malaria, we question the likelihood that the organizations financed through PDP-FF would create enough licensed products or generate significant revenues via sales in rich and poor country markets. The costs of setting up and running PDP-FF could be high. There is also some danger of creating incentives to preferentially pursue vaccine or drug candidates with revenue potential, which may not necessarily be the candidates with the highest public health value.

IRFF would also give stable and predictable funding for five years (but not longer, as under PDP-FF) to PDPs that have been "certified" by the IRFF board as having sound performance and solid portfolios. The original proposal, which aims at strengthening industry collaboration, would also give the PDPs incentives to enter into partnerships with biotechnology and larger pharmaceutical firms, since a proportion of R&D spending under these partnerships would be reimbursed from the Fund. Once certified, individual PDPs would have considerable latitude to manage their own portfolios. IRFF could also improve the sharing of information across product development efforts and reduce duplication, although this would be done through the voluntary actions of participating PDPs rather than as something dictated by the IRFF board. Given the simplicity and automaticity of IRFF financing, its operating costs could be kept low.

On the negative side, IRFF would finance expenditures against business plan targets rather than measurable progress against product development milestones. If business plans are thorough and expertly crafted, then expenditure would be indirectly aligned with advances toward useable drugs and vaccines to solve major neglected-disease problems. However, the link between expenditure and health impact is not guaranteed. As with PDP-FF, resources for individual PDPs, once certified, would flow virtually automatically to reimburse R&D expenditures, regardless of the quality of the underlying R&D activities. Since the time IRFF was proposed six years ago, information sharing among PDPs and private firms working on certain neglected-disease technologies (e.g., malaria medicines, TB drugs, AIDS vaccines) has improved considerably, so the case for IRFF having a role in this may be less compelling than it was earlier. Moreover, if IRFF only subsidizes collaborations with firms, then it could bias PDP decisions on partnerships.

FRIND would exercise stronger overall control of spending across neglected-disease R&D and would hold tight reins over individual product development projects by releasing funds on a milestone basis and (its advocates claim) swiftly killing nonperforming projects. It would open up channels for allocating donor funds directly to private sector product developers, rather than having public and philanthropic funds flow indirectly to industry via PDPs.

The underlying assumption is that FRIND could do a better job than either individual donors or the scientific advisory committees of individual PDPs at picking neglected-disease product development opportunities. This assumption is highly controversial, and we were not able to gather sufficient evidence in our assessment to reach a view on it or to find a consensus position from the experts we interviewed. However, we do note the dangers inherent in a highly centralized R&D financing strategy, especially for early-stage projects where there is considerable scientific uncertainty. We also question whether a single organization could develop and apply a clear metric for judging the expected benefits from investments in drugs and vaccines for a diverse set of diseases, such as African sleeping sickness, Chagas disease, and malaria. The costs of setting up and operating FRIND, while not quantified by its proponents, would appear to be large.

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 we estimate might require roughly $150 million annually or $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.

Search for Greater Consensus, More Solid Facts on Neglected-Disease R&D

As our review of the strengths and weaknesses of the three proposals highlights, each one has been designed to address specific and different problems in the current neglected-disease R&D system. This begs the question, which problems, if solved, would give us the most leverage to accelerate R&D for neglected diseases? In our interviews with over 50 experts, we found little consensus on this point. While some experts believed that funding predictability was important for PDPs, there was no agreement as to whether greater predictability would result in better decision making and resource allocation within a PDP; a number of interviewees felt it would have the opposite effect—making the PDPs too complacent. Some experts claimed that because PDPs already have robust portfolio management processes, increased central oversight via a pooled fund's portfolio management committee was not necessary; others maintained that PDPs make poor spending decisions and that the current system needs to be radically reformed.

This finding from our work suggests that much more needs to be done to evaluate the performance of PDPs and other product developers. The financing gaps that need to be filled in the coming years must be better quantified (the Bill and Melinda Gates Foundation has commissioned a study in this area, to be released in 2011). The portfolio practices and the efficiency of PDPs, both in allocating resources and in running their organizations, should also be more widely evaluated and the results collected and shared systematically with donors and experts on R&D policy.

Even if all of this is done, however, we acknowledge that in the end, views about the efficiency of not-for-profit and commercial R&D organizations—and about the virtues and drawbacks of centralized versus decentralized management of R&D portfolios—will still be subjective and open to interpretation. In such circumstances, the debate over pooled funding arrangements for neglected-disease R&D requires more active involvement of product development organizations, funders, and advocates so that different views can be aired and consensus sought.

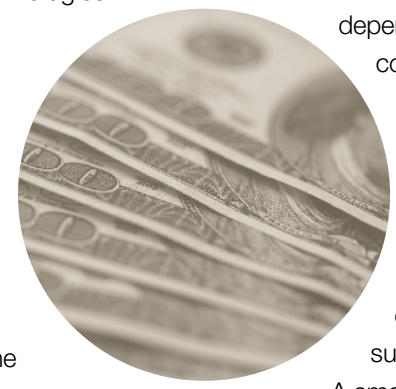
Conclusion

Based on our analysis of the three pooled funding ideas—PDP-FF, IRFF, and FRIND—and our assessment of the current environment and the mood of the donors, we are fairly pessimistic about the prospects of seeing one or several of these ideas launched in the next few years. The case for investing time and resources in establishing any of the three funds, in their current form, is weak at present.

Even though all three pooled funding ideas face significant technical and practical barriers at this time, the work that has been done by their proponents to develop these ideas is still useful and could be leveraged, in one form or another, going forward. The innovative concept behind PDP-FF—especially its attempt to tap into capital markets through public sector guarantees—may be worth further study, even if such a fund does not materialize any time soon. In the same vein, a scaled-down version of FRIND that focuses on financing a subset of high-priority efficacy trials has some technical merit and might stand a better chance of being embraced by the donors; it could be worthwhile to take another look at such a reduced version of FRIND. IRFF's relative simplicity could also be worth testing through a pilot, if and when a critical mass of new and existing donors decides that it is ready to experiment with the Fund's concept of channelling a pool of extra resources to product development through "automatic" reimbursement of certain PDPs, a concept that has proven highly effective in independent assessments.

PDP-FF—Overview

The PDP-FF, championed by IAVI in partnership with the Aeras Global TB Vaccine Foundation, intends to increase resources for PDPs so that funding is more stable and more likely to align with predicted needs, establish flexibility in funding for PDPs, and overcome donor fragmentation.[1] The proposal is currently based on the needs of two vaccine PDPs but could be broadened to include other health technologies.



The PDP-FF would frontload funding for global health research by issuing bonds through capital markets, building on recent experience with the International Finance Facility for Immunisation (IFFIm) (see Figure 3). Individual PDPs would receive a predetermined share of the fund, but the proposal provides little detail on the criteria that might be used for assessing needs and rationing resources if demand exceeds the supply of funding available. Funders would come together to establish allocation guidelines, taking into account the availability of promising vaccine candidates and the current and future prospects of funding from other sources.

Donors could support the Facility in a number of ways. Donors with credit ratings, including sovereign nations or some private sector entities, could provide guarantees for bond repayment. These commitments would be legally binding and help ensure stable PDP revenues for 10 to 15 years. Donors who may be unwilling or unable to provide bond guarantees could make grants directly to PDP-FF or pay premiums on sales of vaccines to developing countries (similar to donor payments under the Advance Market Commitment). Projections suggest that the PDP-FF could raise between $2.2 and $6.9 billion ($0.9 to $2.3 billion in present value terms), generating $29 to $73 million annually for each PDP for 15 years.

A unique aspect of the PDP-FF is its potential for some level of self-financing through the sale of products to high- and middle-income countries. The revenue generated from royalties would be returned to the Facility, with the exact nature of royalty agreements between product developers and manufacturers depending on how much PDPs have contributed to the IP surrounding the individual product.

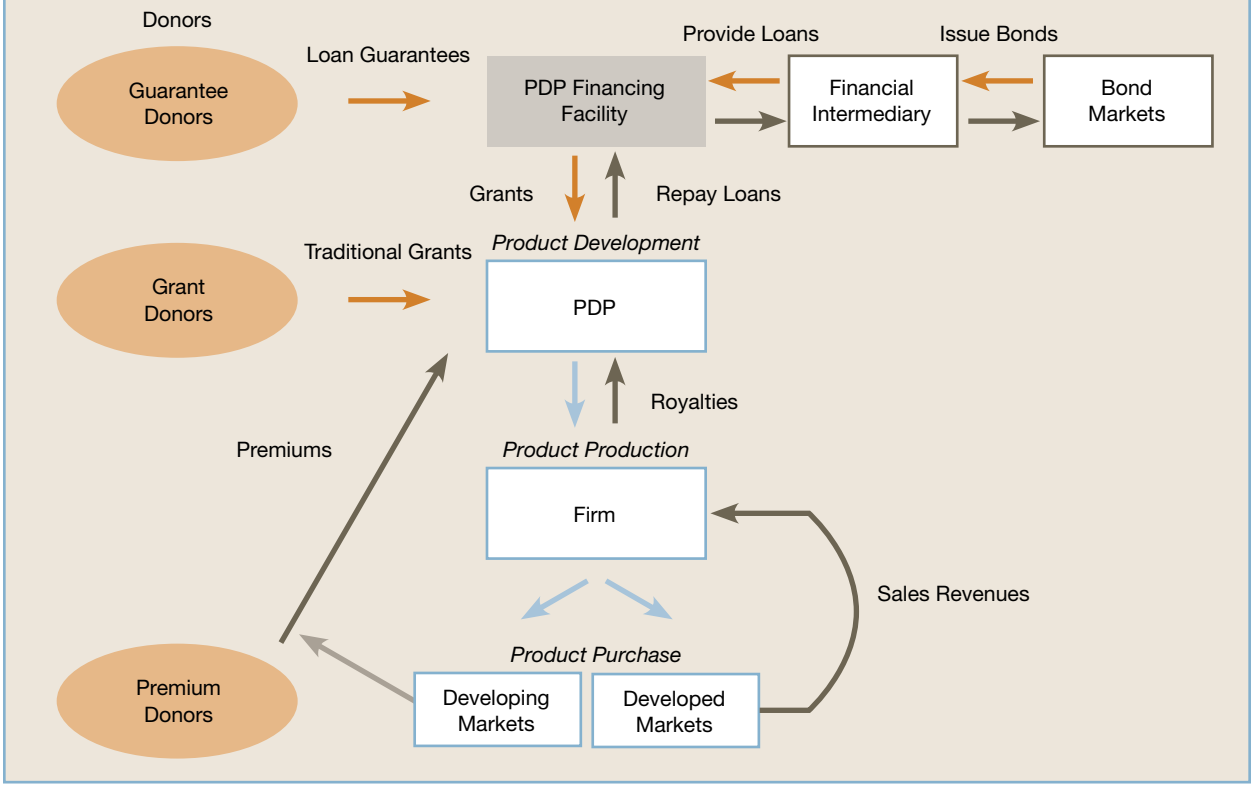
A modest secretariat consisting of a full-time CFO with audit capacity and a number of support staff would manage the PDP-FF, but the majority of human resource support would be supplied in-kind by participating PDPs. A small board representing a range of stakeholders would approve allocations, adjust disbursements, and monitor the operations of the Facility.

The proponents recognize that there are some inherent risks posed by the Facility. They note that there are

- possible shortfalls in revenue streams (the prospect of which might make donors reluctant to provide guarantees);
- possible problems in agreeing upon appropriate royalty rates with industrial partners (which is difficult to do retrospectively for products that are well advanced and likewise difficult to do for those at early stages when commercial prospects are highly uncertain);
- a possible unwillingness of the World Bank to act as a financial intermediary;

[1] IAVI, *Financing for Research and Development of Global Health Technologies: Design and Feasibility of a Product Development Partnership (PDP) Financing Facility*, (New York, NY: IAVI, 2009).

Figure 3: PDP-FF



Source: Adapted from IAVI PDP-FF Concept Note (unpublished)

- problems in agreeing upon allocation and governance arrangements;
- possible reductions in core grant funding from donors who might decide to offer bond guarantees.

PDP-FF—Assessment Findings

Resource Mobilization: Is the fund likely to draw more resources into neglected-disease R&D from existing or new donors?

Of the three proposals, PDP-FF places the greatest emphasis on generating new funds and provides donors with different options for supporting product development though donor guarantees, grants, and premiums. The whole approach hinges on having sufficient donors willing to provide legally binding guarantees. The pool of these donors is limited to entities with a credit rating, and some may find it challenging to enter into multiyear agreements, given their current legislative frameworks and budgeting systems.

On the other hand, PDP-FF has the potential to attract donors who are interested in innovative financing and keen to reward success in R&D. It could also appeal to donors wanting to back approaches that lead to financial sustainability.

One political limitation is the complexity of launching a new bond facility in the midst of widespread concern about financial engineering following the global financial crisis. This could be somewhat mitigated by working with established financial agencies like the World Bank.

Donors may also find the PDP-FF attractive for products close to commercialization, but these may

not be the products that target the greatest global health needs. Products that generate royalties in middle- or high-income markets might not be the products most needed by the poor.

Frontloading poses another risk in that leveraging future funding now might dry up resources for product development later on—donors may be unwilling to commit funding again.

Predictability: Would the fund be likely to make resource mobilization more predictable in the long-term and disburse funding more predictably to R&D organizations?
Yes, if successfully established, the PDP-FF would offer predictable funding for the PDPs. Donors would commit to legally binding guarantees, which would allow the Facility to issue bonds. These rules would allow the PDP-FF to create firm 10- to 15-year funding plans with selected PDPs.

Although the PDP-FF model provides predictable funding for individual PDPs in the long-term, the day-to-day operations of the Facility and its ability to disburse funds in a timely and efficient manner will influence predictability in practice. A risk connected with high financial predictability for the PDPs is that this could lead to an "entitlement" mentality and inhibit PDPs from killing poorly performing projects unless the PDPs enforce rigorous portfolio management in other ways.

Flexibility: What restrictions does the fund have in terms of disease area, technology type, R&D stage, and institutional eligibility, and are these restrictions sensible?
The degree of flexibility depends on how the PDP-FF would be designed and which diseases, technologies, R&D stages, or types of activities would be eligible for financing. To ensure that the PDPs concentrate on vaccine candidates with good chances of becoming marketable products, the proponents of PDP-FF have suggested that a ceiling would be set on the share of funds that could be allocated to discovery and preclinical work. From the perspective of the individual PDPs benefiting from the Facility, they would have a great deal of flexibility to choose the specific vaccine projects that they would pursue—other than the stipulation, mentioned above, that they focus on clinical stages of product development.

Portfolio Management: Is the fund likely to improve the effectiveness of not only resource allocation or portfolio decision making across development efforts where donors are making the decisions but also portfolio management within PDPs?
This is not a major focus of PDP-FF. PDPs would manage their own portfolios, with little involvement from the PDP-FF. There would be limited possibilities for reallocating resources across PDPs.

Transaction Costs: How great are the initial setup and ongoing transaction costs of the fund and to what extent are they justified?
Experience from the IFFIm suggests that there are likely to be substantial upfront establishment costs. Since the allocations to PDPs are established at the outset, ongoing transaction costs would be low but would depend upon the nature of the check-ins between the fund and PDPs at periodic intervals, as well as bond issuance costs.

Intellectual Property Policies: Do the fund's policies on IP strike the right balance between fostering access to the technologies it supports and offering the fund the best choice of partners for R&D activity?
This is not a feature of the proposal—PDPs would continue to manage their own IP. As noted above, the revenue-generation goal carries the risk that PDPs will aim for projects where they can obtain favorable IP terms, which may limit partnering options.

Improving Coordination and Information Sharing: Would the fund be likely to improve coordination and information/resource sharing amongst PDPs and across R&D efforts more generally?

The proposal accepts that agreeing on PDP allocations will require coordination but does not specify how this will take place.

IRFF—Overview

The Pharmaceutical R&D Policy Project originally proposed the Industry R&D Facilitation Fund in a 2005 report supported by Wellcome Trust.[2] This report suggested that industry participation in PDPs was associated with more successful and cost-effective outcomes and that PDP/industry partnerships were lacking prior to 2005, partly as a result of unpredictable funding. At the time of the report, the collective PDP funding gap for the four PDPs studied in the report was estimated to be between $130 and $190 million per year.

To overcome this gap and strengthen partnerships, the IRFF was proposed to attract fresh funding, increase its predictability for PDPs, and encourage them to work more closely with industry. The fund would also allow donors to diversify risk by allowing them to invest in a portfolio of PDPs.

The IRFF would establish a fund for neglected-disease product development, with shares allocated to qualifying PDPs (see Figure 4). To participate, a nonprofit research group would submit a business plan to the Fund that demonstrates a focus on neglected diseases, strong access provisions, a novel product portfolio, sound management, and scientific teams to manage operations. The IRFF would also expect to be able to review at least two years of operating history and a sound forward-looking budget. By evaluating PDP portfolios and plans, the Fund would take some of the burden of due diligence from donors. This might appeal to small donors or donors who are new to funding neglected-disease R&D yet lack the capacity to carry out their own diligence.

If a PDP is approved to access the fund, the IRFF would reimburse a portion of the PDP's expenditure (e.g., 80%) on partnerships upon meeting goals detailed in the business plan.[3] The partial reimbursement would help ensure that PDPs are prudent in their use of the Fund and put up other forms of risk capital. Once a PDP's funds are replenished, it can use these resources to take on additional projects and partnerships.

The reimbursement structure provides a strong incentive for PDPs to share the information necessary to allow IRFF to develop central oversight. The IRFF could also serve as a hub providing PDPs with centralized legal, human resources, and regulatory support. IP negotiations would remain the responsibility of the PDPs.

The IRFF would aim to reward successful PDPs, under the assumption that high-performing PDPs who reach milestones quickly would draw more resources from the Fund. The quality of R&D, however, depends on how well milestones are defined and evaluated.

A small secretariat would be responsible for accrediting PDPs, reviewing their product portfolios, making reimbursements, and coordinating fundraising and donor communication.

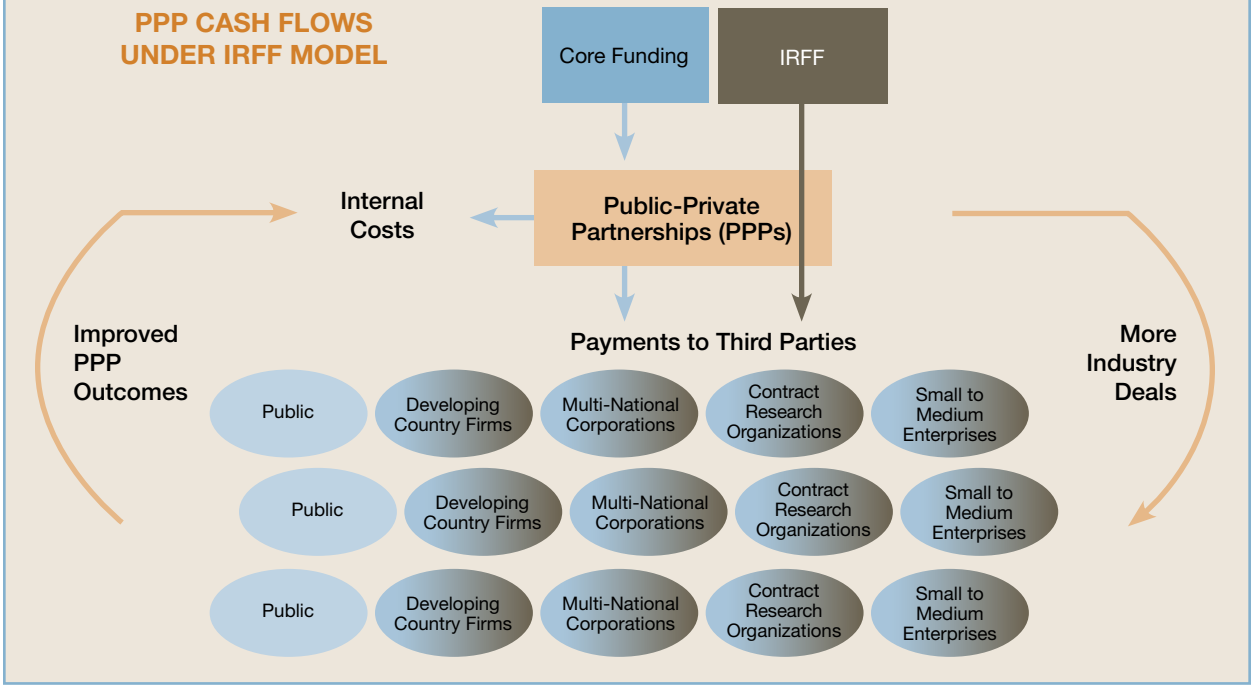
IRFF—Assessment Findings

Resource Mobilization: Is the fund likely to draw more resources into neglected-disease R&D from existing or new donors?

[2]Pharmaceutical R&D Policy Project, *The New Landscape of Neglected Disease Drug Development*, (London: London School of Economics and Political Science and the Wellcome Trust, 2005).

[3]The proposal stated that only industry partnerships would be reimbursed, however, the proponents have subsequently verbally revised this industry-only restriction.

Figure 4: IRFF



Source: Adapted from Pharmaceutical R&D Policy Project, "The New Landscape of Neglected Disease Drug Development," 2005

Under current conditions, this seems unlikely, or has only limited potential. Donors already feel they are investing in a diversified portfolio by giving grants to several PDPs. Interviews revealed that most existing donors in this space are not keen to lose control of decision making regarding how their funds are allocated. Some potential donors who are new to neglected-disease R&D and lack due diligence capacity might be interested.

Predictability: Would the fund be likely to make resource mobilization more predictable in the long-term and disburse funding more predictably to R&D organizations?

Yes, revenue mobilization would increase for the limited five-year period of the IRFF and for the accredited PDPs eligible for IRFF reimbursement, if the Fund is successfully created and enough money is mobilized from donors to cover the five-year needs of the PDPs. This would be an improvement relative to the status quo of three/five year grants, but not as predictable as the PDP-FF.

Flexibility: What restrictions does the fund have in terms of disease area, technology type, R&D stage, and institutional eligibility and are these restrictions sensible?

IRFF would restrict funding to accredited PDPs only. In the original proposal, these were PDPs developing new drugs, not vaccines or diagnostics. It is unclear whether additional PDPs could become accredited during the five-year life of IRFF or whether new projects not included in accredited PDPs' portfolios could also become eligible.

IRFF funds would be relatively flexible from the individual PDP perspective, within the framework of their approved business plans. Our initial research suggested that IRFF reimbursements would be limited to PDP partnerships with industry, but this aspect has recently been verbally revised by the proponent.

Portfolio Management: Is the fund likely to improve the effectiveness of not only resource allocation or portfolio decision making across development efforts where donors are making

the decisions but also portfolio management within PDPs?
Like FRIND, IRFF would have the central oversight and information necessary to enable donors to agree on a rational, evidence-based approach to resource allocation across product developers. However, the IRFF secretariat would not seek to impose portfolio management on individual PDPs. The underlying assumption is that the accredited PDPs, as demonstrated through their business plans, have the systems and incentives to manage their own portfolios effectively.

One issue with IRFF is that it could encourage PDPs to spend more, without focusing on developing products with large health impact or getting products to patients faster. More incentives for quality, health impact, and speed might help. These could be incorporated into the milestones for releasing reimbursements to the PDPs.

Transaction Costs: How great are the initial setup and ongoing transaction costs of the fund and to what extent are they justified?
Moderate. To create IRFF, donors would have to develop structures and invest in processes to agree on priorities, design the resource allocation and common reporting mechanisms, and review and accredit PDPs. During implementation, there would be further institutional costs associated with the IRFF secretariat and its review of PDP performance against milestones and reimbursements of expenditures incurred by the PDPs.

If the IRFF ended up replacing the efforts of numerous existing donors, each separately undertaking due diligence and monitoring activities, then transaction costs could actually decline. However, this is not likely to happen, since existing donors have shown limited interest in IRFF. In this case, IRFF would add to the overall burden of administrative costs in neglected-disease R&D, both for donors and for PDPs who could have additional reporting requirements to meet.

Intellectual Property Policies: Do the fund's policies on IP strike the right balance between fostering access to the technologies it supports and offering the fund the best choice of partners for R&D activity?
IRFF would work through PDPs to maintain the IP status quo.

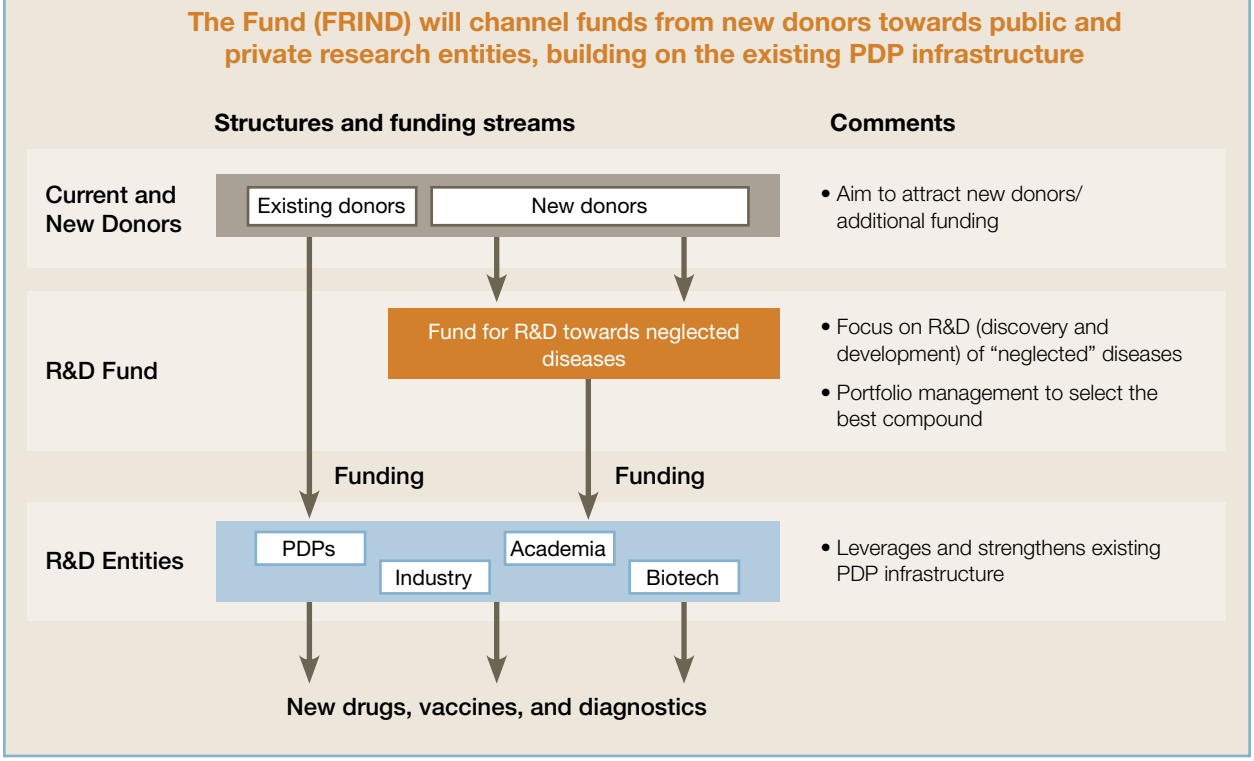
Improving Coordination and Information Sharing: Would the fund be likely to improve coordination and information/resource sharing amongst PDPs and across R&D efforts more generally?
As with FRIND, central oversight could be used to facilitate better coordination and information sharing. The IRFF proposal specifically mentions a potential role in serving as an information clearinghouse and providing platform services to PDPs. However, there are alternate ways to achieve these objectives, and some work is already in progress through donor-PDP consortia for certain diseases and products (e.g., TB drugs, AIDS vaccines, microbicides).

FRIND—Overview

The FRIND, championed by Novartis, focuses on putting in place a mechanism that its proponents say would avoid wasteful duplication in neglected-disease R&D and ensure that the most promising projects access financing.[4] The proponents argue that current product pipelines (mostly for neglected-disease drugs) are maturing, and existing resources are insufficient to support candidates through to registration. Its backers say the FRIND would attract additional funding from existing donors, as well as from new donors like developing country governments.

[4]Herrling P, "Making Drugs Accessible to Poor Populations: A Funding Model," *Global Forum Update on Research for Health Update 5*, (2008): 152–155.

Figure 5: FRIND



Source: Adapted from Dalberg Global Development Advisors

FRIND would exercise a high degree of control and oversight of neglected-disease R&D, using an Executive Board that would govern on behalf of donors, a Health Economic Expert Committee that would propose funding allocation across diseases and technologies according to estimated "returns," and a Scientific Advisory Committee that would perform due diligence on funding requests from PDPs and private biopharma firms (see Figure 5).

Most or all donor funding would flow through the FRIND and would be disbursed to projects on a milestone-to-milestone basis. Projects that fail to meet milestones would stop receiving support from the Fund. PDPs' Scientific Advisory Committees would continue to manage their internal portfolios, but the FRIND committees would make judgments about which PDPs are performing best and merit financial support from the Fund. There is also mention of housing the N2D2 research platform within the Fund, supporting discovery activities for all diseases.[5]

Originally, the proposal suggested that FRIND would only fund late-stage drug development work in malaria and TB, all stages of R&D for viral leishmaniasis, Chagas' disease, and human African tripanosomiasis and discovery work for other neglected diseases. Based on these guidelines, the proponents projected a resource need of $6-10 billion over ten years to meet R&D needs for the ten diseases. An allocation formula was not developed, but early modelling suggested that 75% of the funding might go to late-stage work for TB and malaria.

[5]The N2D2 proposal, or the idea to create a Network for Neglected Diseases Discovery, which was originally conceived by Paul Herrling and Trevor Jones, aims to facilitate collaboration between pharmaceutical firms and PDPs on compound library screening.

Subsequent iterations of the FRIND proposal have looked at the option of "partial portfolio management," whereby only a subset of the disease and technology space is funded. More recent discussions with proponents have revealed an even narrower option, in which FRIND would fund only the "strongest compounds in late-stage development." The proponents explained that a focus on late-stage candidates recognizes the potential benefits of having many innovative projects at the earlier phases of R&D without centralized portfolio control of the kind embodied in FRIND and the value of carefully rationing the more expensive late stages of product development.

FRIND would own exclusive licenses to the technology developed with the Fund's support, but only for the indication that had been financed. The proponents recommended creating an IP pool to which developers must donate licenses, allowing FRIND to enhance access for the poor by influencing the location of manufacturing and market price. Subsequent to publication of the consultation draft of this report, we were informed that FRIND's IP policies are evolving and that the proponents are reconsidering this issue.

FRIND—Assessment Findings

Resource Mobilization: Is the fund likely to draw more resources into neglected-disease R&D from existing or new donors?

Hard to say. FRIND has the potential to attract donors who are unable to carry out the due diligence themselves. But the interviews we carried out for this study suggest that most donors are not convinced by this "one-stop shopping" argument, with the exception of some corporate foundations that may be interested in getting into the R&D space. FRIND might be more appealing to donors who want to invest in a portfolio of late-stage products with higher probabilities of success.

Predictability: Would the fund be likely to make resource mobilization more predictable in the long-term and disburse funding more predictably to R&D organizations?

By putting together a very large pool of donor funding, FRIND seeks to increase the predictability of the overall neglected-disease financing envelope for successful compounds. A $6-10 billion Fund would certainly increase such predictability if it could be realized (which seems doubtful under current circumstances). At the level of individual PDPs and biopharma firms interested in neglected-disease drug and diagnostics R&D, FRIND could actually reduce predictability of funding, since money would be tied to specific approved projects and would be halted if milestones are not met. This milestone-by-milestone disbursement approach is designed to rectify perceived inefficiencies in the current grant funding system by incentivizing performance. In the Phase III FRIND variation, funding would be secure for the duration of the efficacy trials.

Flexibility: What restrictions does the fund have in terms of disease area, technology type, R&D stage and institutional eligibility and are these restrictions sensible?

The proponents of FRIND have considered several different options for the scope of the Fund and have not reached firm decisions in regard to the technology types, disease areas, R&D stages, and types of activities/investments that would be eligible for support. In the earliest iterations of the FRIND proposal, its proposed scope was very wide, giving the Fund's board broad latitude to operate. In a more recent variation, FRIND would be restricted to late-stage clinical trial funding only. Other eligibility options have been considered as well.

From the point of view of PDPs and other product development organizations, FRIND's financing would be tied tightly to specific projects, giving these organizations little flexibility in deciding how to use the money.

Portfolio Management: Is the fund likely to improve the effectiveness of not only resource allocation or portfolio decision making across development efforts where donors are making the decisions but also portfolio management within PDPs?

The original proposal aimed to give FRIND the dominant, if not exclusive, role in financing neglected-disease R&D with tremendous control over portfolio management decisions. Stakeholders interviewed for this study were skeptical about the political and technical advisability of such an approach, arguing that too much centralization would stifle initiative by individual PDPs and firms. How could a single organization make rational choices across a wide range of diseases and drug candidates, they argued, given the huge scientific uncertainties involved and the difficulty in using a single metric of "public health return" to choose among different investments?

Also, since FRIND seems to be unlikely to receive support from the largest funders for neglected-disease R&D, it is doubtful that FRIND can mobilize enough resources in a single pool to give it meaningful portfolio leverage.

The variant of FRIND that would have the Fund focus on Phase III trials seems more realistic from the political, financial, and technical perspectives. In terms of portfolio management, if a critical mass of donors joined such a Fund, then it might be able to choose and sequence the funding of efficacy trials with the greatest public health impact potential.

FRIND's proponents assume that there is duplication of R&D efforts and ongoing portfolio management weaknesses in many PDPs—FRIND would help to solve these problems. The evidence base is too weak to assess whether these assumptions are valid.

Transaction Costs: How intensive are the initial setup and ongoing transaction costs of the fund and to what extent are they necessary and/or justified?

The level of decision making and central oversight necessary for the FRIND will determine the magnitude of its transaction costs. These would be smallest in the Phase III variant but potentially quite large in the full portfolio management option.

A central premise of FRIND is its milestone funding approach and emphasis on central oversight and technical monitoring. This makes FRIND more transaction-intensive than the IRFF and PDP-FF proposal, which approach management with a lighter touch.

Intellectual Property Policies: Do the fund's policies on IP strike the right balance between fostering access to the technologies it supports and offering the fund the best choice of partners for R&D activity?

FRIND would own exclusive license to the technology for indications that the Fund has financed. We suggest that this requirement may be too restrictive for some technology categories and likely to limit the Fund's partnering options. We understand that the IP policy is being reconsidered.

Improving Coordination and Information Sharing: Would the fund be likely to improve coordination and information/resource sharing amongst PDPs and across R&D efforts more generally?

In the full portfolio management option of FRIND, central oversight would facilitate better coordination and information sharing. In the partial portfolio management option, sharing would be limited to the sectors covered by the Fund, which could be quite valuable within disease areas. We can see good potential for housing public-private collaborations and coordinating R&D information to support and facilitate information exchanges across technologies and diseases.

INSTITUTIONS INTERVIEWED

Aeras Global TB Vaccine Foundation
Anacor
AusAid
AVAC
Bayer
Bill and Melinda Gates Foundation
BIO Ventures for Global Health
Credit Suisse
Dalberg Global Development Advisors
Department of Foreign Affairs Ireland
Drugs for Neglected Diseases Initiative
European Malaria Vaccine Initiative
Foundation for Innovative New Diagnostics
GlaxoSmithKline
Imperial College London
International AIDS Vaccine Initiative
International Partnership for Microbicides
Lion's Head Global Partners
Malaria Vaccine Initiative
The McLaughlin-Rotman Centre for Global Health
Medicines for Malaria Venture
Merck
Morgan Stanley
National Chemical Laboratory
National Science and Technology Development Agency
Netherlands Ministry of Foreign Affairs
Novartis
Philbridge
Policy Cures
Program for Appropriate Technology in Health
Results for Development (former World Bank staff)
Sanofi Pasteur
Sequella
TB Alliance
Special Programme for Research and Training in Tropical Diseases, WHO
TropMedPharma
UK Department for International Development
University of Dundee
US National Institute of Health, Fogarty International Center
Wellcome Trust
World Health Organization

RESULTS FOR DEVELOPMENT INSTITUTE

R4D

Results for Development Institute

1875 Connecticut Avenue NW

Suite 1210

Washington, DC 20009

Tel: (202) 470.5711

Fax: (202) 470.5712

info@resultsfordevelopment.org

resultsfordevelopment.org