

# **COMPARATIVE ANALYSIS OF INNOVATIVE FINANCING PROPOSALS FOR HEALTH R&D**

## **Draft for EWG members**

### **Notes for EWG members**

Two documents are included here:

1. The analysis. This compares innovative financing proposals according to their R&D target, thus proposals aimed at funding basic research are compared against each other; proposals aimed at funding product development are compared against each other, and so forth. (The R&D target areas are those set out in the original Framework document that was approved.)
2. A reference document, with a brief paragraph on each proposal. You may find it helpful to refer to this up as you read, as many of the proposals are specialized or obscure and you may not be familiar with them.

When you are thinking about the findings could we note that, although all criteria are important, some are easier to address than others. For instance, it is relatively easy to re-target a proposal to give a better DC health impact – e.g. by fine-tuning the list of diseases, by providing a tighter product profile that suits DC needs. However, it is very difficult to change the fundamentals of how a proposal operates. It would be helpful for you to keep this in mind when you are reviewing the analysis on each of the three main criteria: DC impact, financial aspects, and operational efficiencies and feasibility.

Finally, the analysis report is a draft working document (you will see some references and checks are still outstanding, as are the Methodology and Glossary; and that the formatting is still to be done).

Once we have your feedback, we will finalise the recommendations and submit the final document to yourselves and to Sir George.

There is one further point to note. This report was framed by the proposals that we received or that are in circulation in the policy community: these were almost exclusively devoted to basic research and product development, with virtually no proposals focused on operational research. This is therefore not covered by this report. Health systems research is also excluded, as this was covered by the World Bank-UK review of Innovative Financing of Health Systems.

Looking forward very much to hearing your thoughts.

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## Background

The cost of funding health R&D is driven by several key factors:

### *Is the disease Type I, II, or III?*

Type I diseases (e.g. hypertension, diabetes) are prevalent in both high and low income countries, and thus have substantial commercial markets and R&D activity. The cost of DC-specific development (e.g. additional clinical trials or inclusion of new viral strains) can therefore be substantially offset against commercial investments that are already being made to reach Western markets. For these diseases, industry interest is likely higher; and only partial donor funding is needed (full funding would simply crowd out private investment).

Type II diseases are 'incident in both rich and poor countries, but with a substantial proportion of the cases in the poor countries'. These diseases have modest semi-commercial markets that can be leveraged (e.g. travellers' and military malaria, European TB patients). For these diseases, industry interest is likely to be lower; and donors will need to provide substantially more funding to make up the private shortfall.

Type III diseases occur overwhelmingly or exclusively in developing countries (e.g. Chagas' disease, Buruli ulcer) and have no commercial market and limited R&D. Industry interest is likely to be almost non-existent; and donors are likely to need to provide virtually all funding.

### *Does the disease have a sound science and technology (S&T) base?*

Diseases with a sound S&T base (e.g. pneumonia vaccines) are less risky : Donor funding will need to be only minimally inflated for risk, along the lines of standard industry metrics. Diseases with a weak S&T base are more risky e.g. HIV vaccines, Buruli ulcer: Donors will need to fund the R&D themselves or provide incentives that are highly inflated for risk.

### *What kind of R&D is needed?*

Different types of R&D pose very different levels of cost and difficulty, with implications for the size and choice of funding mechanism.

For basic research and discovery, individual project costs are relatively low - in the hundreds of thousands to perhaps \$2-3 million. However, scientific uncertainty at this tends to drive overall costs up, with multiple projects failing and being replaced by others before success is reached.

For all products, early development (preclinical testing and smaller clinical trials) is relatively cheap, costing in the hundreds of thousands for diagnostics, to tens of millions for drugs and vaccines. By contrast, late development (large-scale clinical trials and manufacture) is far more

expensive, costing a few millions for diagnostics, but up to \$150-250 million<sup>i</sup> for drugs; and \$500-800 million for vaccines, if plant construction costs are included. <sup>ii</sup> These figures include cost of failure. Of course, only a select few products will reach late-stage development.

A special category is R&D of new products based on existing medicines. This can be substantially cheaper due to lower risk but also to the ability to apply existing test and trial data to the new product. For instance, fixed-dose combinations; re-formulation of existing anti-malarial drugs; addition of new DC strains; or extension of existing products to new diseases are all relatively economical.

### *Who is the target group?*

Different types of R&D require different skillsets and are carried out by different actors. Basic research is generally conducted by academics and public institution; product discovery predominantly by small and large companies and PDPs, although public groups also play a role; and large-scale product development by large companies and PDPs. DC firms dominate manufacturing and distribution for the developing world, and IDC firms are increasingly moving into product development.

These groups each have very different cost structures, business models and needs. For instance, large multinational companies can invest more of their own resources and take higher risks before they receive a return on investment (RoI), or may even be able to conduct not-for-profit research. However, if market incentives are being used, they are likely to require a far higher RoI than small or IDC firms. On the other hand, most small companies live hand-to-mouth: they need ongoing capital during the R&D process and cannot afford to do not-for-profit work. However, they can often be satisfied by a far smaller RoI, if a market incentive is being used.

### *How well does the proposal match the needs of the target group?*

One of the most cost-effective ways to reduce donor spend is to better target incentives to the most appropriate groups. The less suitable an incentive is to its recipient, the larger it must be to overcome the increased risk and greater skills gap this poses for them. It is very unlikely that a single proposal could be sized and designed to efficiently meet the differing needs of Western and IDC manufacturers (e.g. for vaccine plant construction); of academics and SMEs (e.g. for drug discovery); or of PDPs and multinationals (e.g. for clinical development). Failure to adequately match proposals to their target groups will inevitably lead to failure, waste or both.

Finally, funders or recipients may reject apparently good proposals because they do not meet their political, corporate or legislative practices.

The acid test is thus a) does the proposal perform well and b) is it acceptable to the target funders and developers. The following analysis seeks to make these judgments on a wide range of innovative financing proposals for developing world health R&D.

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## Fundraising

Table with list of proposals (see overview of proposals)

Broad category	Mechanism
Frontloading support	Issuing bonds and rescheduling debt payments
	IFFnd
	PDP-FF
Increased voluntary contributions (consumers and business sector)	Voluntary consumer contributions (lotteries, digital tax as voluntary)
	Voluntary private sector contributions (including De-Tax)
Increased non-voluntary contributions (consumers and business sector)	Digital tax non-voluntary
	Patent Fees/Green IP (GIP)
	Pharmaceutical Company Taxation
	FTO
Increased public and philanthropic funding for health R&D	Increased Efficiency of Revenue Collection and initiatives to reduce tax evasion and tax havens, (and appropriation of proceeds for R&D)
	Diverting Existing Resources to health R&D for DCs (e.g. De-Tax)
	New Direct Taxes (taxes on business)
	New charges on Services or Access Rights - ETS
	New Indirect Taxes (taxes on consumption) - see also digital tax
	New Donor Funds (public and philanthropic)
Reduce risk and uncertainty (not included in further analysis as not a fundraising mechanism)	Measures to reduce investment uncertainty and reducing investment risk through pooling

These proposals fall into two main groups. A number of fundraising proposals are specifically structured to allocate some or all of the funds they raise to health R&D. These are: IFFnd; PDP-FF; FTO, taxation of pharmaceutical profits and Patent-fees/Green IP. Of these, taxation of pharmaceutical profits, Fast track option (FTO) and Patent-fees/Green IP source their funds from the pharmaceutical industry and R&D process; while both PDP-FF and IFFnd aim to make funds available for health R&D purposes through frontloading of funding backed by government guarantees.

A series of other proposals have no allocation component i.e. the funds they raise could be allocated anywhere, from cleaning up the environment, to building reserves against a future financial crisis, to health R&D. Some of these are

specific proposals to tap into known funding streams, including creating a new direct tax or levy (e.g. currency transaction levy), an indirect tax (e.g. airline solidarity contribution), or front loading funding (e.g. diaspora bonds). Others are still at the broad conceptual level e.g. diverting existing resources to health R&D, or getting more funding from existing donors. What is missing from all these proposals is a strategic connection to health R&D, or even an allocation mechanism to do so. The absence of an allocation solution leaves policy makers and funders without a reason to establish a funding stream (Where would it go? How would it be used?).

## Performance against criteria

Funding proposals are assessed against five criteria:

- Fundraising capacity
- Funding quality (defined as degree of certainty over revenue forecasts; breadth of geographic scope; absence of inefficient conditions or distortionary tax effects; and presence of spill-over benefits to the global good and development agenda)
- Additionality of funding
- Likelihood of allocation to health R&D (only for proposals without an allocation component)
- Operational efficiency and feasibility

### Fundraising capacity and funding quality

The total value of the collective fundraising proposals needs to be sufficient for the task at hand. Although no estimates exist on how much is needed for overall health R&D, current global neglected disease funding is US\$3 billion/annum (leaving some NDs significantly underfunded) thus any new financing mechanism may need to raise **two to three times** as much, although more research is needed to better quantify funding needs. If the cost of all health R&D is included, not just neglected diseases, the costs are much higher. In order to garner funds of this size, any new funding mechanism therefore needs to be future-proofed by being as broadly-based as possible –this means contributions from governments, consumers, philanthropics and the business sector. See table x below for sizing details.

The following table sorts the fundraising mechanisms by size of potential revenue raised, from largest to smallest; and notes funding quality of each.



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Table x: Financials

	<b>Source of revenue</b>	<b>Potential size of revenue</b>	<b>Start up investment</b>	<b>Quality of funding</b>
Increasing Efficiency of Revenue Collection - Initiatives to reduce tax evasion and tax havens, (and appropriation of proceeds for R&D)	Increased public funding	US\$ billions: Substantial- to the order of US\$1,600 billion	<i>Not known, but would have technical set up costs</i>	<i>Moderate</i>
Patent Fees/Green IP (GIP)	Increased private investment	US\$ billions: ~50 billion/annum 'tax' and litigation, \$100's of millions 'premium' source	<i>Not known, but would have technical set up costs</i>	<i>Moderate</i>
Raising Additional Revenue through Direct Taxes	Increased public funding	US\$ billions: Tobin tax could raise \$33-60bn/year	<i>Low</i> <i>not known, but would have some technical set up costs.</i>	<i>High</i>
New Indirect Taxes (taxes on consumption) - see also digital tax	Increased public funding	US\$ billions: Arms trade ~5 billion, CPMF ~20 billion for Brazil only, potentially more if implemented in US or globally	<i>Low</i> <i>not known, but would have some technical set up costs.</i>	<i>High</i> <i>Note: CPMF was withdrawn, see note on political sustainability below</i>

	<b>Source of revenue</b>	<b>Potential size of revenue</b>	<b>Start up investment</b>	<b>Quality of funding</b>
New Donor Funds (public and philanthropic)		<p>US\$ billions:</p> <p>Estimates on additional funding for health might amount to some \$7.4bn by 2015 from traditional donors (optimistic assumptions), and that Southern contributions <i>might be</i> in the range of \$9.5bn to \$12.1bn per annum.</p> <p>Using these estimates, and assuming 10% could be earmarked for health R&amp;D, new donor funds could amount to between \$1.6bn and \$1.95bn per annum</p>	<i>Already incurred</i>	<i>High</i>
Diverting Existing Resources to health R&D for DCs (e.g. De-Tax)	Increased public funding	<p><b>Do NOT provide additional funding</b></p> <p>US\$ billions:</p> <p>\$8.5 bn dispersed by Global Fund to date, 10s of billions for ODA</p>	<i>\$0-\$5m</i>	<i>High</i>
IFFnd	Frontloading support	<p><b>Do NOT provide additional funding</b></p> <p>US\$ billions:</p> <p>\$2 billion frontloaded since 2006</p>	<i>\$0-\$5m</i>	<i>Low</i>
New charges on Services or Access Rights - ETS	Increased public funding	<p>US\$ billions:</p> <p>Example:</p> <p>~\$1.3bn from EU emissions allowances in Germany ETS market in 2008</p>	<i>\$0-\$5m</i>	<i>Very high</i>

	<b>Source of revenue</b>	<b>Potential size of revenue</b>	<b>Start up investment</b>	<b>Quality of funding</b>
Voluntary consumer contributions (lotteries, digital tax as voluntary)	Increased private contributions or donations	<p>US\$ hundreds of millions:</p> <p>Example:</p> <p>~980 million/annum expected from Airline ticket voluntary solidarity contribution (traveller's tax)</p> <p>~\$750 million/annum from postpaid mobile phone services globally, expected to grow</p>	<p>No known for most, but would have technical set up costs.</p> <p>\$5-\$10m - a new lottery could have major up-front costs</p>	High
FTO	Increased public funding	<p>US\$ hundreds of millions:</p> <p>Hundreds of millions of dollars</p>	\$0-\$5m	Very high
Pharmaceutical Company Taxation	Increased public funding	<p>US\$ hundreds of millions:</p> <p>Estimates for LMIC are in the order of \$160m, if profits \$16bn and tax 1%)</p>	Low, although unknown	Low/moderate
Voluntary private sector contributions (including De-Tax)	Increased private contributions or donations	<p>US\$ hundreds of millions:</p> <p>Example:</p> <p>~\$130m raised by RED</p> <p>De-Tax is estimated to raise \$138m in Italy, where it is being piloted.</p>		Very high
PDP-FF	Frontloading support		Low, although unknown	High

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In terms of voluntary consumer contributions, of which lotteries is one, forecasts are more predictable though there are questions on the extent to which people would shift their support from other lotteries, and the extent to which a development focused lottery would attract altruistic consumers.

### **Additionality**

Additionality of funding is crucial since diversion of existing funding streams is extremely difficult, and would require advocates to make a case for DC health needs above the needs of those in other areas where funds are currently being spent. Two proposals do not provide additional funding:

- IFFnd
- Diversion of existing funds to health R&D

### **Likelihood of allocation to health R&D**

Likelihood of allocation to health R&D depends on:

- The extent to which the proposal is being discussed for other uses (and therefore less likely to be dedicated to DC health R&D)
- The extent to which funds are likely to be (or best suited to be) earmarked to other priorities

Several proposals had a moderately high chance of being allocated to health R&D (see Table X), including new donor funds, and additional voluntary revenue streams from consumers and businesses, a proportion of whom are interested in and willing to support improved health for the developing world. As noted in the G-FINDER report, voluntary consumer and business funding streams have been barely tapped for neglected disease R&D.

*Table X: Non-allocation specific fundraising mechanisms*

<b>Mechanism</b>	<b>Broad category</b>	<b>Likelihood the funds could be allocated to health R&amp;D</b>	<b>Strong case for and/or being discussed for other uses</b>
New Donor Funds (public and philanthropic)	Increased public funding	Medium	
New Indirect Taxes (taxes on consumption) - see also digital tax	Increased public funding	Medium	
Voluntary consumer contributions (lotteries, digital tax as voluntary)	Increased private contributions or donations	Medium	Some but not all are being discussed for other uses

Voluntary private sector contributions (including De-Tax)	Increased private contributions or donations	Medium	Some but not all are being discussed for other uses e.g. De-Tax for health systems financing
Diverting Existing Resources to health R&D for DCs	Increased public funding	Low	
Issuing bonds and rescheduling debt payments	Frontloading support	Low	
Increased Efficiency of Revenue Collection and initiatives to reduce tax evasion and tax havens, (and appropriation of proceeds for R&D)	Increased public funding	Low	Yes
New Direct Taxes (taxes on business)	Increased public funding	Low	Some but not all are being discussed for other uses
New charges on Services or Access Rights - ETS	Increased public funding	Low	Yes

### Operational efficiency and feasibility

Operational efficiency was assessed in terms of risk management, technical feasibility and long term functioning. The top performing proposals overall were:

- Voluntary private contributions
- Direct taxes
- Voluntary consumer contributions

Five approaches scored well in relation to risk management, as they have a funding stream based on mandatory contributions once established, and a diversity of funders:

- Increasing Efficiency of Revenue Collection - Initiatives to reduce tax evasion and tax havens, (and appropriation of proceeds for R&D)
- New Direct Taxes (taxes on business)
- New Indirect Taxes (taxes on consumption) - see also digital tax
- Pharmaceutical Company Taxation
- Patent Fees/Green IP (GIP)

Three approaches scored well in relation to the ease with which the mechanism could be operationalised, having minimal legal, technical or administrative hurdles:

- Voluntary consumer contributions (lotteries, digital tax as voluntary)
- Voluntary private contributions (detax, lotteries, digital tax as voluntary)
- New Donor Funds

A further key factor was political feasibility, in particular the extent to which a proposal or approach is politically sustainable in the long term. Here most proposals did well with the exception of Patent fees proposal and taxes. Although we note that any tax can be removed or amended, but in practice taxes that are fair and allocated properly can stay.

Mechanism	OPERATIONAL ISSUES (Risk, technical, long term functioning, interactions, excludes accountability)
Voluntary private contributions (detax, lotteries, digital tax as voluntary)	★★
New Direct Taxes (taxes on business)	★★
Digital tax non-voluntary	★★
Voluntary consumer contributions (lotteries, digital tax as voluntary)	★★
Initiatives to reduce tax evasion and tax havens, (and appropriation of proceeds for R&D)	★★
New Indirect Taxes (taxes on consumption) - see also digital tax	★★
IFFnd	★★
New Donor Funds (public and philanthropic)	★★
Issuing bonds and Rescheduling debt payments	★★
PDP-FF	★
Diverting Existing Resources to health R&D for DCs (e.g. De-Tax)	★
New charges on Services or Access Rights - ETS	★
FTO	★
Patent Fees/Green IP (GIP)	★
Pharmaceutical Company Taxation (Brazil)	★

## Acceptability to funders

Funders felt that solutions need to be broad-based and to include new sources of funding.



The nature of the allocation component was very important to them. They wanted and needed to know what the money would be used for (What will it deliver? When?), and to be able to assess the associated risk (i.e. the likelihood of a health return on their investment). These two factors alone explain why non-allocated funding streams can be less attractive for funders. In general, they preferred to fund broad solutions or areas, rather than narrow ones, and funding targets needed to be 'politically acceptable' (noting that 'political acceptability' tends to be defined more narrowly in difficult economic times). They also preferred solutions that did not require in-depth technical knowledge of the target area in order to make good decisions, such as approaches that included a mechanism to allocate funds to priority areas and/or to best projects within these areas.

Leaving aside the question of allocation, funders also exhibited preferences for certain types of fundraising mechanisms. Government funders were attracted to mechanisms that are simple, automatic, can be operationalised fairly easily, and are future-proofed. An international tax or levy was also viewed as more appropriate than a national tax, which would put implementing countries at a disadvantage to non-implementing countries. Funders were not convinced of the value of spending more expensive 'future dollars' on R&D, noting that mechanisms that "spend expensive money on risky things are not so good": this reduces the attractiveness of the PDP-FF and IFFnd, both of which fund R&D projects which, by their nature, have a high failure rate. Funders were also aware of the scope to reduce inefficiencies in existing funding patterns and arrangements.

## Conclusions

### Least likely to work for health R&D

The fundraising proposals least likely to work for health R&D are those that are already spoken for, or where there is a low likelihood they will be earmarked for health R&D including:

- Diverting Existing Resources to health R&D for DCs
- Increased Efficiency of Revenue Collection and initiatives to reduce tax evasion and tax havens, (and appropriation of proceeds for R&D)
- New charges on Services or Access Rights - ETS

In its current form the funding component of patent fee/Green IP is too hard to operationalise, however some elements of it could perhaps be pulled out e.g. an additional tax or fee on patent applicants, which could be earmarked for health R&D.

## Most likely to work for health R&D

In terms of meeting the key objectives of additionality, size, likely to be applicable for health R&D and a broad base, the optimal combination of proposals is:

<i>Mechanism</i>	<i>Examples</i>	<i>Qualifications, enhancements and linkages</i>	<i>Potentially raising</i>
New Indirect Taxes	Digital tax on internet users	Would require effort to be operationalised and would need sustained political momentum, but could be both DC and West in scope	\$2bn
Voluntary private and consumer contributions	Mobile phone voluntary solidarity contribution	Revenue stream not guaranteed and so needs broad based or used in combination with others (as suggested here)	\$1bn
New donors funds		Could include funding from DCs as well as other non-traditional donors	~\$1.6bn - \$1.95bn
Tax on pharmaceutical profits		Would require efforts to sustain political commitment to the mechanism and would incur start up costs to be operationalised. Has advantage of raising and spending funds in the same area (pharmaceutical R&D)	~\$160m (LMIC only)
<b>Total</b>			<b>~\$4.8bn - \$5.15bn</b>

This mix of funding streams provides funds from governments, business (including the pharmaceutical industry) and consumers, and covers both West and DC. It would potentially raise an additional \$5bn per annum. When combined with *current* neglected disease R&D investments of \$3bn per annum (insert GFINDER ref), this would be highly likely to cover all neglected disease R&D funding needs. This level of funding would not, however, be sufficient to fund all health R&D relevant to developing countries (e.g. operational research, health systems research).

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## R&D capacity building in DCs

Six proposals were submitted to the EWG with a focus on building health R&D capacity in developing countries.

<b>Mechanism</b>	<b>Framework position (s)</b>	<b>Category</b>
Regional Health R&D coordination offices	Research & development	Push all
Pharmaceutical Company Taxation (Brazil)	Research & development	Push all
Life Science Convergence	Development	Push Co's
SBIR for DCs (International)	Early and Late development	Push Co's
SBIR's national programmes in DCs	Early and Late development	Push Co's
Revolving Fund to Finance R&D for NTDs	Research & development	Push all

We can comment on these only in the most general terms. Firstly, a full review of the field would be a far bigger job than the EWG could do in the time allowed, since the submitted proposals represent only a small subset of the many capacity-building approaches in circulation or already implemented. A further hurdle is that the submitted proposals cannot reasonably be compared even with each other, since some focus on funding R&D (Revolving Fund, SBIR programmes, Brazilian pharmaco tax), others include a regional coordination component (Regional Health R&D Coordination offices), while yet others include investment in R&D infrastructure (Life Science Convergence centres). Finally, most proposals were tabled in a very general form with limited detail on which to base analysis.

We therefore note only a few key points. The major difference in thinking about R&D capacity building is whether it is health-driven or innovation-driven. Health-driven R&D tends to occur within academia and public institutions and to be funded from national health and medical research budgets. It tends to focus on operational and health systems research, as well as biomedical basic research and early product development. It is often collaborative, and can be driven either by national priorities or by the interests of individual researchers. This type of R&D benefits from coordination, national and regional, particularly in terms of priority setting; and from international networking. Some funding programmes already exist to support IDC health research capacity, for instance the Wellcome Trust currently partners with the Indian Government on several programmes, including:

- A £5m partnership with the Public Health Foundation of India to create new Indian Institutes of Public Health

- A new £4.5m South Asia Centre in India to increase the infrastructure to carry out research on management of chronic diseases (e.g. diabetes, mental illness, cancers)
- A £5.5m award to reduce maternal and child mortality and morbidity by building a global network of scientists and field sites to generate research evidence to improve policy and practice
- An £80m partnership to boost biomedical research by funding Indian biomedical science fellowship programmes

By contrast, innovation-driven R&D tends to occur within companies (biotechs, SMES and, in the IDCs, in large companies); to focus on product development from discovery through to registration; and to be funded from science and technology budgets or through private equity capital.<sup>1</sup> It is usually competitive and driven by commercial targets, but it is absolutely crucial to note that in DC settings commercial targets often have significant overlap with public health targets, including for both non-communicable diseases (NCDs) and “neglected” infectious diseases. Unlike in the West, both NCDs and infectious diseases remain common maladies affecting hundreds of millions of local people in DCs. (See the recent McLaughlin Rotm<sup>2</sup>an Centre report on product pipelines in the South.<sup>3</sup>) Tuberculosis, malaria, pneumonia, the helminth infections and the diarrhoeal illnesses have high burdens of disease in all the DCs, and less globally prominent diseases such as dengue, leprosy and leishmaniasis also have significant presence in several IDCs. There will, of course, still be cases where investment is commercially unattractive, even for DC firms with lower cost structures; and, for these, both domestic public funding and external philanthropic or double-bottom investment are more likely to be needed.

Innovative Developing Countries invariably invest national resources into both approaches. Two of the world’s top five public funders of neglected disease R&D are now Brazil and India - although both invest far less in proportion to their GDP than do several Western countries. Both also have active and extensive small business investment programmes:

- India has several large schemes in place **Insert from Prof Ganguly**

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<sup>1</sup> Of course, these are generalizations, for instance Brazil’s neglected disease research programmes are now located in their Department of Health in order to better align and integrate health and science

<sup>2</sup> Rezaie Rahim,, Frew Sarah, Sammut Stephen et al. Brazilian health biotech—fostering crosstalk between public and private sectors. *Nature Biotechnology*, June 2008, 26 (6.):DC627-DC644

<sup>3</sup> Sarah E. Frew, Victor Y. Liu and Peter A. Singer (2009). "A Business Plan To Help The ‘Global South’ In Its Fight Against Neglected Diseases." *Health Affairs*, Vol 28 No.6 pp.1760-1773

- Brazil invested ~US \$22 million into ND R&D in 2007 [Insert G-FINDER ref] and supports its domestic small business through initiatives such as the Technological Innovation in Small Businesses (PIPE) program. Additionally, the Brazilian pharmaco tax proposal is well-sized to further support IDC neglected disease but would require sign-on of one or more high-income countries as IDC portfolios move into late-stage development; and substantial public decision-making to determine which projects should best be funded

The *extent* to which these IDCs require external donor support for innovation programmes, as commercial Foreign Direct Investment needs to be taken into account (e.g. the GSK-Ranbaxy partnership; LIST A COUPLE OF OTHER), as well as domestic private sector investment. For example, Indian firms already invest actively into NCDs suitable for both local and international markets, with a dual licencing strategy built into R&D programmes from the very first; while many also have neglected disease R&D programmes ranging from “re-tooling” (e.g. generic variants, fixed-dose combinations) to genuinely novel R&D conducted by a smaller (but growing) number of firms.

It is nevertheless clear that investment into IDC innovation is extremely promising, offering a high health return on investment and avoiding many of the problems associated with incentivizing Western firms to conduct this R&D – since R&D is designed to meet DC markets and needs. Of the above proposals, those best targeted to supporting IDC innovation are the national and international SBIR programmes, and Life Science Convergence centres, although the international SBIR programme would likely be more complex to operate, as it requires international fund collection, project selection and investment allocation. However, it is crucial to remember that these ideas represent only the tip of the innovation iceberg.

The Least Developed Countries (LDCs) are in a different situation since, unlike IDCs, they often have a rudimentary private biomedical sector and therefore predominantly focus on public-health driven R&D. However, even here, the situation is not cut and dried. We note, for instance, that Life Science Convergence centres, which build on small local innovation hubs, are now operational in two LDCs (Tanzania and Rwanda), with a further virtual centre in Ghana.

While much of the discussion around incentives – and the vast majority of proposals in circulation, operation or submitted to the EWG – are focused on public researchers and Western product developers, it seems to us that IDCs will increasingly be the source of new products for developing countries, with reliance on Western developers decreasing over time. We therefore believe that a renewed focus on the IDC commercial sector should be a policy priority going forward.

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## Basic research and product discovery

Target groups:

Academics, PDPs, small and large companies

Thirteen proposals are designed to fund basic research and product discovery for the developing world, with around half of these already implemented (highlighted in grey in Table X). The target groups for these initiatives are academics, PDPs, and small and large companies.

### Performance against criteria

Table X: Proposals to fund Basic Research and Discovery, with performance ratings

CATEGORY	MECHANISM	DEVELOPING COUNTRY IMPACT	OPERATIONAL & FEASIBILITY	DATA GAPS
Alongside IP Pull Impact Payment funds	Cancer prize fund	↑ ↑		?
	Economic Prize system	↑ ↑ ↑		??
	Health Impact Fund	↑ ↑ ↑		??
	Chagas Disease Prize Fund for the Development of new treatments, diagnostics and vaccines	↑ ↑ ↑		?
	Priority Medicines and Vaccines Prize Fund (PMV/pf)	↑ ↑ ↑		??
Alongside IP Pull prizes	Biomedical R&D Treaty	↑ ↑ ↑		??
	Prize fund for development of low cost RDT for TB	↑ ↑ ↑		?
Push Co's	IAM Innovation Fund	↑	★★	??
	Neglected Diseases R&D Tax Breaks (Thai proposal)	↑	★★	?
	R+D grants to industry without Wessner		★★★	?
Push PDPs	Industry R&D Facilitation Fund (IRFF)	↑ ↑ ↑	★★★	?
	Product Development Partnerships	↑ ↑ ↑	★★★	?
TBD	InnoCentive	↑ ↑	★★	?

### DC Impact

Eight proposals have a high potential DC impact, of which one (PDPs) is implemented:

- Push funding via (PDPs , IRFF)



- Proposals that work alongside the IP system (Chagas prize, TB prize, Priority Medicines and Vaccines Prize Fund, Economic Prize system, Health Impact Fund and Biomedical R&D Treaty)

One further proposal performed slightly less well, but still sufficiently high to warrant their inclusions:

- Milestone prizes (Innocentive style)

Another proposal, the IAVI Innovation Fund, scored moderately well despite lack of data on key points, suggesting it is worth further examination.

Proposals that do not clearly and specifically target DC needs performed less well, for example Direct R&D grants schemes for the private sector (US Small Business Innovation Research (SBIR), UK Small Business Research Initiative (SBRI) & the Wellcome Trust's Seeding Drug Discovery Grants) since firms are likely to target commercial needs over DC needs (e.g. malaria products for travelers, Western disease strains etc). These approaches are also less likely to include or encourage technology transfer to, or capacity building with, DC groups; or to encourage recipients to take DC suitability and price issues into consideration in the design of their research and discovery programmes. Poor targeting could, however, relatively easily be addressed to make these programmes more DC-appropriate.

### **Operational efficiency and feasibility**

Five proposals score high on operational efficiency and feasibility, of which all have been implemented save for the IRFF.

- PDP mechanisms (PDPs, IRFF)
- Direct R&D grant schemes for small companies (US and UK small business grants SBIR, SBRI; Wellcome Trust Strategic Drug Development)

Despite data gaps, two further proposals performed sufficiently well to warrant their inclusion:

- Milestone prizes (Innocentive style)
- IAVI Innovation Fund

Proposals that have already been implemented scored universally well on operational efficiency and feasibility. We should clarify that this was not because they were already in operation, but rather that they were already in operation because they are feasible and easier to operationalise. Non-implemented

proposals fared quite differently. Of these, only one (the IRFF) scored well. Most of the Alongside-IP proposals ranked very poorly (TB, Chagas and cancer prize funds, PMV/pf and Biomedical R&D Treaty) due to the need for new and complex central mechanisms, and annual review and funding allocation decisions. Two other Alongside IP proposals ranked poorly, but had substantial data gaps that made judgment difficult (Health Impact Fund and Economic Prize system).

## Financial aspects

Funding needs to match its target R&D activity. In the case of basic research and discovery, this generally means short-term projects of 2-3 years costing up to a few million dollars each, and spread across a wide range of institutions and organizations globally, including academic and public research institutions, Western (and increasingly IDC companies) and PDPs. Proposals should ideally match this funding pattern, while seeking to better align this disseminated activity with DC health goals. Funding “quality” must also be taken into account, including additionality; certainty of revenue; reliability and applicability of mechanisms; absence of inefficient conditions; and additional benefits e.g, lower R&D time and cost.

Assessment against these metrics showed that the highest performing proposals on financial aspects are:

- Innocentive
- Direct R&D grant schemes
- IRFF

Innocentive is an extremely cost efficient way to solve technical or research questions and, by carefully defining desired outcomes and Target Product Profiles, can be closely aligned with DC priorities. The grant programmes are well sized for financing individual projects, although alignment with DC priorities depends on the interests of individual donors. The IRFF is also well sized to achieve its goal, has high quality funding and automatically aligns R&D activity with DC priorities (assuming PDPs have been set up in priority health areas). However, it is only designed to cover industry costs (although this could perhaps be extended).

Impact and prize funds are highly effective at aligning R&D with global goals, but it is impossible to comment on their financial aspects due to lack of details, for instance, how much would be allocated to interim basic research and discovery prizes and over what time-frame. If interim prize funding were consistent in size with other milestone-prize funds, and not costly to run, we would expect this element to also be cost efficient.

The three high-performing funding proposals cover, or could cover, basic research and discovery across all diseases.

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## Financials

Financial aspects: Basic research and discovery proposals					
	<b>Revenue Stream (and whether secure)</b>	<b>Annual investment</b>	<b>Annual projects</b>	<b>Scope</b>	<b>Quality of funding</b>
PDP funding (IRFF)	NO for funder VERY for recipient: 80 % of PDP industry payments	~X million USD CHECK	All PDP projects	ND drugs	High
R&D grants to Western orgs (IAVI, WT, SBIR, SBRI)	IAVI: Yes 3 yr commitment from the Gates Foundation & IAVI.  WT :Not mandated  SBIR: Legislated. All US government agencies with R&D budgets > \$100 million give 2.5% of their extramural research funds  SBRI: Not legislated	IAVI: ~\$3m WT: Stg 20 mill SBIR : \$570m SBRI: Phase 1 - £50-100K for 6 months. Phase 2 - \$250-£1 million for 2 years (size of each reward). Total value of grants unknown	IAVI: ~5 projects (15 projects over the 3 yrs) WT: No data SBIR: Total number of grants unknown. Of grantees: 50% had at least 1 peer reviewed publication/ 40% led to a patented invention SBRI: No data	Any diseases (but guided by donor preference - except IAVI solely for HIV)	IAVI: High  WT: Low  SBIR/SBRI: Low

Milestone prizes (Innocentive)	NO	6-9m	Funded 300 problems (~130 solved)	Any diseases (but guided by donor preference)	Moderate
Prize funds	NO	NON ANNUAL - PAY FOR MILESTONES, SHARING INFORMATION & IP AND END PRODUCT Cancer fund: No data (end product only) / Chagas: \$250m/ TB: \$100m/ PMV/pf No data (billions/ 10% donor investment)		<ul style="list-style-type: none"> <li>All cancer products</li> <li>All Chagas products</li> <li>TB diagnostics</li> <li>PMVPF drugs and vaccines</li> </ul>	Low
Impact payments: - <ul style="list-style-type: none"> <li>Econ Prize Fund</li> <li>Health Impact Fund</li> </ul>	NO	NON ANNUAL - PAY FOR END PRODUCT EPF: \$400-800m HIF: A fund of \$6 billion annually to sustain a portfolio of 20 drugs with an average of 2 new drugs per year. \$600 million/year to conduct health impact assessments. Payout per company depends on health impact of product.		EPF: All Canadian ND research HIF: All diseases; only drugs	EPF: Low HIF:Low
Biomedical R&D Treaty	MINIMAL: Treaty but no sanctions for defaulters	No data	No data	All global R&D	Low
ND Tax breaks	MODERATE: Legislated/ govt funded: <ul style="list-style-type: none"> <li>130 -175 % rebate (UK R&amp;D relief)</li> <li>40% (UK VRR relief)</li> <li>Not specified for Thailand's global system)</li> </ul>	UK: \$8m (Stg 5m)	No data	HIV, TB, malaria (UK)  DC diseases for Thailand's global system	Low

## Acceptability to funders and target groups

There was almost unanimous agreement that push funding (including interim payments) was more effective than pull funding for stimulating early R&D, with philanthropic and public funders, PDPs and MNCs all strongly expressing this view. All product developers felt pull funding was too far off to be effective in stimulating early R&D: “Pull funding is quite difficult as it doesn’t fund the actual R&D – getting funding for this is now the rate-limiting step”. “Small companies do not have the capacity to make any internal investment and big pots of money at the end of the R&D process will not suit us at all.”

Within this, responses were nuanced. SME groups noted that milestone pulls (ideally commercial milestone payments) were their preferred approach, as they did not like standard grant push funding. Some US-based groups were less comfortable with push funding than market pulls, saying they found push funding unfamiliar but noting that they “could see it made sense in some cases”, for instance when there wasn’t a market.

Different proposals are more likely to incentivize different developers to make new DC products, as shown in [Table X](#).

Proposals **least likely** to induce researchers and developers in any category to undertake basic research and discovery for DC uses are:

- Pull funding proposals (impact or prize based)
- Biomedical R&D Treaty

## Conclusions

### Least effective proposals (performance and acceptability)

- Pull funding proposals
  - Health Impact Fund
  - Economic Prize system
  - TB, Chagas and cancer prize funds; and PMV/p (NB: The interim prize elements of these proposals could work – see below)
- Biomedical R&D Treaty

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Table X: Likelihood of incentivizing target groups and appeal to funders

	MNCs	SMEs	IDCs	Diagnostics firms	PDPs	Funders
Push funding in general	"We need push upstream to stimulate R&D that isn't happening"	(But in the form of milestone payments - see below)				" ...
Push funding via PDPs	"PDPs need regular funding so any mechanism that gives predictability would be appealing: "PDPs work, and provide a vehicle for the pharmaceutical industry to make contributions"	✗ (Overall, would not respond to this approach)				Public  Philanthropic: "PDPs should be given more funding"
Direct grants to companies	" ...					"It helps pull researchers into new disease areas"
Milestone payments/prizes (as an adjunct to bigger solutions)	✗ (Overall, would not respond to this approach)	"A series of pulls along the dev't path are our No.1 preference - but milestone payments are preferred to prizes"				



## Promising proposals

The IAVI Innovation Fund performed well overall, despite lack of data on key points. This makes it interesting for further exploration as it suggests high potential.

Two proposals performed patchily, with high scores in some areas but very low scores in other areas. These proposals would be interesting to analyse further, with a view to pulling out high-performing elements or amending low-performing ones

- Health Impact Fund (high DC impact; elements that were very attractive to target groups; but very low operational scores)
- Alongside IP-Prize funds - TB, Chagas (high DC impact; the interim prize elements of these proposals may score well on financial issues, but insufficient data to know; very low operational scores)

## Most effective proposals (performance and acceptability)

<i>Mechanism</i>	<i>Proposal</i>	<i>Qualifications, enhancements and linkages</i>
Push funding via PDPs	PDPs IRFF	
Direct grants to companies (Western groups?)	SBIR/SBRI-style WT- SDD IAVI innovation fund	Need re-targeting to NDs before could be used  Existing Western schemes may face some hurdles to expand to NDs (legislative hurdles)  Not automatically aligned with DC health goals (depends on donor preference)
Milestone prizes	Innocentive	Insufficient as a standalone system

All these proposals, except the IRFF, are already implemented but only one (the US small business grants scheme) has a revenue stream; the remainder relying on donor funding.

## Product development

Target groups:

Early development: Small companies, MNCs, PDPs and Public

Late development: MNC, PDP, public (trials)

Twenty five proposals are designed to fund development of products for DCs.

Table X (grey=operational)

CATEGORY	MECHANISM	FRAMEWORK POSITION (S)	DEVELOPING COUNTRY IMPACT	OPERATIONAL & FEASIBILITY	DATA GAPS
Alongside IP Pull Impact Payment funds	Cancer prize fund	Development	† †		?
	Economic Prize system	Development	† †		?
	Health Impact Fund	Development	† †		??
	Chagas Disease Prize Fund for the Development of new treatments, diagnostics and vaccines	Development	† † †		?
Alongside IP Pull prizes	Biomedical R&D Treaty	Development	† † †		??
	Prize fund for development of low cost RDT for TB	Development	† † †		?
Alongside IP Push	Funds (Global Fund for R&D)	Development	† †		??
Pull - market	Paediatric exclusivity (US and EU)	Late Development		★ ★	?
	Orphan drug legislation	Development		★ ★	?
	Priority Review Voucher	Development		★ ★	?
Pull - market	Transferable intellectual property rights (TIIPR)	Development			??
Pull public	Advance Market Commitment (AMC)	Development		★ ★	?
Push Co's	EMEA's SME initiative	Late Development		★ ★ ★	?
	IAVI Innovation Fund	Early development	†	★ ★	??
	Neglected Diseases R&D Tax Breaks (Thai proposal)	Development		★ ★	?
	R+D grants to industry	Development		★ ★ ★	?
Push PDPs	FRIND	Development	† †	★	??
	Industry R&D Facilitation Fund (IRFF)	Development	† †	★ ★ ★	?
	PDP-FF	Development	†	★	?
Push PDPs	Product Development Partnerships	Development	† † †	★ ★ ★	?
TBD	Hatch-Waxman exclusivities	Late development	†	★ ★	?
TBD	InnoCentive	Early development	† †	★ ★	?
TBD	Pharmaceutical Company Taxation (Brazil)	Development	† †	★	??
TBD	Priority Medicines and Vaccines Prize Fund (PMV/pf)	Development	† † †		??
TBD	Prize Fund to Support Innovation and Access	Development	† †		??

Of these, several target only early development (preclinical and early clinical trials) or only late development (Phase III trials to bring products to registration, and plant manufacture), however, the majority aim to fund product development from preclinical through to registration. Over one third of these proposals (11) have already been implemented, as highlighted in grey on Table X.

## Performance against criteria

### DC impact

Five proposals have a high potential DC impact, of which only one is implemented (PDPs, as marked with an asterisk below):

- Proposals that work alongside the IP system (Biomedical R&D Treaty; TB and Chagas prize funds, PMV/pf). The Economic Prize system had a slightly lower rating, but might also be included
- PDPs\*
- Milestone prizes (InnoCentive style\*) had a slightly lower rating, but nevertheless scored sufficiently well to be included

One further proposal - the IAVI Innovation Fund, scored well on DC impact despite data gaps, suggesting that it merits further examination.

A strikingly high number of implemented proposals scored very poorly in terms of potential DC impact - making up 7 of the 8 proposals that scored very poorly. This was generally because they were primarily designed for Western markets, although DC product developers can and do use them (e.g. Orphan drug, paediatric exclusivity, EMEA SME initiative, ND tax breaks and a range of direct grant schemes for companies). However, one proposal specifically intended to incentivise DC product R&D also rated in the bottom five on DC impact (the Priority Review Voucher).

### Operational efficiency and feasibility

For early development, up to Phase II, three approaches covering many proposals scored high on operational efficiency and feasibility, of which all but one (the IRFF) are implemented:

- PDP funding mechanisms (PDPs, IRFF)
- Small business grants (US and UK small business grants; Wellcome Trust Strategic Drug Development programme, EMEA regulatory fee relief, IAVI Innovation Fund)
- Milestone prizes (InnoCentive style\*) scored almost equally well, despite significant data gaps, and are therefore also included

For late development, there were only two approaches that scored well on operational efficiency and feasibility:

- PDP mechanisms (PDPs\*, IRFF)
- SME initiative

Proposals that have already been implemented scored universally well against operational efficiency and feasibility metrics. As noted previously, this is not because they are already in operation, but rather that they are already in operation because they are feasible and easier to operationalise. Of more

interest is an examination of not-yet-implemented proposals. Of these, the IRFF scored very well, reflecting its automated funding allocation process and simple administration; while others ranked poorly due to design weaknesses (the TB, Chagas and cancer prize funds; PVM/pf and Biomedical R&D Treaty). A third group of proposals showed promising trends, but could not be assessed due to lack of data on key operational points (TIPR, FRIND, and the SBIR for DCs): these may be worth further study or development if they rank highly against other metrics.

## Financial aspects

Around \$3 billion per year (G-FINDER REF) is currently invested into global neglected disease R&D, including investments into large late stage trials for pneumonia, TB and malaria vaccines and malaria drugs. However, there is severe underfunding of a wide range of diseases, in particular the most neglected diseases and, even for many high attention diseases, early pipelines are not being filled as quickly as needed. It is therefore clear that billions of dollars of funding will be needed each year, some of which must be additional. CD funding will require ?????

Funding also needs to match VERY different R&D activities, ranging from a few million over a few years for diagnostic development to hundreds of millions over 12-15 years for vaccine development. These activities are conducted by a wide range of players globally but, unlike basic research, there are far fewer groups being targeted by funding. Early product development for the developing world takes place in Western companies (dozen s(?) of firms, or at most a few hundred if small diagnostic companies are taken into account); IDC companies (increasing rapidly); Product Development Partnerships (low dozens); and some academic and public groups. The further down the development pipeline, the fewer groups are involved, with large clinical trials to licence new products being primarily the province of large companies and PDPs.

It is therefore important to select proposals that can raise and/or allocate large sums of money between relatively few groups for late development, as well as smaller sums of money to several hundred competing groups for early development, and in a way that reduces the burden on decision-makers. Funding “quality” must also be taken into account, as noted in the previous section.

For the purposes of assessment, proposals were therefore classified into three categories:

- Those raising and/or investing millions to tens of millions (small)
- Those raising and/or investing hundreds of millions (medium)
- Those raising and/or investing billions (large)

*Small funding proposals:* In this category, two approaches were superior:

- Innocentive

- Grant programmes from individual organizations

As with basic research, Innocentive remains an extremely cost efficient way to solve technical or research questions with minimal donor effort. Grant programmes from individual organizations are well sized for financing individual projects, but require donors to make many complex decisions.

The remaining two approaches are poorly sized, providing rewards that are simply too small to incentivize or finance full product development programmes. This includes Western ND market approaches (Orphan legislation; expedited review and paediatric exclusivity) and ND tax breaks. Orphan legislation (which comes closest) could perhaps be amended to address this (see *Ideas section*).

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Table X: Financials

<b>Financial aspects: Small funding proposals SORT TO PUT BEST ONES FIRST IN EACH CATEGORY (SMALL DONE)</b>					
	<b>Revenue Stream (and whether secure)</b>	<b>Annual investmen t</b>	<b>Annual projects</b>	<b>Scope</b>	<b>Quality of funding</b>
Developer grants by Individual orgs (IAVI, WT, EMEA)	NO	IAVI: \$3m WT: Stg 20 mill	15 projects (IAVI) ? (WT)	Any diseases (but guided by donor preference)	IAVI: High <b>CHECK WHY WT AND EMEA LOW</b>
Milestone prizes (Innocentive)	NO	\$6-9m	Funded 300 problems (~130 solved)	Any diseases (but guided by donor preference)	Moderate
ND market pulls paed excl/expedited review	VERY: Legislated/ market based  - 7-10 yrs market exclusivity per product	Orphan: \$10s of millions per product  Others: Very low	1 finished product	All NDs	Orphan: Moderate  Expedited review: Moderate  Paediatric exclusivity : Low
ND Tax breaks	MODERATE: Legislated/ govt funded:  - 130 -175 % rebate (UK R&D relief) - 40% (UK VRR relief) - Not specified for Thailand's global system)	UK: \$8m (Stg 5m)	~ Half of 10 companies portfolios <b>CHECK MY CALCULATIONS ON THE 150% TAX</b>	HIV, TB, malaria (UK)  DC diseases for Thailand's global system)	Low
<b>Financial aspects: Medium size funding proposals</b>					
Pharmaco tax	MOD FOR FUNDER:	Assume		IDC	Moderate

	Legislated % tax on domestic pharmaceutical sales. Would raise \$160m (LMICs/ MICs only); billions if HIC sign-on  NO for recipients	fully expended i.e. \$160m		portfolios	
Econ prize system (Canada)	NO	\$400-800 m		Global ND portfolio	Low
Gates Grand Challenge	NO	\$100m per year	? How many questions	Any NDs (but guided by donor preference)	?
TB prize	NO	\$100m total		TB diagnostics	Low
Chagas prize	NO	\$250m total		Chagas drugs, diagnostics, vaccines	Low
PDP funding: IRFF	NO for funder VERY for recipient: X % of their expenses	\$??m per year CHECK  ~X million USD CHECK	Industry contribution to PDP projects (early)	ND drugs	High
PDP funding: FRIND	NO	\$600m- \$1 bill per year	All projects (early? Late?)	ND drugs	Moderate
Govt R&D grants to companies	NO	\$600m (NIH) per year	How many grantees per year? 50% had at least 1 peer reviewed publication/ 40% led to a patented invention	Any diseases (but guided by donor preference)	Low

PRV	VERY: Legislated/ market based: \$200m- \$1 bill per product	\$200m- \$1 bill per product	1 product	1 product for any ND	Low
<b>Financial aspects: Large funding proposals</b>					
Health Impact Fund (HIF)	NO	NON ANNUAL - PAY FOR END PRODUCT A fund of \$6 billion annually could sustain a portfolio of 20 drugs with an average of 2 new drugs per year. \$600 million/year to conduct health impact assessments. Payout per company depends on health impact of product.		All diseases; only drugs	Low
Global fund for R&D	NO	\$1.5-4 billion		All DC products	Low
Cancer prize	NO	Billions		DC cancer products	Low
Treaty	MIN: Mandated by treaty but no sanctions for defaulters	Billions		All products	Low
TIPR	VERY: Legislated/ market based	Billions	1 product	1 product for any ND	Moderate
AMC	NO for funder VERY for recipient (Price & volume contract	1.5billion	1 product	1 product for 1 disease (end-stage R&D and purchase )	Moderate



*Medium size funding proposals:* The best-performing approaches were:

- PDP funding, especially IRFF

The PDP funding approaches are realistically sized to achieve their goal, and impose minimum decision-making burdens on donors (in particular the IRFF).

Several proposals are poorly sized, in particular, the Economic Prize Fund and Chagas prize, which are severely under-funded, and the TB diagnostic prize which is overfunded: all have complex decision making processes involving varying combinations of technical experts and representatives from research organizations and developing countries. The PRV is interesting but has low funding “quality” due to uncertainty of revenue estimates (which can lead to substantial overpay for some products); and limited applicability (only countries with effective regulatory priority review capacity can implement it); however, as with many other implemented proposals, it reduces public decision-making to a minimum. |

*Large funding programmes*

- No suitable proposals

The Global Fund for R&D is substantially under-funded, as it is currently insufficient to fund neglected disease R&D, let alone R&D for all DC products, as per its stated target. It also requires very substantial public decision-making input.

The TPR is ‘decision-free’ for public funders but is clearly over-priced, providing billions for 1 product when global neglected disease R&D spend on all neglected disease product R&D is currently or around \$3 billion (somewhat higher if annualized plant construction costs are included). The cancer prize fund and Treaty have insufficient data to make a judgment. The AMC cannot be compared with other proposals since it covers both purchase funds and R&D: we note, though, that Western MNCs suggest the AMC is under-sized, since it provides profit margins well below what they are used to, while IDC firms suggest they find the profit margins generous. It requires a great deal of public decision-making in the selection and contract stage but, once in place, requires minimal further decisions by public funders. It also applies to only one product.

## **Acceptability to target groups|**

The strong preference from both funders and developers was for combined push and pull to support the development process. Push funding was seen as suitable for early or late development, and for building infrastructure to support product development (e.g. developing trial sites). One firm noted that having late-stage push funding, “... helped us decide to do additional DC studies, rather than just doing Western trials and then offering DCs a cheaper access price on the finished product.” Pull funding was seen as best suited to late development, while milestone pull prizes worked best for early development.

Industry and philanthropists took a more nuanced view of pull incentives than many public funders. They saw pulls as being most useful for end-stage development and rollout, and in particular for extension work on existing R&D programmes: “Pull incentives can encourage opportunistic investments (provide the final added incentive needed)” and “they steer existing R&D towards the needs of DCs”. Pull incentives also had the merit of making certain R&D areas attractive, “building a landscape where industry wants to invest and take on the risks of developing a product”. However, they believed pulls would not work for diseases where the basic science was missing e.g. HIV vaccines; while some pulls (e.g. AMCs) were suited to vaccines, but unsuited to drug development due to variable market size.

Public funders, on the other hand, tended to take a more “blunt instrument” view of pull incentives, seeing them as helpful for most R&D areas. They also had very different perceptions of the optimal pull size, with industry noting that the public offering of a \$1.5 billion AMC was “barely profitable for large companies” and “only worked because products were already in late-stage development when the AMC was announced”. Multinational companies said an AMC “would need to be substantially larger than \$1.5 billion to support full product development”.

Different proposals are more likely to incentivize different developers to make new DC products, as shown in [Table X](#).

Proposals **least likely** to induce developers in any category to make new DC products are:

- TIPR: “Too politically unpopular”
- Tax breaks: Unattractive to small companies and less relevant to large companies
- Health Impact Fund and other impact based pull proposals: “Not attractive to us in its current form”; “Measuring impact is an inexact science – anything that introduces uncertainty is almost impossible to overcome from an incentive perspective.” “A utopian idea but the reality would be a nightmare to implement in terms of assessing impact and ‘worth’”. “Very expensive to implement and very unattractive to small companies” BUT many groups nevertheless identified this approach as definitely worth further exploration
- Large end-stage prizes: “\$100K won’t incentivize firms to enter the field”; “Prizes as the main pull at the end don’t de-risk the development process.”
- Solutions outside the IP system were unappealing to all groups: “Anything that blow apart IP is a nightmare for us”; “We can never ever support something that gets rid of the IP system”; “We’re not in favour as wouldn’t fit with our business model”. As a result, the Biomedical R&D Treaty received a universal “No” from interviewees

Overall, philanthropic and developer preferences were closely aligned. However, public funders diverged from developers in many areas, often putting in place or supporting proposals that developers are unlikely to respond to, and avoiding proposals that are most likely to stimulate developers to invest in making new products for DCs.

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Table X: Likelihood of incentivizing target groups and appeal to funders

	MNCs	SMEs	IDCs	Diagnostics firms	PDPs	Funders
Push + pull	"The best option combines them, and offers different incentives for early and late-stage R&D"					"Both are needed"
Public markets & public purchase commitments	"Our preference is a purchase commitment"; "a long-term commitment (10-15 years) from a procurement agency like GAVI or UNICEF would be best"				"purchase of existing vaccines would be the best signal".	✗ Public
AMCs	"tend to be market-distorting rather than market supporting"; "We're trying to persuade governments to do a purchase fund, not an AMC". "They're OK but not a magic bullet"	✗ "had too many conditions and was only for one disease"	yes or no?	✗ "big incentives are appealing to some policy makers but only small amounts are needed for diagnostics, since manufacturers normally take a proven technology and extend it for ND use"	No data	
PRV		"a good match for the SME model but would likely need additional up-front funding"	"incentivises MNCs to partner with us or buy-out our IP "	✗ "priority reviews do not exist for diagnostics; even if they did, PRV doesn't provide an 'up front' incentive for manufacturers"		
Orphan drug Paediatric exclusivity						Public
Push funding via PDPs	PUT IN A COUPLE OF QUOTES ACROSS THE MCN/IDC/ PDP	✗				Public Philanthropic
Direct grants to companies	"...useful to subsidise clinical trials in DCs"					
PDP-FF	"Mixing together commercial and not-for profit models is messy"	"Companies don't like the public sector taking royalties on profits, even if those profits are allocated back to improving DC health."			"We like the long-term, low admin approach"; "A 10-year grant would be simpler and would omit the need for a PDP-FF"	
Milestone pulls/ prizes (as an adjunct to bigger solutions)	✗	"A series of pulls along the dev't path are our No.1 preference –but milestone payments are preferred to prizes"				
Regulatory efficiencies	PUT IN QUOTES FOR MNC, SME ETC			"the most immediately effective incentive would be eliminating regulatory barriers, such as WHO's diagnostic pre-qual program (or have it recognize prior approvals by rigorous regulatory authorities)"		✗ Public funders: "interesting and valuable, but we wouldn't fund it"  Philanthropic: "We really like these, as they mitigate risk all the way along".

	MNCs	SMEs	IDCs	Diagnostics firms	PDPs	Funders
Push + pull	"The best option combines them, and offers different incentives for early and late-stage R&D"					"Both are needed"
Public markets & public purchase commitments	"Our preference is a purchase commitment"; "a long-term commitment (10-15 years) from a procurement agency like GAVI or UNICEF would be best"				"purchase of existing vaccines would be the best signal",	✗ Public
AMCs	"tend to be market-distorting rather than market supporting"; "We're trying to persuade governments to do a purchase fund, not an AMC". "They're OK but not a magic bullet"	✗ "had too many conditions and was only for one disease"	yes or no?	✗ "big incentives are appealing to some policy makers but only small amounts are needed for diagnostics, since manufacturers normally take a proven technology and extend it for ND use"	No data	
PRV		"a good match for the SME model but would likely need additional up-front funding"	"incentivises MNCs to partner with us or buy-out our IP "	✗ "priority reviews do not exist for diagnostics; even if they did, PRV doesn't provide an 'up front' incentive for manufacturers"		
Orphan drug Paediatric exclusivity						Public
Push funding via PDPs	PUT IN A COUPLE OF QUOTES ACROSS THE MCN/IDC/ PDP	✗				Public Philanthropic
Direct grants to companies	"...useful to subsidise clinical trials in DCs"					
PDP-FF	"Mixing together commercial and not-for profit models is messy"	"Companies don't like the public sector taking royalties on profits, even if those profits are allocated back to improving DC health."			"We like the long-term, low admin approach"; "A 10-year grant would be simpler and would omit the need for a PDP-FF"	
Milestone pulls/ prizes (as an adjunct to bigger solutions)	✗	"A series of pulls along the dev't path are our No.1 preference –but milestone payments are preferred to prizes"				
Regulatory efficiencies	PUT IN QUOTES FOR MNC, SME ETC			"the most immediately effective incentive would be eliminating regulatory barriers, such as WHO's diagnostic pre-qual program (or have it recognize prior approvals by rigorous regulatory authorities)"		✗ Public funders: "interesting and valuable, but we wouldn't fund it"  Philanthropic: "We really like these, as they mitigate risk all the way along".

## Conclusions

### Least effective proposals (performance and acceptability) overall

- Biomedical R&D Treaty
- TIPR
- Large endstage prizes (TB, Chagas, cancer, PMV/pf, Prize Fund to Support Innovation and Access)
- Economic prize system
- ND tax breaks

### Promising proposals

- FRIND –good scores on all criteria, despite large data gaps: Very promising

Performed patchily, with high scores in some areas but very low scores in other areas. These proposals would be interesting to analyse further, with a view to pulling out high-performing elements or amending low-performing ones:

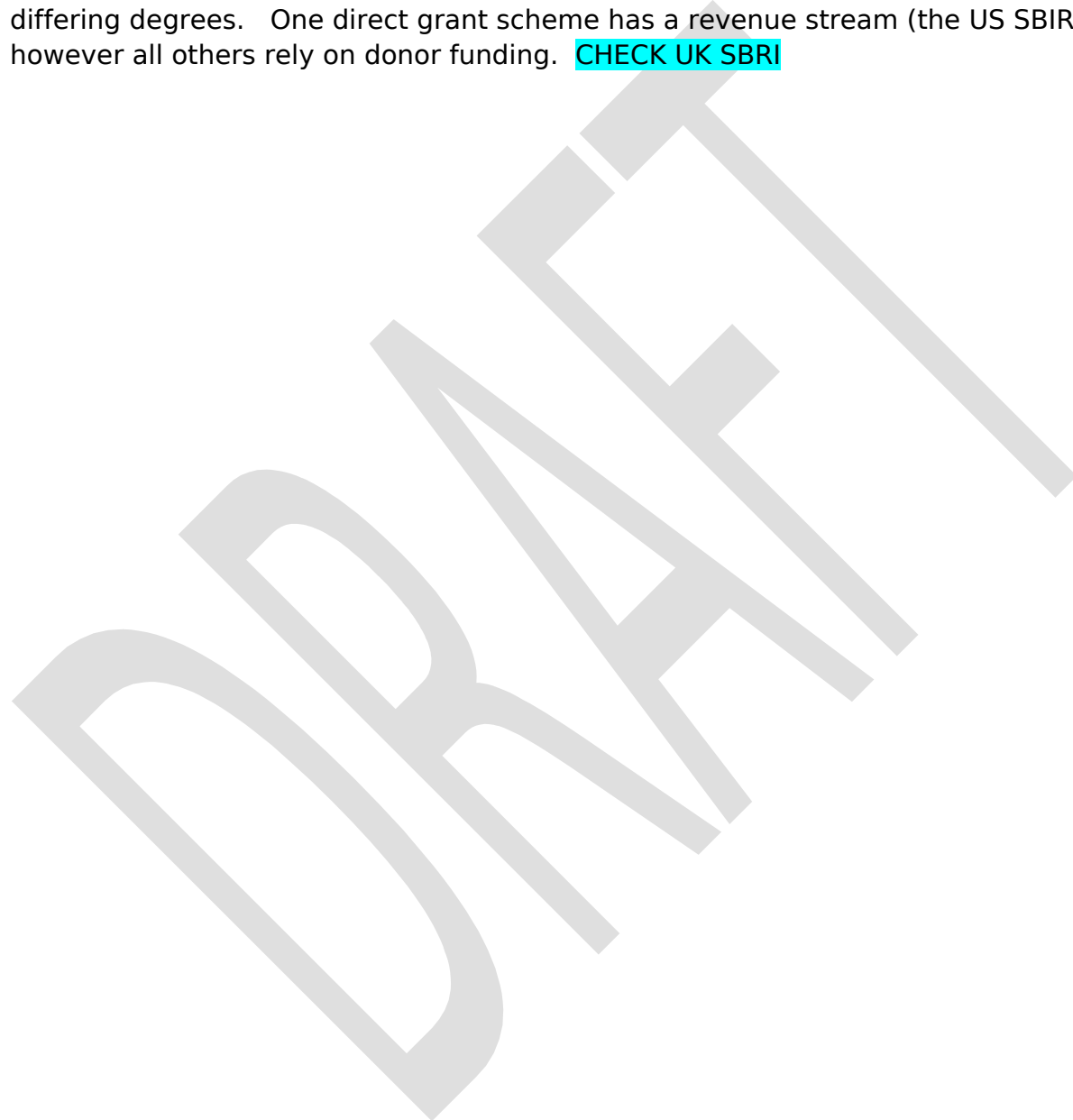
- PRV: Return on investment is highly variable for both the developer and the funder, as payout size and DC product are not linked to each other. Needs amendment to tighten it up and ensure better DC impact and value for money
- Orphan drug legislation: Performs moderately well on operational and financial aspects; could be greatly improved to increase DC impact
- HIF : As before

### Most effective proposals (performance and acceptability)

<i>Mechanism</i>	<i>Proposal examples</i>	<i>Qualifications, enhancements and linkages</i>
Procurement funds		<i>To add later</i>
PDP funding proposals	particularly IRFF	Limitations in that they only work with PDP diseases
Direct grant schemes for small companies	SBIR style	But only if properly designed to meet DC needs, needs re-targetting.
Research prizes/ Milestone	Innocentive style	But only for small companies

prizes		
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Collectively these proposals provide, or could provide, good coverage for development R&D for all DC diseases. All proposals are already implemented, to differing degrees. One direct grant scheme has a revenue stream (the US SBIR), however all others rely on donor funding. [CHECK UK SBRI](#)



## Manufacturing and Distribution

Target groups:

Manufacturing: MNCs, Generic manufacturers, PDPs

Distribution: public, MNCs and Generic manufacturers

Thirteen proposals are designed to fund manufacturing and distribution of products for DCs. Only two proposals have been implemented, these being the two publicly funded pull mechanisms, highlighted in grey in Table Y. Both apply only to selected DC products.

Table Y (grey=operational)

CATEGORY	MECHANISM	FRAMEWORK POSITION (S)	DEVELOPING COUNTRY IMPACT	OPERATIONAL & FEASIBILITY	DATA GAPS
Alongside IP Pull Impact Payment funds	Health Impact Fund	Manufacturing & Distribution	† †		??
	Cancer prize fund	Manufacturing & Distribution	† †		?
	Economic Prize system	Manufacturing & Distribution	† † †	★	?
	Chagas Disease Prize Fund for the Development of new treatments, diagnostics and vaccines	Manufacturing & Distribution	† † †		?
	Priority Medicines and Vaccines Prize Fund (PMV/pf)	Manufacturing & Distribution	† †		???
	Prize Fund to Support Innovation and Access	Manufacturing & Distribution	† †		??
Alongside IP Pull prizes	Biomedical R&D Treaty	Manufacturing & Distribution	† †		??
	Prize fund for development of low cost RDT for TB	Manufacturing & Distribution	† † †		?
Alongside IP Push	Funds (Global Fund for R&D; Canadian ND Innovation Fund)	Manufacturing & Distribution	† †		??
Pull public	Advance Market Commitment (AMC)	Manufacturing & Distribution	†	★ ★	?
	Minimum Volume Guarantee / Access RH (Reproductive Health)	Manufacturing & Distribution	†	★ ★	???
TBD	Cap to Fund (C2F) Model	Manufacturing & Distribution	†		???
TBD	Patent Fees/Green IP (GIP)	Manufacturing		★	?

Although grouped together, these proposals take quite different approaches to underwriting broad DC access to new products. The Alongside-IP pull mechanisms are focussed on increasing DC patient access by allowing generic or fixed low-price access immediately a new product is registered, therefore they do not need a product purchase fund. The Advance Market Commitment and Cap2Fund models work on the principle of earlier access to low-priced products, however both first allow a high-priced window of varying duration to provide returns to the developer. The Minimum Volume Guarantee (and procurement funds in general) also bring



prices down to the lowest competitive level, however they can only do so when patents have expired and competition is possible. For patented products, prices can be driven down through economies of scale, but not to the levels achieved by generic competition.

## Performance against criteria

### DC impact

- Most of the Alongside-IP prize proposals scored well on DC impact, due to their ability to provide patients with immediate low-price access to new products.

By contrast, the two public pull funds (AMC and Minimum Volume Guarantee (MV), both of which are implemented) have an average performance against DC impact. The MVG scored very well in areas where it is applicable (i.e. where generics are already available) but it does not encourage early generic production and thus scored less well on overall access, DC capacity building and technology transfer. The AMC scored less well due to its failure to preferentially incentivise low cost-of-goods R&D approaches and low prices, and relatively weak technology transfer stimulus. Cap 2 Fund did not perform as well as it has a long delay in access to lower generic prices compared to other proposals, and no price subsidy during this period.

### Operational efficiency and feasibility

- There were no high-ranking proposals.

Proposals that scored moderately well were:

- The Minimum Volume Guarantee, despite lack of data on many key points, suggesting it has high potential and is deserving of further exploration
- The AMC would have performed better, but was dragged down by the difficulty of putting each AMC in place and the requirement to raise large new tranches of funding for each new product, thus also scoring poorly on political feasibility.

The remaining mechanisms suffered from lack of data but, even taking this into account, performed so poorly as to not merit inclusion. The Green IP/patent fee proposal, in particular, is so complex as to be almost inconceivable.

Of the higher-scoring proposals, the MVG is already in place for reproductive health products and could be applied to any disease, although we note that its maximum benefits can only be achieved where off-patent products are available. The AMC

applies to one product only and would be very difficult to scale up to give broad disease and product coverage.

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<b>Financial aspects: Manufacturing and Distribution Mechanisms</b>				
	<b>Revenue Stream (and whether secure)</b>	<b>Funding for manufacture and distribution</b>	<b>Scope</b>	<b>Quality of funding</b>
MVG	Efficiency so no revenue needed where sales exist.  If <u>no</u> existing purchases, then N/A  Yes for developer (purchase contract)	<b>No funding needed</b> , as existing purchases are pooled. Savings of \$3-11m in first 3 years, giving a return on investment of 0.6 - 2.4. Est. start-up costs \$5m for the first 3 years, then self-sustaining through user fees.	Reproductive health products (oral contraceptive/ devices)	High
Patent fees/ Green IP	Yes: From patent office revenues, insurance premium, and tax from patent transactions +	<b>Billions</b> available to:  - allow Compulsory Licenced generic production (IP owner recompensed from Fund) & boost tech transfer to enable this - subsidise LIDC prices	ARVs initially Any product potentially	High
Cap to Fund (C2F) Model	Efficiency so no revenue needed  To a degree for developer (fixed cap on profits; but unclear over how long returns will be earned)	<b>No funding needed, allow generic competition after “Profit cap” has been reached</b>  Profits caps negotiated per product.  No funds for purchase for LMICs	Could apply to any product	High
AMC	NO for funder  YES for developer (purchase commitment)	<b>Yes:</b> \$1.5bn/10years <b>for ~200 million doses annually</b> shared amongst the contracted vaccine manufacturers (likely <10); subsidised for LMICs  Will require higher sums for future AMCs (if novel products). Start up costs relatively high, not self-sustaining.	Vaccines for one disease	Moderate
HIF	No	<b>Billions/year ~6billion/year or 0.01% of global income needed for rewards proportional to health impact over a 10 year period for new products and 5 years for incremental</b>	DC products	Moderate

		<p><b>R&amp;D. 10% of this figure would be needed to measure health impact.</b></p> <p>No funds for purchase for LMICs (although suggests this may be needed)</p>		
Econ prize system (Canada)	No	<p><b>100s of millions from 5% of Canada's aid budget annually to buy-out IP and reward developers based on health impact of innovation.</b></p> <p>No funds for purchase for LMICs</p>	ND products	Low
Disease-specific Prize Funds	No, for cancer prize an percentage of DC cancer budget	<p><b>100s of millions split across :</b></p> <ul style="list-style-type: none"> <li>- End prize for product - based on health impact (except for TB prize)</li> <li>- Open info reward (% of End prize)(Except for cancer prize)</li> <li>- IP made available to a licensing pool to get prize</li> </ul> <p>No funds for purchase for LMICs</p>	All cancer products All Chagas product TB diagnostics	Low
Prize Fund to Support Innovation and Access	No	<ul style="list-style-type: none"> <li>- <b>Billions? /year but funding source not identified.</b> End prize - based on health impact</li> <li>- Open info reward (% of End prize)</li> <li>- IP made available to a licensing pool to get prize</li> </ul> <p>No funds for purchase for LMICs (although suggests this may be needed)</p>	All DC products	Low
Priority Medicines and Vaccines Prize Fund (PMV/pf)	No, <b>sourced from 10% of donor funding</b>	<p><b>Billions/year</b></p> <ul style="list-style-type: none"> <li>- End product prize (80%) - based on health impact</li> <li>- Open info reward is an additional prize</li> <li>- IP made available to pool to get prize</li> </ul>	All DC products	Low

		No funds for purchase for LMICs (although suggests this may be needed)		
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## Financial aspects

- Minimum Volume Guarantee (for off-patent products)
- Green IP (with provisos)
- Cap2Fund (with provisos)

The Minimum Volume Guarantee is the most cost-effective mechanism, since it does not require funding and provides lowest generic prices to patients, however this assessment only extends to off-patent products; benefits are far lower when applied to new products. For novel products, both Green IP and Cap2Fund performed well, with strong provisos: Green IP only perform well if all the proposed revenue streams can be mobilised (in our view, this is highly unlikely – see operational); while for Cap2Fund success will depend on the final ‘multiplier’ chosen, which determines how much profit the developer will be allowed to receive; and does not include a fund to purchase or subsidise products for the poorest in LIDCs, who cannot afford even commercial generics.

The AMC performed less well due to its failure to harness competitive or volume pricing (this being the trade-off to stimulate R&D); while, for impact-based proposals, the return to each developer cannot be known, reducing its potential score on value for money. Most prize funds also require an additional unquantified (and sometimes unmentioned) fund to purchase or subsidise products in LIDCs.

## Acceptability to funders and target groups

Product developers unanimously preferred public purchase funds to support manufacture and rollout of DC products – perhaps unsurprisingly, as this is a traditional market solution that matches their business models. End prizes were seen as only suitable for smaller firms and specific targets, with larger diagnostic firms being most likely to respond to them.

Impact-based end-prizes, and specifically the HIF, were viewed as interesting by all groups, however there was a unanimous view that they needed substantial amendment to be feasible: if this work could be done, many groups including large companies, PDP and funders say they might respond to this approach.

In general, public funder preferences aligned fairly poorly with developer preferences.

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Table X: Likelihood of incentivizing target groups and appeal to funders

	MNCs	SMEs	IDCs	Diagnostics firms	PDPs	Funders
Purchase funds(Not MVG specifically)	"Our preference is a purchase commitment";				"purchase of existing vaccines would be the best signal"	✗ Public
AMCs	"We're trying to persuade governments to do a purchase fund, not an AMC". "They're OK but not a magic bullet"	✗ "Has too many conditions and is only for one disease"	yes or no?	✗		
Impact based prizes to put IP into a pool (HIF in particular)	? "Might be attractive for areas where there is NO market"; "interesting"  BUT "No attraction In its current form"; "Anything that introduces uncertainty is almost impossible to overcome from an incentive perspective."	✗ "A utopian idea but would be a nightmare to implement"; "Firms wouldn't know how many other companies they were competing with for a share of the impact fund"			? "Aligns the incentive with the outcomes we really want - but is it workable?" "Should definitely be in our 'to be explored more' basket"	? "Creates a market where this isn't one already"; "Like the idea <i>in theory</i> BUT "needs more automaticity"; "impractical"
End prizes (cash) to put IP into a pool	✗ Have a place for the right diseases and the right kinds of organizations ( <u>prob for smaller organizations</u> )  BUT  "Milestone payments not for the full R&D process"; "Should work within the IP system"; "Only effective if as big as the expected market returns"	✗		"Larger diagnostic firms can respond more to prizes"; "Many diagnostic firms would probably be interested in prizes that reward <u>interim</u> outputs"	? Not sufficient as a stand-alone; Would have to be VERY large"; Prize has to be same as value of selling IP"  BUT "Can incentivize really out-of-the-box thinking" ; IP-giveup might work for diseases with no market; "I wouldn't want to give up IP but I would if I had to"	Yes, could be viable; Would be happy to fund smaller-prizes directed to specific uses; Prizes as the main pull at the end don't de-risk the development process



## Conclusions

### Least effective proposals (performance and acceptability)

- Green IP is judged as operationally impossible

### Promising proposals

The impact-based proposals had very poor operational efficiency and feasibility, which rendered them unattractive to funders and developers, however they performed well on DC impact and had some elements of interest. These positive elements make them interesting as a method of rolling out affordable products to DC patients, particularly in low or no profit disease areas. They should be analysed further with a view to pulling out high-performing elements or amending low-performing ones. The lead proposal to focus on is the Health Impact Fund.

### Most effective proposals (performance and acceptability)

No manufacturing and distribution proposals performed really well, with those below being only partial solutions. This is a major problem for developers, who view final purchase as the most important pull; and for those groups who have already invested a great deal in R&D of new products that are now moving close to registration.

<i>Mechanism</i>	<i>Proposal</i>	<i>Qualifications, enhancements and linkages</i>
Purchase funds	E.g. MVG	For generics in its current form.
End-prizes	Cash prizes	Likely only for diagnostics: cheaper and quicker; allows funder and developer needs to better align. Operational issues would need to be improved

These proposals cover, or could cover, generics and novel diagnostics. Diagnostic cash prizes have not been implemented and would rely on donor funding. However, there are no suitable proposals to underwrite broad manufacturing and distribution of novel products for DCs.

## Efficiencies

Target groups:

MNCs, Generic manufacturers, PDPs, SMEs

The vast majority of R&D financing proposals focus on funding the existing unwieldy R&D system, rather than on streamlining or improving it. Only seven proposals were targeted at R&D efficiencies to reduce R&D costs and deliver innovations to patients more quickly.

Of these, Removal of Data Exclusivity has not been implemented; and DC regulatory harmonization (regionally, as well as with WHO and relevant Western regulatory processes) has begun but is nowhere near complete. The remaining proposals have been partially or fully implemented, **as marked in grey in the Table below**. All major Western regulatory authorities provide expedited regulatory review for priority products (EMA, FDA etc). The EC IMI is well established (only in Europe); and a variety of open source schemes are operating for research and discovery, including a formal Open Source Drug Discovery programme funded by the Indian Government, and various informal Open Source collaborations. The UNITAID patent pool comes into full operation in early 2010; while the GSK patent pool was launched in the first half of 2009.

CATEGORY	MECHANISM	FRAMEWORK POSITION (S)	DEVELOPING COUNTRY IMPACT	OPERATIONAL & FEASIBILITY	DATA GAPS
Early pipeline efficiencies	Opensource	Research	↑ ↑	★ ★	?
		Development	↑ ↑	★ ★	?
	Patent pools - GSK	Development	↑		???
	Pre-competitive R&D platform – govt funded (e.g. EC Innovative Medicines Initiative (IMI))	Research			★ ★
Development				★ ★	?
Late pipeline efficiencies	Patent pools - UNITAID	Development	↑ ↑ ↑	★ ★	?
		Manufacturing	↑ ↑	★ ★	??
	Expedited Approvals	Late development		★ ★	?
	Removal of data exclusivity	Manufacturing and distribution	↑		??
Regulatory alignment	Developed/Reference Country regulatory alignment	Late development	↑ ↑ ↑	★ ★	?

These proposals fall into two categories:

- Research to develop tools that improve efficiency, such as surrogate markers to reduce trial times, platform technologies, and methods to improve the predictive value of trial data. Since this is research, it requires funding. Only one proposal falls into this category - the EC-IMI, which has a budget of Euro 2 billion over 5-10 years, half from the pharmaceutical industry and half from the European Commission

- Efficiencies themselves, e.g. streamlining or harmonising existing systems. These require very little funding - only the minimal investments needed to amend existing processes, or to operate the efficiency mechanism - but they can be long and difficult to implement, especially across jurisdictions. All other proposals fall into this category.

## Performance against criteria

We note that efficiency proposals are not assessed on financial aspects, as it is difficult or impossible to estimate the value generated, and many have little or no dollar-cost (as opposed to cost in time and effort).

### DC Impact

While efficiencies tend to benefit all products, some have a higher DC impact than others. The proposals that scored well were:

- **DC regulatory harmonisation** (extremely well)
- UNITAID patent pool (extremely well, but only covers HIV drugs)
- Open-source R&D scored somewhat less well but sufficiently high to warrant inclusion

The GSK patent pool proposal applies to multiple neglected diseases but was difficult to judge due to lack of information on key points.

Both the EC-IMI and expedited review by Western regulators scored poorly. The EC-IMI platform is unlikely to deliver high DC value even if it chose to include a developing country disease strand, since product developers are likely to focus on more commercially relevant aspects (e.g. travel or military applications); issues such as DC price and formulation suitability are not likely to be prioritized; and technology transfer and DC capacity building are non-existent. Expedited review by Western regulatory authorities is also of limited benefit to DC patients, who must still wait for national regulatory review and approval and WHO prequalification (for some products).

### Operational efficiency and feasibility

Lower cut-off points were used to assess the efficiency proposals since, almost by definition, they require change in current systems and thus are harder and slower to put in place, particularly across several jurisdictions. Using these lower cut-offs, many proposals scored well for operational efficiency and feasibility:

- DC regulatory harmonisation
- Expedited approvals (may have scored higher but had some data gaps)

- UNITAID patent pools (despite substantial data gaps)
- Pre-competitive platforms
- Open source

The GSK patent pool, and Removal of Data Exclusivity had insufficient data to make an assessment.

Table X: Likelihood of incentivizing target groups and appeal to funders

	MNCs	SMEs	IDCs	Diagnostics firms	PDPs	Funders
Tools to cut R&D cost & time	"We would be VERY interested in ways to reduce the cost of, and simplify, R&D - this is a real gap"; "Surrogate marker work is "incredibly important" to accelerate and simplify R&D"; "Yes, yes, yes!"				✓ "Efficiencies are tremendously helpful...but they don't appeal to people who don't have to do the R&D"; "We now spend one-third of our funding on developing enabling and platform technologies"; "Yes!! These have a very high value"; "The problem is that governments don't want to fund R&D efficiencies because they want bling"	Philanthropic "We really like these, as they mitigate risk all the way along - an enabling environment makes things cheaper"; "We must reduce regulatory costs: It didn't use to cost this much to make a drug" ✗ Public "Yes, very interesting and valuable, but we wouldn't fund it" (NB: EC has funded it, but G-FINDER confirms overall limited spend on platform tools and technologies
More efficient & harmonized systems	"A harmonized regulatory system across many countries would be very, very significant in terms of de-risking"; "...would be an enormous help to companies working on DC products - currently, the entire burden is on developers"; "More cooperation and harmonization between DC ethics committees is necessary"	"International regulatory (EDL, WHO drug prequal, WHOPEs etc) needs a major overhaul"; IP transaction costs are too high"		"Diagnostic companies are being deterred from getting involved in R&D of diagnostics for poor countries as the WHO system is so messy and slow it isn't worth it"; "Improved WHO efficiency and transparency would remove the "scare factor" for diagnostic companies"	"These are very important and should be one of the main focus areas"	Public Yes, interested in regulatory harmonization, WHO systems, ethics committee line-up
Patent pools	"Can make sense for					

## Acceptability to funders and target groups

Investing into efficiency tools was seen as a top priority for product developers and philanthropic funders, as seen in Table X, however public funders were cooler on the idea. It seems likely that public reluctance to invest in this area is a false economy, costing more dollars than it is saving.

By contrast, there was a strong consensus across all groups on the need for more efficient and harmonized systems, with regulatory processes being a clear front-runner.

## Conclusions

### Least effective incentives (performance and acceptability)

- Removal of data exclusivity

- Expedited approvals

### Promising proposals

- Open-source. While not clear that many developers would use this approach, it nevertheless scored sufficiently highly to warrant further exploration
- UNITAID patent pool. Scores very well on DC impact and operational/feasibility, but may need additional work to make it attractive to product developers across many diseases (they need a reason to put their IP into the pool)

### Most effective **incentives** (performance and acceptability)

<i>Proposal</i>	<i>Qualifications, enhancements and linkages</i>
DC regulatory harmonisation	
Pre-competitive R&D platforms	ONLY if DC focused – strong proviso

These proposals would cover all DC diseases, and both early and late development. DC regulatory harmonization does not require a revenue stream, and is partially underway. Pre-competitive platform programmes are also underway (some in commercial areas; others in ND areas), however they have no revenue streams and rely on donor funding.

<sup>i</sup> Pekar N, editor (2001) *The Economics of TB Drug Development*. New York: Global Alliance for TB Drug Development. Available: [http://www.tballiance.org/downloads/publications/TBA\\_Economics\\_Report.pdf](http://www.tballiance.org/downloads/publications/TBA_Economics_Report.pdf)

<sup>ii</sup> Serdobova I, Kieny MP (2006) Assembling a Global Vaccine Development Pipeline for Infectious Diseases in the Developing World. *Am J Public Health* 22 (9): 1554—1559. Available: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1551949>