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DELPHI FORESIGHT ANALYSIS

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Summary

The INNOVA-P2 project seeks to develop a plan for amending the current Intellectual Property Rights (IPR) regime for rewarding pharmaceutical innovations. Amendments to the current system are required if reasonably priced health care is to be delivered to patients in all areas of the world. The INNOVA-P2 project focuses on a potential two-tiered patent system, which would create a new patent (Patent-2) that is complementary to existing monopoly patents, leaving innovators free to choose the traditional approach to recouping the costs of medical innovation, or adopt the Patent-2 approach. Reward would be in proportion to the positive impact on health globally. From this, the Health Impact Fund (HIF) scheme has been designed to facilitate innovation in the pharmaceutical sector regarding the treatment of neglected diseases or diseases of poverty. A critical issue regarding the effectiveness of the HIF is the acceptance by key stakeholders and end-users, including industry and national governments, and international organisations. A two stage, international, expert stakeholder Delphi survey (N=25) was conducted to identify:

- Potential barriers to implementation of the Patent-2 scheme, and how these can be overcome.
- Requirements for acceptance, harmonisation and implementation of the Patent-2 scheme globally and by individual stakeholders.
- The conditions and approach required to develop an international consensus policy.

The results of the Delphi survey suggest that there is considerable stakeholder and end-user support for an HIF scheme in principle, although some practical difficulties will require resolution prior to practical implementation of an HIF. These include the focus of the scheme (in terms of diseases included, size of the scheme, appropriate and effective metricisation of health impacts, and whether the HIF should include other health interventions over and above pharmaceutical developments). Potential diversion of funding from other initiatives was also perceived as problematic, and would need to be considered through effective international harmonisation of funding practices.
Introduction

The INNOVA-P2 project seeks to develop a plan for amending the current Intellectual Property Rights (IPR) regime for rewarding pharmaceutical innovations. The existing IPR rules for incentivising pharmaceutical research have been interpreted as causing problems regarding innovation with regard to the treatment of neglected diseases, or diseases of poverty. Long recognised among international health experts, this fact has come to be more widely understood through the AIDS crisis, where there is tension between the health care needs of poor patients and the need for drug companies to recoup research and development investments (Barnard 2002). Despite recognition of the need to amend the current system in order to deliver reasonably priced health care to patients around the world, the implementation of concrete activities in this regard has not occurred, in part because of pragmatic difficulties in actioning change. The INNOVA-P2 project suggests that reforms of the existing patent system are achievable through application of a potential two-tiered patent system, (“Patent-2”) (Pogge 2005). This scheme would create a new patent (Patent-2) that is complementary to existing monopoly patents, leaving innovators free to choose the traditional approach to recouping the costs of medical innovation, or adopt the Patent-2 approach. Patent-2 holders would not have veto powers over the reproduction of their inventions (as is currently the case), thus allowing medicines to become available at competitive market prices more rapidly. Patent-2 holders would instead be rewarded, out of public funds, from a Health Impact Fund (HIF) in proportion to the impact of their invention on the global burden of disease (GBD), or health impact (Hollis and Pogge 2008; and Banerjee, Hollis and Pogge 2010; see also www.healthimpactfund.org).

Forging a consensus regarding implementation of the Patent-2 scheme is the ultimate objective of INNOVA-P2. A critical issue regarding the effectiveness of the HIF is the acceptance by key stakeholders and end-users, including industry and national governments, and international organisations. This consensus refers to agreement on a realistic roadmap that this scheme will need to follow in order to achieve global endorsement beyond the timeline of the project. This task can be achieved by policy consensus that is based on credible foresight analysis. The aim of the research presented in the current report was to identify potential stakeholder and end-user perceptions of implementation preferences, as well as perceived implementation barriers, relevant to the potential operationalisation of an HIF scheme.
The Patent-2 scheme will only be successful if there is agreement across policy, industry and end-users regarding the appropriateness of its aims, its perceived justice, sustainability, and the international harmonisation of relevant policy initiatives and their implementation. Identification of relevant experts for the database focused on the need to obtain expert opinions regarding:

- Potential barriers to implementation of the Patent-2 scheme, and how these can be overcome.
- Requirements for acceptance, harmonisation and implementation of the Patent-2 scheme globally and by individual stakeholders.
- The conditions and approach required to develop an international consensus policy.

To enable an effective international foresight analysis to identify consensus (or lack of it) across important stakeholder groups, 26 experts from relevant stakeholder groups were surveyed using a two round Delphi survey.

**The Delphi method**

The inclusion of international expertise demands the use of a methodology that makes it feasible to consult with disparate experts. International workshops, whilst facilitating the interactive exchange of opinions, may incur prohibitive costs and raise pragmatic problems in terms of time and travel. Furthermore, such events can generally only involve a small number of participants, and their outputs may be constrained by social and political processes that often result in sub-optimal decision-making (e.g. Rowe, Wright, and Bolger, 1991). Questionnaires allow the surveying of diverse and numerous experts in different geographical locations at reasonable costs, while eliminating group interaction and thus pre-empting problematic social and political processes (e.g. the group’s position being overly influenced by dogmatic or high-powered individuals). However, surveys do not provide for interaction and debate. As a consequence, though a survey is useful in scoping different opinions, it cannot offer the prospect of conflict resolution.

Participant input was obtained using the Delphi methodology. Delphi (Rowe and Wright 1999) is an iterative technique used for the systematic measuring and aiding of forecasting activities and decision making, and has been applied in a variety of disciplines. Delphi provides a structure to facilitate group communication on a specific task, and is recognised as being an effective procedure
when reliable consensus of opinion needs to be obtained from diverse groups, including key end-users, such as the pharmaceutical industry, policy advisors and makers, funding bodies and public health authorities. Delphi involves sequential collection of questionnaire data interspersed with controlled opinion feedback.

Delphi methodology (e.g. Linstone and Turoff, 1975) was used to investigate the views of international experts from disparate geographical regions. This methodology involves the repeated polling of experts, whose answers are used as feedback in subsequent rounds. By providing feedback from the answers of others, Delphi creates interactivity and dialogue, as may be achieved in group meetings, while at the same time allowing for the benefits of a computerised survey, in terms of cost, access to more participants and a wider distribution of experts than might otherwise be possible. Specifically, Delphi methodology is characterised by having at least two rounds in which opinions are recorded and fed-back to participants – who remain anonymous to one another so as to pre-empt some of the potentially negative processes previously discussed (i.e. removing indicators of power, reducing conformity pressures, enabling opinion change without fear of ‘losing face’). Often there is an exploratory round, in which key issues are identified, followed by one or more rounds of focused, quantitative questions. At the end of the process, the ‘group’s’ position is indicated by the average response to the particular questions – though the extent of agreement/disagreement is also noted (Delphi generally aims to acquire a consensus position, though – importantly - the process may instead help to establish that there are fundamentally un-reconcilable positions too). Beyond these basics there is considerable variation in how Delphi surveys are implemented, such as in terms of the nature of feedback provided, the size of sample chosen, and the number of rounds used. Generally, pragmatic factors influence how any Delphi is implemented. For example, in real-world applications there are rarely more than two structured rounds since experts tend to be busy and unprepared to contribute beyond these. However, research suggests that most change of opinion takes place over the first two rounds anyway, so that further rounds are unnecessary (i.e. there are insignificant degrees of change over subsequent rounds – see Rowe, Wright, and Bolger, 1991). Pragmatic factors also tend to influence the numbers of respondents used, although there is no clear evidence for any particular sample size being better than another. In terms of feedback used, there is some, limited, evidence that feedback of rationales for decisions allows better discrimination of estimate/forecast quality on subsequent rounds than does feedback of statistical information alone.
In this study, rationales for experts’ stated judgments are collected and used as feedback in subsequent rounds. Regardless of the way in which Delphi is implemented, however, empirical research has generally shown that the method (in its various forms) leads to better (e.g. more accurate) judgments and forecasts than regular interacting groups. Delphi has also proven to be a useful method for eliciting international expert opinion within the domain of governance, for example, relating to food risk analysis, or development of research policy and agenda setting for future research activities (Wentholt, Rowe, König, Marvin, and Frewer, 2009; Frewer, Wentholt, Marvin, Ooms, Fischer, Coles, and Rowe, in preparation).

In order to identify potential barriers to successful global implementation of the Patent-2 scheme, an international Delphi foresight exercise was conducted to complement Innova-P2’s reality-check work in China and India (Workpackages 2 and 3).

**Methods**

At the outset, an international database of experts was established, who were to be contacted regarding potential participation in the Delphi Survey. Potential experts were identified through collaboration and discussion with other Innova-P2 consortium members. Thus personal contacts were utilised, together with the application of the cascade methodology. This approach has been proven to be effective in recruiting potential participants to international Delphi surveys in previous research (Frewer, Wentholt, Marvin, Ooms, Fischer, Coles, and Rowe, in preparation). Policy actors, end-users and other stakeholders, including those drawn from the international community of relevant policy advisors and policy makers, pharma-industry actors, academia and public and private funding bodies, were identified.

In an initial round of consultation, a semi-structured questionnaire (Annex 1) in MS Word format was developed by Wageningen University (partner 7) in consultation with other Innova-P2 project partners. An invitation to experts to participate in the survey, an explanation of the Delphi process, and a summary of the HIF scheme was also prepared (Annex 1) and was circulated by email to 65 experts, stakeholders and end-users identified in the database. Participants were also provided with weblinks to key documents relating to Patent 2 and the HIF approach (www.healthimpactfund.org). The purpose of round 1 was to enable participants to comment on the various aspects of the proposed HIF approach, its potential acceptability to different stakeholders, to
identify potential barriers to successful implementation of the scheme, to suggest ways in which the scheme might require modification and consider critical success factors relevant to policy development and valorisation together with possible mechanisms and timescales for implementation.

The initial invitation to participate in the study made clear that the Delphi methodology used was an iterative process that would require commitment to at least two rounds of responses.

The anticipated outcome and analysis of this first round semi-structured questionnaire was to provide qualitative information relevant to policy implementation together with expert stakeholder input to the development of a second quantitative questionnaire. The results of round 1 were analysed to identify whether any consensus views had emerged. Minority consensus was classified as reflecting 50-79% agreement with 80% or more agreement being classified as a majority consensus.

The second quantitative questionnaire [Annex 2] was circulated to those respondents who had replied to the first questionnaire, again by email in MS Word format. Round 2 focussed on ranking the barriers and critical success factors identified in round 1. A statistical summary (mean group response) was included in the second round, in order to provide feedback to participants regarding anonymous group responses to individual items. Participants were also informed of those responses for which consensus views had emerged. Views for which there was a consensus in round 1 were not considered for further discussion in round 2.

Results

Delphi round 1.

All questions were developed following consultation with the Innova-P2 project consortium. The key questions asked in round 1 were as follows:

- Is there broad stakeholder and end-user support for the HIF?
- What are the most important barriers to treating diseases of poverty and neglected diseases?
- Are any refinements to the HIF required to address these barriers (including pragmatic issues related to implementation of the scheme).
- Are the estimated resources needed and assessment measures used appropriate in terms of implementation?

A combination of qualitative and quantitative questions was applied to solicit expert and stakeholder opinion regarding these issues. The profiles of participants who responded to round 1
questionnaire are provided in Table 1. Of the initial participants invited, (65 in total) 24 responded, resulting in a round 1 response rate of 39%. Of the participants involved in round 1, all but 1 responded to the second round questionnaire.

Table 1.

Professional affiliations of experts involved in round 2 of the Delphi Questionnaire.

<table>
<thead>
<tr>
<th>Type of organisation</th>
<th>Country of professional affiliation (n).</th>
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<tbody>
<tr>
<td>Pharmaceutical companies and providers</td>
<td>Denmark (1)</td>
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<td>France (1)</td>
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<td></td>
<td>United Kingdom (1)</td>
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<td>International organisations</td>
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<td>National government</td>
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<td>Health services</td>
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<td>NGOs</td>
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<td>Academics</td>
<td>Belgium (1)</td>
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<td>China (5)</td>
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<td>Netherlands (1)</td>
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<td></td>
<td>United Kingdom (2)</td>
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<tr>
<td>Other Stakeholders and end-users</td>
<td>Denmark (2)</td>
</tr>
<tr>
<td></td>
<td>Netherlands (2)</td>
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<td>United Kingdom (2)</td>
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Participants with industrial affiliations, and from developing, (as opposed to emerging) economies were slightly under-represented (Table 1). Other key stakeholder and end-user groups (representatives of regulatory and ethical bodies, IPR lawyers, patient groups, for example), did not participate, although such individuals were included in the original database. In contrast, researchers from academic institutions were over-represented. It is possible that relevant opinions from representatives of these groups might be reflected by the international and NGO participants, but this cannot be assumed to be the case. It has therefore been decided that, in order to validate the results from rounds 1 and 2, a third and final (quantitative) phase will ensure the generalisability of findings across all interested stakeholder constituencies. The results of this final survey will be reported elsewhere. Inspection of self-reported job titles indicates that the majority of participants were relatively senior within their organisations. Women were, however, under-represented (83% of the sample were male).

Consensus opinions identified in round 1.

Agreement across participants was obtained regarding the following issues, which were not subsequently followed up in the second round of the Delphi study. As discussed, for the purposes of
the Delphi exercise, agreement of more than 80% was assumed to indicate reasonable consensus across the sample (see Wentholt et al, 2009; Wentholt et al, in Press; Frewer et al, submitted). In this study, the categories “agree strongly” and “agree” were merged to indicate general agreement. The results indicated that participants agreed on the following items.

- ‘There was a need to adopt “special measures” regarding the treatment of neglected diseases
- The HIF would provide a greater incentive for the pharmaceutical industry to develop tools to fight diseases of poverty
- An HIF scheme would encourage commercial pharmaceutical companies to collaborate with publicly funded research initiatives
- Pharmaceutical interventions should be eligible for an HIF payment
- Health system innovations should be eligible for a HIF payment

These items were not followed up in the second round of the Delphi. In addition, 74% of participants agreed or agreed slightly, and 17% had no opinion that “in addition to national Governments, other donors, such as private foundations, will be willing to fund an HIF scheme”. The low level of disagreement associated with this item suggested that reasonable consensus existed across the participants, and no further questions were asked regarding this issue.

Participants were also asked to estimate the financial size of the fund required annually to enable the fund to be implemented. Almost 60% of participants were unable to estimate whether the proposed size of the fund (US$6bn) was appropriate to fund an HIF scheme. The remaining participants provided a wide range of estimates, and indicated in the quantitative response category provided that they were uncertain of the accuracy of these estimates. This suggests that a convincing economic analysis of the financial resources required will be essential if institutional and industrial “buy-in” to the HIF scheme is to occur.

**Delphi round 2.**

**Open-ended responses from round 1.**

Round 2 items were developed from round 1 responses, in particular from the qualitative responses of participants. Two researchers involved in the study separately coded these open-ended responses,
developing a coding scheme grounded in the data available. Following development of the coding scheme, participant responses were subsequently recoded using the scheme. Where disagreement occurred, the two researchers discussed the appropriate code for a particular response until agreement was reached. The categories identified were then used to develop quantitative responses for inclusion in round 2.

**Barriers to effectively treating neglected diseases**

In round 1, participants were asked to describe potential barriers to treating neglected diseases. Following coding, a range of potential barriers were identified (figure 1). In round 2, participants were asked to rate the extent to which they perceived each potential barrier to represent an important or unimportant barrier to the treatment of neglected diseases. Specifically, participants rated each barrier on a 5 point scale, anchored from “very important” to “very unimportant”. The results are summarized in Appendix 3, *Figure 1, Barriers to treating neglected diseases*.

All of the potential barriers identified from participant responses in round 1 were rated, in terms of importance, over the midpoint of the scale (i.e. were regarded as at least slightly important). However, the barriers rated as being most important included *lack of political will* (national and international), *the cost of medicines*, *local infrastructure problems*, and *lack of innovation in the pharmaceutical sector targeting diseases of poverty*. Of these, perceived *lack of cohesion between different national funding initiatives* is worth mentioning, as this relates to the development of more efficient and harmonised strategies utilising existing resources, rather than the allocation of new resources to the problem of neglected diseases.

**Incentives for the private sector to invest in treating or curing neglected diseases**

In round 1, participants were asked to provide qualitative responses to identify what would incentivise the private sector to invest in treating or curing neglected diseases. The coded categories of responses are provided in Appendix 3, *Figure 2, Incentives for the private sector*. Participants were asked to rate the extent to which they agreed that each of the items identified would incentivise industry investment (five point scales, anchored by “completely agree” to “completely disagree”). Greatest disagreement was linked to *international government regulation* (tied to resource allocation),
and corporate social responsibility (either voluntary or compulsory). Greatest agreement focused on profitability (including, for example, the development of new markets, respect for intellectual property rights, and industry compensation).

Participants also agreed that the potential to develop effective public-private partnerships would also incentivise industry to direct innovative activities to the treatment of neglected diseases.

**Barriers to successful implementation of an HIF scheme**

In round 1, participants were asked to provide qualitative responses to identify potential barriers to successful implementation of an HIF scheme. The coded categories of responses are provided in Appendix 3, Figure 3, Barriers to a successful implementation of an HIF scheme. In round 2 of the Delphi, participants were asked to rate each potential barrier in terms of its importance in potentially preventing successful implementation of an HIF scheme. Participants rated each barrier on a 5 point scale, anchored from “very important” to “very unimportant”. All of the barriers identified in round 1 were rated above the midpoint of the scale as representing, to some extent, important barriers to implementing the scheme. The most important barrier related to “end-of-pipe” delivery of pharmaceuticals. “Buy-in” (for example, by stakeholders, including industry, and developing country governments) was also regarded as potentially problematic. The issue of having enough resources allocated at the start-up of the scheme was also rated as a potentially important barrier.

**Measuring the impact of an HIF scheme**

In the original proposal for the HIF scheme, QALYS were identified as the potential metric by which health impact could be measured following health interventions. Health impact is the basis for payments from the scheme. In round 1 of the Delphi, participants were asked to suggest alternative measures which could be used to metricise health impacts. Responses were coded, and are provided in Appendix 3, Figure 4, Appropriate impact measure. In round 2 of the Delphi, participants were asked to rate the extent to which they agreed or disagreed that each of the measures identified would represent an appropriate metric for assessing health impact. Participants were asked to rate the relevance of each metric from high to low, on a five point scale anchored by “very high relevance” to “very low relevance”. All the metrics assessed were, on average, rated below the midpoint of the
scale. Of all the alternatives, the need to develop new metrics “specific to the needs of developing countries” was rated most positively.

The ability to effectively metricise health impact is an essential element of the scheme, insomuch as pharmaceutical payments from the scheme are contingent on measurable impact. The lack of agreement across the participant sample might, therefore, represent an important barrier to implementation of the HIF scheme overall. However, the specialist knowledge required to test and validate appropriate metrics of health impact may also have resulted in participant uncertainties in responding. Given the importance of this particular issue, further assessment of the appropriateness of potential measures is required. In may be worth investigating whether the use of multiple measures (including developing country specific measures) and triangulating the results is the most appropriate to take. This may be particularly relevant if the HIF is to include pharmaceutical delivery in developed, as well as developing countries, as Health Impact Measures may not be equally sensitive in different socio-cultural contexts. Against this, at least some common metric is required to enable comparative analysis between the developed, and developing, world.

It should be noted that some participants found it difficult to answer this question, perhaps as a consequence of lack of specialist knowledge.

Other issues relevant to the implementation of an HIF scheme

In round 1 of the Delphi, participants were asked to identify any other issues they thought relevant to the implementation of an HIF scheme. Their qualitative responses were coded, and are summarized in Appendix 3, Figure 5, Other issues relevant to the HIF scheme. In round 2 of the Delphi, participants were asked to rate each potential issue in terms of its importance. Participants rated each barrier on a 5 point scale, anchored from “very important” to “very unimportant”. The highest level of agreement was obtained regarding the need to develop an inclusive governance structure for an HIF scheme, involving all major stakeholders, the need to focus on diseases other than Malaria, HIV and tuberculosis, and the need to develop local capacity and capability in health care. Participants also agreed that there was a need to pilot and further refine an HIF scheme before it could be “rolled out”.

Current IPR systems act as a disincentive to pharmaceutical innovation regarding neglected diseases
In the first round, considerable disagreement was identified regarding the extent to which participants perceived that “current IPR systems acted as a disincentive for developing treatments or cures for diseases of poverty”. The question was again asked in the second round, (participants rating their agreement or disagreement with the statement on five point scales anchored by “agree completely” to “disagree completely”, and asked to explain their answers using open-ended responses. Around 26% indicated agreement and 43% disagreement with the statement, the rest neither agreeing nor disagreeing, or indicating that they had no opinion regarding this issue.

Inspection of the qualitative responses indicated a wide range of potential reasons for this lack of consensus, varying from the need for IPR to incentivise innovation, through to overestimation of the role of IPR in treatment development.

For example;

“Not patentable’ products do not get developed because the financial incentives do not exist”

(Director of policy, health organization, UK).

“I think the influence of IPR is slightly overestimated…it is possible to respect IPR and develop more treatments for neglected diseases”

(Academic, the Netherlands)

The importance of (protection of) IPR as potential barrier to the treatment of neglected diseases has not been resolved by the Delphi study.

An HIF scheme would provide an incentive for commercial companies to develop cures not treatments

In the first round, considerable disagreement was identified regarding the extent to which participants perceived that an HIF scheme would provide an incentive for commercial companies to develop cures rather than treatments. The question was again asked in the second round, (participants rating their agreement or disagreement with the statement on five point scales anchored by “agree completely” to “disagree completely, and asked to explain their answers using open-ended responses. Around 50% of the participants agreed with the statement in the second round, the remainder neither disagreeing or disagreeing, or expressing no opinion. Disagreement tended to be linked to uncertainties associated with the financial mechanisms underlying the scheme.
“To be a true incentive for research, a mechanism such as HIF should provide clear visibility on possible financial compensations at a very early stage in the design of an R and D project”

(Pharmaceutical company, Vice President, France)

Participants who agreed that the scheme would act as an incentive, in contrast, tended to present arguments associated with increased certainty of reward mechanisms.

*If the health impact is captured well, a medicine that cures AIDS, for example, would be given the same value as 10 or 15 years of chronic AIDS treatment. It would be a lot more convenient for companies to receive a reward for providing one treatment, than to receive exactly the same reward for providing treatment during 15 years*.

(Academic researcher, international)

“Treatment may be more attractive to commercial companies as they are likely to sell more of a treatment product rather than a cure”

(Research funder, Director, UK).

**Would an HIF scheme primarily benefit developing, as opposed to developed, countries?**

In round 1, considerable disagreement was identified regarding whether the primary beneficiaries of an HIF scheme would be in developing, as opposed to developed, countries. The question was again asked in round 2, with provision of feedback from open ended responses from round 1. In round 2, 77% of participants agreed that the benefits of an HIF scheme would apply primarily to developing countries, and so this was treated as a (marginal) consensus agreement.

**Discussion**

In summary, there was participant agreement regarding the need for an HIF fund, and consensus that such an approach would facilitate the treatment of neglected diseases. However,
some issues needed to be addressed if the final implementation was to be successful. In particular, participants were uncertain as to whether the size of the fund, and the health impact measure(s) to be used as the basis for payments from the fund, were appropriate, and needed to be further thought through. In addition, participants indicated that various barriers (in particular related to stakeholder “buy-in”) needed to be overcome if the fund was to be implemented successfully. Concerns related to the focus of the HIF were also identified. For example, participants indicated that the focus of the HIF should extend beyond the “big three” (HIV, malaria and tuberculosis). The results also suggest that innovations in pharmaceutical development alone are unlikely to reduce disease incidence, unless they are linked to additional innovations in local health delivery infrastructures, and capability and capability building regarding health care provision in developing countries. Without these additional innovations, disease treatment and prevention would not be efficacious. A question arises as to whether these should also be included as innovations in an HIF. Concerns were also raised as to whether the scheme could potentially divert funding from other related research, and further cost-benefit analysis may be needed in this regard.

Several issues have been highlighted that merit further discussion. The first is related to the “end-of-pipe” problem, insomuch as it is not only the issue of novel pharmaceutical development which needs to be addressed when discussing prevention or treatment of diseases of poverty. Delivery of pharmaceuticals to end-users in developing countries, the development of efficacious local health service infrastructures, and the development of “political will” (both local and international) are also important elements of optimising health. On one hand, interventions designed to reduce such social or infrastructural problems may appear as less attractive to researchers in this area, as academic peer approval is more geared towards approving and rewarding research delivering the development of new pharmaceutical treatments than research proposed on the intervention and redevelopment of existing health related-structures and services. However in terms of overall impact on population health in developing countries, it is well-established (Tanner, Lengeler and Lorenz 1993) that in most cases improvements in health care delivery is likely to have a bigger effect than the implementation of a new pharmaceutical product. For example, in many developing countries only a minority of the population have access to modern healthcare treatment. In addition, limitations in the capacity of medical staff available to provide health services may mean that by no means all patients receive the correct diagnosis. Capacity limitations in the health care systems can also limit the
effective management of a treatment. All these factors together affect any attempt at reduction of disease burden and reduce the overall impact of any new pharmaceutical intervention. For example, if a pharmaceutical company develops a new product and the original intervention was effective in 50% of the cases treated while the new product is 90% effective, this will not however lead to the disease incidence being reduced by a health impact of 80%. Even assuming there is no shortage of product available, if only 35% of the population have access medical care, only 65% of those receive a correct diagnosis and therefore the new product and if the treatment is only managed effectively for 75% of the patients then there will only be an improvement in population health (impact) of around 7% over the old product. However if at the same time the pharmaceutical company could also improve capacity for diagnosis and management to say 75% and 85% then the health impact for the same product would increase to around 12% over the old product. Improving access to health care would have an even more dramatic effect on health impact. Combining development of a new pharmaceutical product with a reduction of exposure to the disease would also increase impact significantly, for example by provision of bed-nets alongside malaria treatment or prevention. The results of the Delphi survey confirm this view by suggesting that the development of an effective health impact measure is likely to register optimal improvements in health if both novel pharmaceutical development and local health service and infrastructures issues are considered. However, including both in the proposed HIF may result in a scheme which is too complex and difficult to implement.

Some limitations of the Delphi study need to be mentioned. The first relates to the representativeness of participants in terms of geographical and institutional affiliation. In particular, participants from developing countries and industry were under-represented. The key results of the Delphi study will be used to develop a survey instrument, which will be circulated to a much larger number of stakeholders and end-users internationally. It is hoped that the resulting data will be analysable in terms of cross-sectorial and regional differences between groups of participants, enabling a systematic comparison of concerns and preferences regarding the implementation of the HIF scheme to be made. This will be detailed in the final project report.

Conclusions
The results of the Delphi survey suggest that there is considerable stakeholder and end-user support for an HIF scheme in principle, although some practical difficulties will require resolution prior to practical implementation of an HIF. These include the focus of the scheme (in terms of diseases included, size of the scheme, appropriate and effective metricisation of health impacts, and whether the HIF should include other health interventions over and above pharmaceutical developments). Potential diversion of funding from other initiatives was also perceived as problematic, and would need to be considered through effective international harmonisation of funding practices.

References


APPENDIX 1.

Round 1 Delphi Questionnaire
Dear,

We would like to invite you to participate in a high level expert group as part of the EU funded INNOVA project investigating the feasibility of a Health Impact Fund (HIF) system to promote investment into new medicines while also enabling widespread access. The purpose of this survey is to obtain your opinions on the potential effectiveness and acceptability of such a system.

The Health Impact Fund (HIF) is a new way of stimulating research and development of life-saving pharmaceuticals. To provide wide access to the most effective pharmaceuticals, prices need to be low enough for people to afford – but low prices don’t create strong incentives for innovators to invest in research and development. The proposed HIF is an optional mechanism that offers pharmaceutical innovators a supplementary reward based on the health impact of their products, if they agree to sell those products at designated low prices. The proposed Fund is to be financed mainly by governments. More information about the HIF can be found in several languages in the e-Library at www.healthimpactfund.org.

Delphi Foresight
We are using the Delphi method for our survey. Delphi is an iterative method of gathering expert opinion involving at least two rounds of questionnaires. The aim is to provide participants with (anonymised) feedback regarding areas where there is consensus (or lack of it) among participants. A second Delphi round can then be used to see whether or not the feedback from the first round has an impact on participant opinions.

What does it involve?
In this first round of the Delphi survey, we would like you to comment upon the various aspects of the proposed HIF framework, and to identify factors which may potentially act as barriers to its successful implementation. In the second round, we will provide you with feedback from all of the participants the first round, either in the form of percentage responses to specific items or new questions developed from participant observations in the first round.

The use of the Internet for data collection rather than bringing together an expert group, saves participants’ time and allows us to anonymise feedback from participants. Each participant will only be identified by a code number. The final report will include a list of participating organisations, but individuals will not be identified and the answers given by each participant will be treated as confidential.

How long does it take?
We estimate the first round questionnaire will take approximately 30 minutes to complete (Word format). A second round questionnaire is likely to be shorter, and developed from you answers to the first round questionnaire. When completed, please return by email or fax to lynn.frewer@wur.nl - Fax: +31 317 484361
Delphi Study
The purpose of this Delphi Foresight study is to promote high level policy discussions on the HIF concept, to provide a feasibility check and to assess the level of stakeholder support for the new system in both the developed and developing world and amongst pharmaceutical companies and other pharmaceutical product developers, development agencies, international organisations, national governments and health services, NGOs, patient groups, scientists, IPR lawyers, academics, regulatory and ethical bodies and other stakeholders. The expert group for this study consists of about 50 high level experts drawn from the above stakeholder groups.

Delphi methodology is an iterative method of data collection involving at least two rounds of questionnaires. It is a particularly useful tool for gathering expert opinion from widely dispersed groups of high level stakeholders. The aim is to provide participants with (anonymised) feedback regarding areas where there is consensus (or lack of it) among participants. A second round of Delphi can then be used to see whether or not the feedback has an impact on participant opinions.
FAQs on the Health Impact Fund
A Proposal of Incentives for Global Health

The Health Impact Fund is a new way of stimulating research and development of life-saving pharmaceuticals. To provide wide access to the most effective pharmaceuticals, prices need to be low enough for people to afford – but low prices don’t create strong incentives for innovators to invest in research and development. The proposed Health Impact Fund is an optional mechanism that offers pharmaceutical innovators a supplementary reward based on the health impact of their products, if they agree to sell those products at designated low prices. The proposed Fund is to be financed mainly by governments.

How will it work?
Pharmaceutical innovators holding valid patents can elect to sell their product globally at a low price designated by the Fund. In exchange, they will be paid by the Fund annually for ten years based on their product’s assessed health impact. Participating firms will also offer zero-priced licenses of relevant technology required for manufacturing and selling the product following the ten years.

How much will each firm earn?
The low price will be set to cover manufacturing costs, so firms’ profits will derive from payments from the Fund. Each year, the Fund will have a fixed pay-out – perhaps $5bn – to be distributed among the products firms elect to register. This annual pay-out will be shared among firms in proportion to the assessed global health impact of their drugs in the preceding year. Thus, products will be rewarded strictly in proportion to their health benefits.

What drugs will be included?
The Health Impact Fund would be most attractive for products that are expected to have a large global health impact but relatively low profitability under monopoly pricing. For example, a drug treating a disease mainly afflicting poor people will be an excellent candidate for registration, since typically such products cannot earn high profits. Any pharmaceutical product is eligible, but payments will be largest for those products with the largest health impact. Thus, the Fund will provide important additional incentives to develop drugs for neglected diseases.

How will it affect consumers?
Consumers will benefit from the availability of new drugs at low prices.

Are patent rights affected?
No. Innovators retain their patent rights. They can elect to give up the freedom to charge monopoly prices in exchange for health impact payments from the Fund. Firms will make this election only when they expect higher profits from these payments than from monopoly prices.

How will the Fund be financed?
Governments and other donors would commit to long-term funding. Much of the Fund’s cost to taxpayers will be offset by savings on medicines that would otherwise have been bought at much higher prices. But its greatest benefit is that patients will gain access to important medicines that, without the Fund, would have been too expensive or even non-existent.

How does this relate to AMCs?
These are complementary systems: Advance Market Commitments (AMCs) fix a supplementary payment in advance, but only for vaccines that meet specific pre-announced criteria. The Health Impact Fund rewards any effective vaccine or drug, based on its health impact. Products receiving payments under an AMC would be ineligible for health impact rewards.

What is Incentives for Global Health?
IGH is an international, interdisciplinary collaboration of scholars and experts in public health, economics, ethics and law founded by Dr. Thomas Pogge of Yale University.

How can I find out more?
More information on the proposed mechanism is available at: www.incentivesforglobalhealth.org
Most of the questions in this survey involve simply selecting one response from a number of options. Please use an ‘X’ to indicate which response you select.

For open-ended questions you are free to write as much or as little text as you wish.

Evidence shows that there are diseases or health conditions that have not been allocated as much investment by the private sector compared to other diseases specifically in terms of drug or treatment development. These diseases are popularly referred to as “neglected diseases or diseases of poverty”. Such diseases are mostly, but not exclusively, found in developing countries. Important examples include malaria and tuberculosis.

1. What are the most important barriers to effectively treating neglected diseases and diseases of poverty (open–ended question)

1……………………………………………………………………………………………………………………

2……………………………………………………………………………………………………………………

3……………………………………………………………………………………………………………………

2. Consider you answer to the first question. Do you think that special measures need to be adopted to overcome these difficulties?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>No Opinion</th>
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</thead>
</table>

3. What could incentivise the private sector to invest in treating or curing these diseases or health conditions? (Open-ended question)

............................................................................................................................................................

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4. Current IPR systems are a disincentive for developing treatments or cures neglected diseases or diseases of poverty

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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</thead>
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</table>
The following questions focus on the HIF. We are interested in your opinions regarding the potential effectiveness and acceptability of a HIF-based system.

5. The HIF would provide a greater incentive for the pharmaceutical industry to develop tools to fight diseases of poverty.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

6. An HIF scheme would provide an incentive for commercial companies to carry out research and development on tools to provide cures rather than treatment.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

7. An HIF scheme would encourage commercial pharmaceutical companies to collaborate with publicly funded research initiatives.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

8. Barriers to the implementation of an HIF scheme can be identified.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

If you think there are barriers please explain what these are:

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9. An HIF scheme would help to resolve the ‘last mile’ problem of delivering of pharmaceutical product to patients in developing countries.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>
10. An HIF scheme would deliver health benefits for developing countries.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

11. An HIF scheme would deliver health benefits for developed countries

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

12. An appropriate measure of health impact assessment for use in an HIF scheme would be a Qalys measure.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

13. Better measures of assessment or measurement of impact compared to a Qalys can be identified

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

If you think better measures exist please explain what these are.

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14. Pharmaceutical interventions should be eligible for a HIF payment.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
</table>

15. Health system innovations should be eligible for a HIF payment.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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</thead>
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25
16. In addition to national Governments, other donors such as private foundations, will be willing to fund an HIF scheme

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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17. Do you believe that 6 billion US dollars per year would be a reasonable minimum for operation of a HIF?

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
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If you disagree, what do you believe would need to be the minimum annual size of a Health Impact Fund for it to provide an effective incentive as an alternative to the normal IPR approach?

US $ per year  ........................................

<table>
<thead>
<tr>
<th>US $ per year</th>
<th>I don’t know</th>
<th>No opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>US $...........</td>
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</table>

18. The cost of an HIF scheme will be offset by savings in national health budgets?

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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19. What effect would an HIF scheme have on publicly-funded and not-for-profit research initiatives on neglected diseases such as those of public private partnerships (IAVI, MMV, TB Alliance etc.)? (Open ended question)

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20. What effect would an HIF scheme have on research funded by private foundations (Bill and Melinda Gates Foundation, Wellcome Trust etc.)? (Open ended question)

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21. What effect would an HIF scheme have on existing schemes funded by international organisations (e.g. WHO), the EU and national governments (NIH, DFID, Global Fund, EDCTP). (Open ended question)

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22. Would your organization support in principle, the creation of an HIF?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>No Opinion</th>
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23. Please add any other comments you would like to make. (Open ended question)

............................................................

............................................................

We would now like to ask you to answer a few questions about yourself.

24. Please indicate how old you are

<table>
<thead>
<tr>
<th>Under 25 years</th>
<th>25-35 years</th>
<th>36-45 years</th>
<th>46-55 years</th>
<th>56-65 years</th>
<th>Over 65 years</th>
</tr>
</thead>
</table>

25: please indicate your gender

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
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</thead>
</table>

26: Which of the following best describes the sort of organisation you work for? Please mark only one box.

<table>
<thead>
<tr>
<th>Type of company</th>
<th>Your response (mark with a cross)</th>
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</thead>
<tbody>
<tr>
<td>Pharmaceutical company</td>
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<tr>
<td>Other pharmaceutical product developer</td>
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<tr>
<td>Development agency</td>
<td></td>
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<tr>
<td>International organisation</td>
<td></td>
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<tr>
<td>National government</td>
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<tr>
<td>Health services</td>
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<tr>
<td>NGO</td>
<td></td>
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</tbody>
</table>
27. Please write down your job title or job description

Thank you very much for taking the time to complete this questionnaire. Please return by email or fax to Professor Lynn Frewer at lynn.frewer@wur.nl (Fax: +31 317 484361) If you have any questions or comments please contact Lynn Frewer.
Treatments for human immunodeficiency virus illustrate the dilemma between access to and innovation in medicines: second-line therapies have dramatically reduced the burdens of HIV infection in affluent countries but, at a price of $800 to 1,500 per year, are out of reach for the majority of people until the 20-year patents run out. We could insist on lower prices, but that would undermine the incentives for pharmaceutical companies to develop new medicines. By facilitating access we strangle innovation, and by stimulating innovation through strong patents we obstruct access for many people to new medicines they urgently need.

This terrible dilemma can be avoided by introducing a new option: the Health Impact Fund (HIF). This publicly funded pay-for-performance mechanism would give pharmaceutical innovators the option to register any new product. They would promise to make it available at marginal cost wherever it is needed in exchange for annual reward payments based on the product's global health impact during its first 10 years. The reward payments would be a share of a massive annual pay-out, with each registered product receiving a share equal to its share of the assessed health impact of all registered products.

The HIF would foster innovation—especially against diseases concentrated among the poor: tuberculosis, malaria, and other tropical diseases. Such diseases are now neglected because innovators cannot recover their R&D costs from sales to the poor. But with the option of an alternative reward based on health impact, heretofore neglected diseases would become some of the most lucrative R&D opportunities.

The HIF would promote access to new medicines by limiting the price of any registered product to the lowest feasible cost of production and distribution. It would motivate registrants to ensure that their product is widely available, perhaps at even lower prices, and that it is competently prescribed and optimally used. Registrants are rewarded not for selling their product, but for making it effective toward improving global public health.

The HIF will provide optimal incentives only if potential registrants are assured that the rewards will actually be there in the decade following market approval. Core funding of the HIF is therefore best guaranteed by a broad partnership of countries. If governments representing one third of global income agreed to contribute just 0.03 percent of their gross national incomes, the HIF could get started with $6 billion annually. This is a reasonable minimum because the high cost of developing new medicines requires large rewards and because the cost of health impact assessment should not consume too much of the annual budget. If the HIF works well, it could be scaled up through increased allocations and accession of new funders. Governments would have the option of phased withdrawal over a 10-year period.

The HIF can be seen as an annual competition among innovators that ranges over all countries and diseases, with firms earning more money if their product has a larger impact on health. Health impact can be measured in terms of the number of quality-adjusted life years saved worldwide. The QALY metric is already extensively used by private and state insurers in determining prices for new drugs, so employing it in calculating HIF rewards is not a big leap. Taking as a benchmark the pharmaceutical arsenal before the registered medicine was introduced, the HIF would estimate to what extent it has added to the length and quality of human lives. This estimate would be based on data from clinical trials, including pragmatic trials in real-life settings, on tracking randomly selected medicines to their end users, and on statistical analysis of sales data as correlated with data about the global burden of disease. These estimates would necessarily be rough, at least in the early years. But so long as any errors are random, or at least not exploitable by registrants, HIF incentives would be only minimally disturbed.
With the HIF so designed, innovators would register products that can reduce the global burden of disease most cost-effectively. Products with the largest health impact would make the most money — creating exactly the right incentives for innovation. And because the HIF would be an optional system, the rate of reward is certain to be reasonable. If rewards were too high, new registrants would enter and dilute the payments to all registrants. If profits were too low, the reward rate would naturally increase as firms would choose, for more of their new products, to exploit their patent-protected pricing powers instead of registering them with the HIF. Competition would ensure that registered products are rewarded at a rate that is profitable for innovators and maximizes the effect of the HIF.

To be certain that the HIF is cost-effective relative to other public health expenditures, one can stipulate a maximum reward rate; if one year’s funds are not fully used, the remainder can be rolled over into future years. To reassure potential innovators, one can also add some protection against unreasonably low rewards.

By creating incentives to provide important pharmaceutical innovations at low prices, the HIF would easily pay for itself. Through lower drug prices, taxpayers would realize off-setting savings in national health systems, insurance premiums, and direct pharmacy purchases. They would benefit from reductions in counterfeiting, wasteful litigation, and excessive marketing. By stimulating development of important but currently unprofitable medicines, making new high-impact medicines much more widely accessible, and encouraging efforts to ensure that medicines are optimally used, the HIF would greatly reduce the global burden of disease and thereby produce large medical cost savings and gains in economic productivity.

A much fuller account of how the HIF would work can be found in the e-Library at:

www.healthimpactfund.org
APPENDIX 2

Round 2 Delphi Questionnaire
Dear X,

Thank you for completing the first round of the Delphi survey your participation in our survey investigating the feasibility of a Health Impact Fund (HIF), which forms part of the EU funded INNOVA project. The project is examining ways to promote the research and development of tools to reduce neglected diseases. The purpose of the first survey was to obtain your opinions on the potential effectiveness and acceptability of such a system.

We are using the Delphi method for our survey. Delphi is an iterative method of data collection involving at least two rounds of questionnaires. The aim is to provide participants with (anonymised) feedback regarding areas where there is consensus (or lack of it) among participants. This second round of Delphi will then be used to see whether or not the feedback has an impact on participant opinions. We will also provide feedback regarding areas where consensus has been developed. For the purposes of our analysis, we have identified 80% agreement across the sample as the cut-off point for consensus.

The use of the Internet for data collection allows us to anonymise feedback from participants. As before, each participant will only be identified by a code number. The final report will include a list of participating organizations, but individuals will not be identified and the answers given by each participant will be treated as confidential.

How long does it take?

We estimate the first round questionnaire will take approximately 20 minutes to complete. A second round questionnaire is likely to be shorter, and developed from you answers to the first round questionnaire. When completed, please return by email or fax to Lynn.Frewer@wur.nl.
The Health Impact Fund (HIF) is a new way of stimulating research and development of life-saving pharmaceuticals. To provide wide access to the most effective pharmaceuticals, prices need to be low enough for people to afford – but low prices don’t create strong incentives for innovators to invest in research and development. The proposed HIF is an optional mechanism that offers pharmaceutical innovators a supplementary reward based on the health impact of their products, if they agree to sell those products at designated low prices. The proposed Fund is to be financed mainly by governments. More information about the HIF can be found at [www.healthimpactfund.org](http://www.healthimpactfund.org).

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How will it affect consumers?
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Are patent rights affected?
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**How will the Fund be financed?**
Governments and other donors would commit to long-term funding. Much of the Fund’s cost to taxpayers will be offset by savings on medicines that would otherwise have been bought at much higher prices. But its greatest benefit is that patients will gain access to important medicines that, without the Fund, would have been too expensive or even non-existent.

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**What is Incentives for Global Health?**
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**How can I find out more?**
More information on the proposed mechanism is available at:

www.incentivesforglobalhealth.org

We welcome your questions and your involvement.

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Delphi Study
Questions: Round 2

First of all, we would like to provide you with some feedback from participant’s responses in the first round.

We have used 80% agreement across the sample on a particular item as the cut-off point for consensus. Using this criterion, consensus was obtained regarding the following issues.

- 87% of participants agreed or agreed slightly with the statement that “The HIF would provide a greater incentive for the pharmaceutical industry to develop tools to fight diseases of poverty”.
- 96% of participants agreed or agreed slightly that “An HIF scheme would encourage commercial pharmaceutical companies to collaborate with publicly funded research initiatives”
- 83% of participants agreed or agreed slightly that “Pharmaceutical interventions should be eligible for an HIF payment”
- 80% of participants agreed or agreed slightly that “Health system innovations should be eligible for a HIF payment”.

These questions will not be investigated further in the 2nd round of this study.

In addition,

- 74% of participants agreed or agreed slightly that “In addition to national Governments, other donors such as private foundations, will be willing to fund an HIF scheme”. As 17% had no opinion, and 9% disagreed, this question will not be explored further in round 2.
- Almost 60% (57%) of participants were unable estimate whether the proposed size of the fund (US$6bn) was appropriate to fund an HIF scheme. Given that participants generally found it difficult to provide revised estimates, the issue of the appropriate size of the find will not be further explored in the second round.

We would like to give you some additional feedback on the round 1 responses, and ask some further questions regarding the HIF fund based on your previous answers.
Q 1. In round 1, there was complete consensus regarding the need to adopt “special measures” regarding the treatment of neglected diseases. Following on from this, we asked participants to list what were, in their opinion, the most important barriers to effectively treating neglected diseases and diseases of poverty. We have categorized these responses into “types of barrier” and they are summarized below.

*Please indicate the extent to which you think each of the following represents an important barrier to the effective treatment of neglected diseases. Please rate each from “not important at all” to “extremely important”.*

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Not important at all</th>
<th>Slightly important</th>
<th>Moderately important</th>
<th>Important</th>
<th>Extremely important</th>
<th>No opinion</th>
</tr>
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<tbody>
<tr>
<td>Poor access to medicine</td>
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<tr>
<td>Lack of diagnostic tools</td>
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<tr>
<td>Lack of treatments</td>
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<tr>
<td>Lack of incentives for pharmaceutical companies to develop treatments</td>
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<tr>
<td>Government’s health care input (national)</td>
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<tr>
<td>Lack of resource (general)</td>
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<tr>
<td>Local health care infrastructure inadequate</td>
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<tr>
<td>Lack of political will (international)</td>
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<tr>
<td>Poor sanitation</td>
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<tr>
<td>Local health care infrastructure inadequate</td>
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<tr>
<td>Cost of medicine (general)</td>
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<td>Patents and licensing</td>
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<tr>
<td>Government’s health care input (national)</td>
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<tr>
<td>Lack of cohesion in funding initiatives</td>
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<tr>
<td>Cost of medicines (individuals cannot afford them)</td>
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<td>The lack of priority spending on healthcare in the developing world economies</td>
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<tr>
<td>Shorter term treatments need to be identified</td>
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</table>
Q 2. In round 1, we asked what could incentivise the private sector to invest in treating or curing these diseases or health conditions. We have categorised these answers into “types of incentives”.

Please indicate the extent to which you agree or disagree that each of the following would act as an incentive for the private sector to invest in treating or curing neglected diseases.

<table>
<thead>
<tr>
<th>Issue or activity relevant to incentivising the private sector</th>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither agree or disagree</th>
<th>Disagree Slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facilitating Private Public Partnerships</td>
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<tr>
<td>Create the potential for the industry to make profits</td>
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<tr>
<td>Creation of new markets for pharmaceutical products</td>
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<tr>
<td>Compulsory corporate social responsibility (for example, in terms of allocating research and development budgets)</td>
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<td>International government encouragement</td>
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<tr>
<td>Voluntary corporate social responsibility</td>
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<tr>
<td>Voluntary corporate social responsibility</td>
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<tr>
<td>Economic compensation from international governments and organizations for investing in research and development budgets.</td>
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<tr>
<td>Respect for intellectual Property Rights</td>
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</table>

Q 3. In round 1, 61% of participants agreed, or agreed slightly, and 25% disagreed, or disagreed slightly, that current IPR systems are a disincentive for developing treatments or cures neglected diseases or diseases of poverty. The remainder of participants did not express an opinion.

We would like you to answer this question again, this time providing additional information to explain your response. If you would like to change your opinion, please do so.
Current IPR systems are a disincentive for developing treatments or cures for neglected diseases or diseases of poverty

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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</table>

Please explain your answer

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Q 4. In the first round, there was considerable disagreement among participants regarding whether “an HIF scheme would provide an incentive for commercial companies to carry out research and development on tools to provide cures rather than treatment”. 43% of participants indicated that they agreed or agreed slightly with the statement. 26 % disagreed or disagreed slightly with the statement. The remainder indicated that they neither agreed nor disagreed, or did not have an opinion on the issue.

We would like you to answer this question again, this time providing additional information to explain your response. If you would like to change your opinion, please do so.

An HIF scheme would provide an incentive for commercial companies to carry out research and development on tools to provide cures rather than treatment

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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Please explain your answer

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Q 5. 87% of participants in round 1 agreed or agreed slightly that barriers to “Barriers to the implementation of an HIF scheme can be identified”. Following on from this, we asked participants to list what were, in their opinion, the most important barriers to implementing an HIF scheme. We have classified these responses into groups and they are summarized below.

Please indicate the extent to which you think each of the following is an important barrier to successful implementation of an HIF scheme. Please rate each from “not important at all” to “extremely important”.

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Not important</th>
<th>Slightly important</th>
<th>Moderately important</th>
<th>Important</th>
<th>Extremely important</th>
<th>No opinion</th>
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<tbody>
<tr>
<td>Raising funding (general)</td>
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<tr>
<td>Raising funding (from national governments)</td>
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<tr>
<td>Developing country governments “buying in” to the scheme</td>
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<tr>
<td>Developed country governments “buying in” to the scheme</td>
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<tr>
<td>Uncertainty about the potential size of financial incentives for industry</td>
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<td>Uncertainty about the potential risks, costs and benefits to industry</td>
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<tr>
<td>The HIF scheme does not deal with “end of pipe” problems</td>
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<tr>
<td>The HIF scheme does not deal with available healthcare personnel</td>
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<td>The HIF scheme does not deal with diagnosis methods and facilities</td>
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<tr>
<td>The HIF scheme does not deal with drug distribution systems to remote areas</td>
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<tr>
<td>The HIF scheme does not deal with information and education of the healthcare chain (including patients and communities)</td>
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<tr>
<td>Lack of cohesion between (inter)national development policies and (inter)national research agendas</td>
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<tr>
<td>Lack of stakeholder “buy-in”</td>
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<tr>
<td>Lack of adequate funding at the “kick-off”</td>
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<tr>
<td>Methods for effectively measuring impact are not available</td>
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<tr>
<td>Cross-national differences in regulations and policies</td>
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<tr>
<td>Problems with donor and pharmaceutical company interactions</td>
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<tr>
<td>Uncertainty about resources required to operationalise an HIF</td>
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</tbody>
</table>
The “patent problem” is not adequately resolved.

Q6. In round 1, we asked whether “An HIF scheme would deliver health benefits for developing and developed countries”. The results are summarised graphically below.

The results seem to suggest that the participants were more certain that the HIF scheme would benefit health in developing countries, but this conclusion was somewhat uncertain.

Please indicate the extent to which you agree or disagree with the following statement.

*An HIF scheme would deliver greater health benefits to developing, as compared to developed, countries.*
Q 7. In round 1, around half the sample 52% agreed that an appropriate measure of health impact assessment for use in an HIF scheme would be a Qalys measure. However, 35 % indicated that they agreed, or agreed slightly that better measures could be identified. Various impact assessment measures are listed below. Please indicate the extent to which you agree or disagree that each of these measures would be appropriate for use in an HIF scheme.

Please indicate the extent to which you agree or disagree that each of the following would be an appropriate measure for measuring the impact of an HIF fund.

<table>
<thead>
<tr>
<th>Measure of impact assessment</th>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither agree or disagree</th>
<th>Disagree Slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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</thead>
<tbody>
<tr>
<td>QALYS</td>
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<tr>
<td>DALYS</td>
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<tr>
<td>New measurements specific to the context of developing countries</td>
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<tr>
<td>Mortality (depending on the disease)</td>
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<tr>
<td>Morbidity (depending on the disease)</td>
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<tr>
<td>Relapse (depending on the disease)</td>
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<tr>
<td>Percentage of treatable diseases currently untreated</td>
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<tr>
<td>Socio-economic potential (of country) improved or restored</td>
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<tr>
<td>Preference-based measures</td>
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<tr>
<td>Consumer uptake of pharmaceutical products</td>
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</table>

Q 8. 61 % of participants disagreed, or disagreed slightly, that “the cost of an HIF scheme will be offset by savings in national health budgets?”. Only 9% of participants agreed with this statement. We would like to ask this question again, but, in the second round, ask you to explain your answer.

The cost of an HIF scheme would be offset by savings in national budgets.

<table>
<thead>
<tr>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither</th>
<th>Disagree slightly</th>
<th>Disagree</th>
<th>No opinion</th>
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Please explain your answer

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Q 9. In the first round, we asked
- “What effect would an HIF scheme have on publicly-funded and not-for-profit research initiatives, and research on neglected diseases such as those of public private partnerships (IAVI, MMV, TB Alliance etc.)?“.
- “What effect an HIF scheme would have on research funded by private foundations (Bill and Melinda Gates Foundation, Wellcome Trust etc.)”
- What effect would an HIF scheme have on existing schemes funded by international organisations (e.g. WHO), the EU and national governments (NIH, DFID, Global Fund, EDCTP).

We have categorized these responses into “types of effect”. Please indicate what you think the OVERALL impact of the HIF will be in the different types of organisations.

**The overall impact of an HIF scheme on research funded by public private partnerships would be ....**

<table>
<thead>
<tr>
<th>Very positive</th>
<th>Positive</th>
<th>No effect</th>
<th>Negative</th>
<th>Very negative</th>
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<tbody>
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<table>
<thead>
<tr>
<th>Overall impact</th>
<th>No opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>difficult to predict</td>
<td></td>
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</tbody>
</table>

**The overall impact of an HIF scheme on research funded by private foundations would be ....**

<table>
<thead>
<tr>
<th>Very positive</th>
<th>Positive</th>
<th>No effect</th>
<th>Negative</th>
<th>Very negative</th>
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<table>
<thead>
<tr>
<th>Overall impact</th>
<th>No opinion</th>
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<tbody>
<tr>
<td>difficult to predict</td>
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</table>

**The overall impact of an HIF scheme on research funded by international organisations would be ....**

<table>
<thead>
<tr>
<th>Very positive</th>
<th>Positive</th>
<th>No effect</th>
<th>Negative</th>
<th>Very negative</th>
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<tbody>
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</table>

<table>
<thead>
<tr>
<th>Overall impact</th>
<th>No opinion</th>
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<tbody>
<tr>
<td>difficult to predict</td>
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</tbody>
</table>
Q10. In round 1, participants raised various additional issues which were potentially important when considering the viability of an HIF scheme. These have been coded and are presented as statements below.

*Please indicate the extent to which you agree or disagree with each of the following statements regarding the viability of an HIF scheme.*

<table>
<thead>
<tr>
<th>Issues potentially relevant to the viability of an HIF scheme.</th>
<th>Agree</th>
<th>Agree slightly</th>
<th>Neither agree or disagree</th>
<th>Disagree Slightly</th>
<th>Disagree</th>
<th>No opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>The HIF as currently proposed places too much emphasis on the private sector’s ability to address unmet healthcare needs in developing countries.</td>
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<tr>
<td>The governance structure should be inclusive, involving NGOs, patient associations, development experts and not just large donors.</td>
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<tr>
<td>The HIF should focus on diseases other than the “big three” (HIV/AIDS, TB and Malaria).</td>
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<tr>
<td>The HIF should focus more on chronic diseases (e.g. diabetes, mental health, coronary heart disease) that have major impacts on public health in developing countries but are “neglected” by international funders.</td>
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<tr>
<td>The HIF as currently proposed places too much emphasis on the private sector (as opposed to public sector), being able to address unmet healthcare needs in developing countries.</td>
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<tr>
<td>The HIF should be modeled, piloted, and externally evaluated to explore any unintended consequences, and to further define and limit the scope of the scheme.</td>
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<tr>
<td>The HIF should place more emphasis on capacity and capability building to enable developing countries to take the initiative in treating neglected diseases.</td>
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<tr>
<td>The HIF is likely to act as a greater incentive for small pharmaceutical companies rather than “big pharma”, which is perhaps more likely to apply the HIF to existing products rather than the HIF leading to de novo development of new products.</td>
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</table>

*Thank you very much for taking the time to complete this questionnaire. If you have any questions or comments please contact Professor Lynn Frewer at lynn.frewer@wur.nl Tel: +31 317 482550; Fax: +31 317 484361*
ANNEX 1

The Health Impact Fund

Treatments for human immunodeficiency virus illustrate the dilemma between access to and innovation in medicines: second-line therapies have dramatically reduced the burdens of HIV infection in affluent countries but, at a price of $800 to 1,500 per year, are out of reach for the majority of people until the 20-year patents run out. We could insist on lower prices, but that would undermine the incentives for pharmaceutical companies to develop new medicines. By facilitating access we strangle innovation, and by stimulating innovation through strong patents we obstruct access for many people to new medicines they urgently need.

This terrible dilemma can be avoided by introducing a new option: the Health Impact Fund (HIF). This publicly funded pay-for-performance mechanism would give pharmaceutical innovators the option to register any new product. They would promise to make it available at marginal cost wherever it is needed in exchange for annual reward payments based on the product’s global health impact during its first 10 years. The reward payments would be a share of a massive annual pay-out, with each registered product receiving a share equal to its share of the assessed health impact of all registered products.

The HIF would foster innovation—especially against diseases concentrated among the poor: tuberculosis, malaria, and other tropical diseases. Such diseases are now neglected because innovators cannot recover their R&D costs from sales to the poor. But with the option of an alternative reward based on health impact, heretofore neglected diseases would become some of the most lucrative R&D opportunities.

The HIF would promote access to new medicines by limiting the price of any registered product to the lowest feasible cost of production and distribution. It would motivate registrants to ensure that their product is widely available, perhaps at even lower prices, and that it is competently prescribed and optimally used. Registrants are rewarded not for selling their product, but for making it effective toward improving global public health.

The HIF will provide optimal incentives only if potential registrants are assured that the rewards will actually be there in the decade following market approval. Core funding of the HIF is therefore best guaranteed by a broad partnership of countries. If governments representing one third of global income agreed to contribute just 0.03 percent of their gross national incomes, the HIF could get started with $6 billion annually. This is a reasonable minimum because the high cost of developing new medicines requires large rewards and because the cost of health impact assessment should not consume too much of the annual budget. If the HIF works well, it could be scaled up through increased allocations and accession of new funders. Governments would have the option of phased withdrawal over a 10-year period.

The HIF can be seen as an annual competition among innovators that ranges over all countries and diseases, with firms earning more money if their product has a larger impact on health. Health impact can be measured in terms of the number of quality-adjusted life years saved worldwide. The QALY metric is already extensively used by private and state insurers in determining prices for new drugs, so employing it in calculating HIF rewards is not a big leap. Taking as a benchmark the pharmaceutical arsenal before the registered medicine was introduced, the HIF would estimate to what extent it has added to the length and quality of human lives. This estimate would be based on data from clinical trials, including pragmatic trials in real-life settings, on tracking randomly selected medicines to their end users, and on statistical analysis of sales data as correlated with data about the global burden of disease. These estimates would necessarily be rough, at least in the early years. But so long as any errors are random, or at least not exploitable by registrants, HIF incentives would be only minimally disturbed.

With the HIF so designed, innovators would register products that can reduce the global burden of disease most cost-effectively. Products with the largest health impact would make the most money – creating exactly the right incentives for innovation. And because the HIF would be an optional system,
the rate of reward is certain to be reasonable. If rewards were too high, new registrants would enter and dilute the payments to all registrants. If profits were too low, the reward rate would naturally increase as firms would choose, for more of their new products, to exploit their patent-protected pricing powers instead of registering them with the HIF. Competition would ensure that registered products are rewarded at a rate that is profitable for innovators and maximizes the effect of the HIF.

To be certain that the HIF is cost-effective relative to other public health expenditures, one can stipulate a maximum reward rate; if one year’s funds are not fully used, the remainder can be rolled over into future years. To reassure potential innovators, one can also add some protection against unreasonably low rewards.

By creating incentives to provide important pharmaceutical innovations at low prices, the HIF would easily pay for itself. Through lower drug prices, taxpayers would realize off-setting savings in national health systems, insurance premiums, and direct pharmacy purchases. They would benefit from reductions in counterfeiting, wasteful litigation, and excessive marketing. By stimulating development of important but currently unprofitable medicines, making new high-impact medicines much more widely accessible, and encouraging efforts to ensure that medicines are optimally used, the HIF would greatly reduce the global burden of disease and thereby produce large medical cost savings and gains in economic productivity.

For a much fuller account of how the HIF would work and why it is needed, see www.healthimpactfund.org
APPENDIX 3

Report Graphics

Figures 1-5
What are the most important barriers to effectively treating neglected diseases?

Higher Importance

- Lack of political will (international)
- Poor access to medicine
- National governments' input into health care
- Cost of medicines (individuals cannot afford them)
- Lack of incentives for pharmaceutical companies to develop treatments
- Lack of priority spending on healthcare in the developing world economies
- Local health care infrastructure inadequate
- Lack of treatments
- Lack of political will (national)
- Treatments take too long, shorter treatment regimes needed
- Lack of diagnostic tools
- Poor sanitation
- Lack of cohesion between different international funding initiatives
- Patents and licensing

Lower Importance
Figure 2

Incentives for the private sector to invest in treating or curing neglected diseases

- International governmental regulation/ resources allocation
- Voluntary corporate social responsibility
- Compulsory corporate social responsibility
- Encouragement and promotion by international governmental bodies
- Ensuring respect for intellectual Property Rights
- Economic compensation from international governments and organizations.
- Create the potential for the industry to make profits
- Creation of new markets for pharmaceutical products
- Facilitating Private Public Partnerships

Level of agreement
Figure 3

Barriers to successful implementation of an HIF scheme

Very Important

- "End of pipe" problem
- Adequate funding at "kick-off"
- Stakeholder "buy-in"
- Available healthcare personnel
- Industry "buy in"
- Developed country governments "buy in"
- Lack of cohesion (development policies and research)
- Drug distribution systems to remote areas
- Diagnosis methods and facilities
- Raising funding (national governments)
- Raising funding (international organisations)
- Impact measurement methods
- Donor and pharmaceutical company interactions
- Size of financial incentives for industry?
- IPR issue
- Uncertainty about resources required
- Education of the healthcare chain
- Uncertainty - risks, costs benefits to industry
- Harmonisation of policy
- Developing country government "buy in"

Less Important

1 Low  2  3  4  5 High
Figure 4

Appropriate Impact Measure

Preference-based measures (used in conjunction with Qualys)
DALYS
QALYS
Socio-economic potential (of country) improved or restored
Consumer uptake of pharmaceutical products
Relapse (depending on the disease)
Mortality (depending on the disease)
Percentage of treatable diseases currently untreated
Morbidity (depending on the disease)
New measurements specific to the context of developing countries

Level of Agreement
High Level of Agreement Low
Figure 5

Other issues regarding implementation of an HIF

- Focus more on chronic diseases
- Greater incentive for small pharmaceutical companies
- Too much emphasis on the private sector’s ability to address unmet healthcare needs in developing countries.
- Modeled, piloted, and externally evaluated to explore any unintended consequences.
- Capacity and capability building
- Focus on diseases other than the “big three” (HIV/AIDS, TB and Malaria).
- Inclusive governance structure involving NGOs, patient associations, development experts.