Response to the High-Level Panel and Expert Advisory Group

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The following answers are intended to be responsive to the specific questions asked during the hearing on delinkage mechanisms in London on March 9 2016.

1. **What is the first step towards delinkage?**

While we would welcome a large-scale move to delinkage, we think that at present it makes sense to explore a more modest delinkage model. Any delinkage model needs to have a mechanism for allocating payments to the innovator. Essentially, the three potential models involve grants to pay directly for innovation (as in PDPs), prizes for pre-specified technical achievements (such as the Qualcomm Tricorder XPrize), and rewards based on health outcomes (such as the Health Impact Fund or Senator Bernie Sanders Prize Fund for HIV/AIDS drugs).

For the latter type of mechanism, we believe that the HIF offers a model that can grow over time if successful. The miniHIF will provide evidence on making rewards dependent on outcomes in a competitive framework. The miniHIF could then be followed up with a larger pilot that would provide further evidence to calibrate the model. Ultimately, we envision a permanent HIF with fixed annual reward pools that can start at around $6 billion. The size of these annual pools could be gradually enlarged to induce an increasing percentage of new drugs to opt for HIF-registration.

2. **To what extent will pharmaceutical companies will be involved in delivery in the HIF model?**

In most countries, the responsibility for oversight and delivery of health care rests with governments. But pharmaceutical innovators can make an important contribution to the availability of their drugs. They are responsible, for example, for obtaining regulatory approval as well as for arranging for reliable distribution of their products. Some innovators do not have global capacity and simply hire others to perform these services for them. In either case, applying for regulatory approval and ensuring that their products are in stock at local wholesalers requires substantial resources and will not happen without appropriate financial support. The HIF would provide the financial motivation for innovators to engage in these activities because HIF payments are based on health impact.

In addition, the HIF would encourage pharmaceutical innovators to care about the health gains their registered products achieve. Health gains are enhanced when a medicine reaches patients in optimal condition, when doctors understand which patients can benefit the most from a given product, and when doctors, nurses and patients know how to use a product to optimal effect. Innovators can promote these

goals, for instance, by improving the cold chain, by developing heat stable versions of their drugs, by translating package inserts into local languages or providing other information materials for patients and health care providers, and by developing ways of reminding patients (e.g., with the aid of cell phone technology) to take their medicines at the right times and for the full duration.

3. Does the HIF create a bias towards serving the patients whose health gains are most easily measured?

Perhaps. The HIF is not expected to be a perfect institution. At present, there is a massive bias towards serving high-income patients. Under the HIF, there might be some bias to treating patients with health gains that are relatively easy to measure. For example, mental disorders such schizophrenia cause a large share of the global burden of disease, and yet assessing the health impact of treatments for these disorders is very challenging. To the extent that the HIF underestimated health gains in diseases that are poorly measured, it would not create optimal incentives to develop treatments for such disorders. However, this would encourage firms to develop better measures of health gain and better information about the effects of their products. It should be clear that the HIF would not perfectly address every possible problem: instead it is meant to offer a substantial addition to the existing institutional structure that would better incentivize R&D into diseases mainly suffered by poor people, while ensuring widespread access at affordable prices.

4. Is a financial impact analysis available?

At present we think that the right starting point for analyzing the HIF is to undertake the miniHIF. The financial impact analysis for this is challenging in advance, since we cannot know at present which projects would be selected into the competition. We do know the proposed cost, which would be the budget of the miniHIF, but we cannot know the net cost, which depends on the (presently unknown) specific projects.

However, a feature specific to the HIF and miniHIF proposals is that, by design, they automatically analyze their own cost-effectiveness by measuring the health impact generated by the products they reward. Thus, policymakers will know what value they get for the funds they invest into the miniHIF pilot or the HIF itself.

5. How does a delinkage system choose winners?

An important feature of the HIF approach is that it doesn't choose winners in advance. Instead, it sets a broad goal (improving human health) and applies a general metric, such as QALYs, to assess how well the various registered medicines are doing. Pharmaceutical innovators, the very parties best able to predict what

their R&D efforts might be able to achieve, make the crucial decisions about which R&D efforts to undertake and which new medicines to register with the HIF. The HIF merely rewards these registered medicines differentially, thereby creating winners (medicines that were relatively cheap to develop and produce large health gains) and losers (medicines that were relatively expensive to develop and produce small health gains). These anticipated rewards incentivize pharmaceutical innovators to undertake those R&D projects that they expect to yield the most favorable ratio of health gains to cost.

6. **How does a delinked system deal with the important issues of getting products registered with health authority and distributed?**

In the HIF system, the mechanism for supporting registration and distribution is to offer the firm an outcome-based reward. Since the outcome can only be realized if the product is available on the market, firms are incentivized to perform the activities required to obtain market authorization and to achieve wide diffusion, more or less as we observe in high-income countries today.

7. **What kinds of drugs would be submitted to HIF?**

The Health Impact Fund is intended to be open to any class of drugs or disease. It encourages firms to look for the opportunities that create the largest improvements in health, relative to the risk-adjusted cost of successfully developing a drug. Because the HIF does not limit the types of drugs that can be rewarded, it motivates investment in whatever is most cost-effective. However, if a new drug is developed, the HIF offers a choice: either HIF rewards or the conventional monopoly mark-up. The only drugs for which the HIF would be an attractive choice are those that deliver a significant therapeutic benefit but face relatively low commercial returns. This condition arises typically for drugs that are mainly needed by poor people, where the health gains are very large relative to the commercial value under monopoly pricing. The HIF (unless it had a very large annual budget) would therefore not be attractive for blockbusters such as sofosbuvir and atorvastatin. It would attract registrations mainly of products that deliver large health benefits but are not highly profitable under our current system of patent-based rewards.

8. **What is the ability of firms to game the system if they can just oversell product into the market and there isn't a really tight control on health impact assessment?**

One important challenge for the Health Impact Fund is to ensure that payments are meaningfully proportional to the health impact achieved by each product. If firms could reap rich rewards for very little impact, this would undermine the incentives to register the most effective drugs.

There are various ways for the HIF to ensure that assessed impact is in line with actual impact? First, the HIF would explicitly attempt to base reward payments on health outcomes. Other systems of payment do not have this feature. For example, in our current system, firms earn "rewards" for every unit sold, equal to the difference between the price and the average production cost. These "rewards" are unlikely to be well correlated with therapeutic value because that is not a goal. Explicitly making this correlation a goal, as the HIF does, is important to achieving it.

Second, the HIF would allocate substantial resources to assessing outcomes. While the HIF would rely on data relating to volumes and the results from pre-approval clinical trials (as is common in health technology assessment processes today), it would complement this data by assessing patient characteristics to help refine its estimates of health impact. For example, patient age may be relatively easy to capture in surveys and for some drugs and vaccines that is an important variable. Similarly, the degree to which retails sales are made following a medical diagnosis and dispensed in a clinic, rather than following a patient diagnosis and dispensed without a prescription, could be relevant to assessing the likely effectiveness of the product in a country.

Third, the HIF would preempt gaming by keeping some of its assessment methods confidential and by conducting unannounced random spot checks. It would also have the ability to respond to perceived gaming by adjusting its data collection.

Fourth, the HIF would be aided in preventing gaming by the interests of other participants in the HIF rewards, who would be motivated to watch out for abuse by others, since a larger payment for one firm would lead to smaller payments to others.

Despite all this, any system is subject to gaming by potential participants. The actual operation of the HIF would need to be closely monitored, and its rules and practices might need to be adjusted in light of the observed behaviour of participants.

9. How would the HIF help realize the human right to the highest attainable standard of physical and mental health?

From a human rights standpoint, the present system of pharmaceutical provision is highly problematic in two main respects. Our method of rewarding new medicines with patent-protected markups – globalized through the TRIPS Annex to the WTO Agreement – requires governments to prevent the manufacture and sale of cheap generic versions of new drugs with the result that, in poor countries, the majority of the population cannot afford to buy new medicines. This is a huge disadvantage, especially in regard to medicines for communicable diseases, which often lose their efficacy over time. Millions of patients die because they cannot gain access to important medicines that generic firms would happily supply at low prices if only

they were legally permitted to do so. These deaths, along with a great deal of avoidable suffering and disability from disease, are known side effects of maintaining the R&D incentives that yield the new medicines that more affluent patients are eager to buy: if poor patients could buy the same new drugs cheaply, then affluent patients would also find ways to buy these drugs cheaply, the earnings of pharmaceutical innovators would be much lower, and many R&D projects would never be undertaken.

It is true that patent-inspired R&D will eventually benefit poor patients also: after patent expiration. But the deaths and suffering in the interim are enormous and morally acceptable only if there really is no suitable alternative. And there is a suitable alternative: we can delink the price of the product from the innovators' reward, thus asking patients to pay only for the manufacturing cost.

The other respect in which the present system is problematic from a human rights standpoint has to do with how it drives the selection of R&D projects. Health problems that are common among affluent patients are prioritized; health problems that are largely confined to the poor are shelved because products developed through such efforts cannot be sold at the usual exorbitant patent-protected markups. This violates the idea – central to the human rights discourse – that all human lives are of equal value and that diseases harming and killing poor people should therefore receive the same pharmaceutical attention as diseases harming and killing affluent people. In this regard, as well, the HIF helps rectify the imbalance by conditioning its rewards upon health impact pure and simple, without any regard to whether the patients benefiting are rich or poor, influential or marginalized, articulate or voiceless, educated or illiterate, popular or loathed, charismatic or offensive. Straightforwardly, the HIF guides pharmaceutical innovators toward undertaking those R&D projects through which they can make the most cost-effective interventions for human health, counting all health gains on the same scale regardless of whose gains they are.

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