

The Relationship of the Health Impact Fund and Its Registrants

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Abstract: The success of the Health Impact Fund plan to promote global access to pharmaceutical innovation can only be built upon the bedrock of mutually advantageous relationships with the Fund's registrants. Accordingly, the credibility, predictability, and efficiency of the arrangements that will comprise those relationships are of paramount importance.

This discussion paper considers the relationship of the HIF with its registrants as laid out in in *The Health Impact Fund: Making New Medicines Accessible for All*. This paper evaluates the relationships and arrangements the HIF will offer to registrants, identifies potential concerns in the current plan, and suggests specific prescriptions for their resolution.

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EXECUTIVE SUMMARY

The success of the Health Impact Fund (“HIF” or “Fund”) plan to promote global access to pharmaceutical innovation can only be built upon the bedrock of mutually advantageous relationships with the Fund’s registrants. Accordingly, the credibility, predictability, and efficiency of the arrangements that will comprise those relationships are of paramount importance.

This white paper considers the relationship of the HIF with its registrants as laid out in *The Health Impact Fund: Making New Medicines Accessible for All* (“HIF Book”). This paper evaluates the relationships and arrangements the HIF will offer to registrants, identifies potential concerns in the current plan, and suggests specific prescriptions for their resolution. This analysis is designed to facilitate consultations between Incentives for Global Health (IGH) and potential funders, registrants, and stakeholders in order to generate support and dialogue necessary to bring the HIF into existence. This white paper is also intended to provide an early foundation for the legal and policy work that will be necessary, after those consultations, to structure and draft the contractual arrangements between HIF and its registrants.

The goal of the HIF–registrant relationship must be to align registrant incentives with the sustainable public health outcomes that are the root and standard of HIF’s mission. Critical determinants of success will include the size of the reward, the clarity and predictability of the reward system, and the contractual obligations placed on registrants. It will be essential to convince registrants that the global health impact assessments are transparent and precise. The HIF plan, as currently envisioned, takes many innovative and positive steps in addressing these issues.

There are, however, aspects of the current HIF model which may pose significant structural and contractual challenges to its relationships with registrants. Five such challenges, and this paper’s prescriptions for them, are highlighted here.

Challenge I. Engaging Prospective Registrant Product Developers. The HIF model rewards the supply of products (or, more precisely, the effect of their supply), not their development. Pharmaceutical product development is costly and risky. It will be doubly so for products with high potential global health impact, but which would be unprofitable without the HIF.

Without adequate assurances from the HIF, there will not be sufficient incentive for firms to undertake the necessary capital investments.

Specific prescription: Contractual structures must provide clarity, certainty, and predictability and extend to developers as well as suppliers.

Challenge II. Product Eligibility: The eligibility criteria for products and registrants are critical for the success of the HIF, but remain unclear in the HIF plan.

Specific prescription: Eligibility must be carefully defined, non-discretionary, and designed to promote the registration of the best products. This white paper proposes specific criteria consonant with the mission and objectives of the HIF.

Challenge III. Term and Termination: The health impact based reward system imposes significant risks on and potentially uncertain rewards to potential registrants. The reward system may be subject to abuse and manipulation by registrants. Termination is important for managing risk for both the HIF and its registrants. Too much freedom for registrants to enter and exit the Fund, however, will significantly complicate administration of the health assessment and reward calculations.

Specific prescription: Well-designed entry, term, and exit provisions are necessary to create constructive incentives and manage the risks for registrants and the HIF alike.

Challenge IV. Intellectual Property and Access Conditions: The HIF plan includes intellectual property access conditions that unduly increase risk, undermine the utility of early termination, and are duplicative of the incentives provided under the HIF reward mechanism.

Specific prescription: The intellectual property access conditions proposed in the HIF Book should be limited and, in some cases, omitted.

Challenge V. Dispute Resolution: The global health impact assessment that HIF will conduct of registered products is complex and—for many diseases, types of products, and settings—novel. The stakes are also high. The entire HIF reward will be based on that assessment. There is a potential for disputes and perceptions of opacity and prejudice.

Specific prescription: An internal adjudication body should be established to provide added certainty to health assessments and reward determination and reduce the risk of litigation.

INTRODUCTION

This paper considers the relationship and possible arrangements that may exist between the proposed Health Impact Fund (“HIF” or “Fund”) and the entities that register their pharmaceutical products with it. This analysis is designed to facilitate consultations between Incentives for Global Health (“IGH”) and potential funders, registrants, and stakeholders in order to generate support and dialogue necessary to bring the HIF into existence. This white paper is also intended to provide an early foundation for the legal and policy work that will be necessary, after those consultations, to structure and draft the contractual arrangements between HIF and its registrants.

This paper proceeds in five sections.

The first section of this paper outlines, in brief, the mission and the basic design of the relationship between HIF and its registrants as laid out in the HIF Book.

The second section considers the implications and challenges that the currently envisioned design of the HIF creates for the structure and terms of the registrant relationship.

The third section proposes a possible structure for arrangements between the HIF and its registrants and examines four key areas of that structure in greater depth: product and registrant eligibility; entry, term and termination; intellectual property and access conditions; and internal adjudication dispute settlement.

The fourth section provides a summary of this paper’s recommendations.

The fifth section suggests next steps for structuring and designing the terms of the HIF-registrant relationship.

OVERVIEW OF THE HIF

This analysis begins with a review of the relevant parties in the HIF-registrant relationship and their principal objectives and responsibilities as outlined in the HIF Book.

There are three relevant parties involved in the relationship of HIF and its registrants.

The HIF

The mission of the HIF is to create an economic incentive to (1) develop new, innovative medicines that are important for global health and (2) provide widespread and sustainable access to innovative medicines that are important for global health. HIF will provide that incentive through a fixed fund in which entities may register their pharmaceutical product. The registrants agree to supply that product at an administratively determined low price, in exchange for an annual share of the Fund for ten years. Registrants' share of the HIF will be determined in proportion to the health impact of that registered product relative to all the products registered with the HIF.

HIF will perform the health assessment of registered pharmaceutical products. The health impact assessed will be both global—for all patients who use the registered product—and incremental—based on the additional health impact the product achieves for each year in which it is assessed. The HIF will reward health impact experienced by anyone in the world at an equal rate, without distinction for the type of patient, the disease or condition, the country in which the patient was treated with the product, or sector (public or private) through which the product was provided.

It remains an open question at this point whether HIF itself would enter into the necessary legal agreements with its registrants. The HIF could be established, like the Global Fund to Fight AIDS, Tuberculosis, and Malaria, as a stand-alone entity with its own legal personality and be able to enter into legally binding commitments. Alternatively, the governments, intergovernmental organizations, and foundations that fund and/or host the HIF could enter into the necessary contractual arrangements with registrants, as occurs with the Pneumococcal Vaccine Advance Market Commitment.

This question cannot be resolved here. The answer will depend largely on the donors that fund the HIF and their and registrants' needs and interests regarding the vehicle for these

commitments. This paper assumes, for the purposes of this analysis, that HIF or the contracting entity will be legally able enter into the types of contracts discussed below and that its objectives for doing so will be to fulfill the mission of the HIF. For ease of reference, this paper will refer to this first party as the HIF.

Developers

The second party (“Developer”) will be one or more pharmaceutical or biotech companies that wish to research and develop a pharmaceutical product for registration with HIF. The objective of this party is to develop a product that is eligible for HIF and, subsequently, enter into an agreement to supply the product in return for a share of the Fund.

Suppliers

The third party (“Supplier”) will be one or more pharmaceutical companies that have successfully developed an eligible pharmaceutical product, obtained regulatory approval, and wish to enter into an agreement with HIF to supply that product. The objective for this party to register will be an annual reward payment from HIF for each year the product is registered. That amount of that annual payment is not fixed and will depend on numerous variables, including the size of its fund, the number of registered products, the effective global demand for the product, and the HIF’s estimate of the health impact achieved by the registered product relative to the HIF’s estimate of the health impact achieved by all products registered during that year.

In some instances, the Developer and the Supplier will be the same, but they need not be. The HIF is open to all eligible products, whether they were developed for registration with the HIF, already exist, or would exist irrespective of the HIF.

The HIF does not offer a prize or reward payment for successfully developing an eligible pharmaceutical product; it only offers rewards for supplying an eligible pharmaceutical product pursuant to the terms and conditions of the HIF. The possibility of a reward payment for the supply of a product may stimulate its development, but the HIF will not reward this activity alone.

In exchange for the HIF reward payment, registrants must commit to:

- forego whatever price the registrant could otherwise obtain for its registered product and charge an administratively determined price (near the average cost of production and distribution for that product);
- pay a yearly administration fee to cover the costs of the HIF health impact assessment;
- provide sales data and other evidence required by HIF to conduct its audits and health assessments;
- make a good faith effort to obtain market clearance wherever the registered product is needed;
- authorize the HIF to seek market clearance for the product wherever the HIF determines that the registrant has failed to do so (the costs of which HIF will subtract from the registrant's next health impact reward payment);
- grant to HIF, or its designee, a non-exclusive, royalty-free license to exploit the registered product wherever the registrant has failed to adequately supply it; and
- grant a nonexclusive, royalty-free license to the relevant intellectual property at the conclusion of the HIF ten-year reward period.

A product may be registered with the HIF for as long as ten years. Registrant Suppliers may exit the HIF, however, before the end of that ten-year term. During the registration term, other products may be registered to the HIF as well. There is no maximum or minimum number of products that may be registered with the HIF.

ANALYSIS

In general, the HIF plan is both innovative and timely. There is a clear need for incentives for creating medicines with a significant global health impact and ensuring their widespread and sustained availability. A market-based approach, which does not require wholesale changes to international or national intellectual property laws, should be well-received by potential donors and industry participants alike.

There are, however, several aspects of the HIF model which may pose significant challenges for registrants and the HIF.

Challenges for Registrants

The HIF will be a voluntary arrangement. Critical determinants of HIF's success in attracting Registrants will include the size and predictability of the reward and the contractual requirements placed on registrants.

The HIF health impact assessment-based rewards will be difficult for prospective registrants to predict. Health impact assessments of pharmaceutical products are difficult and complex under the best conditions; for many diseases, types of products, and developing country settings, such assessments are unprecedented. HIF will be a new entity with no track record conducting such assessments. The difficulty of its task will be compounded by the fact that HIF will assess how registered drugs are used in actual practice rather than comparative reviews of medicines based on clinical trial data. In many developing country settings, far more basic data, like effective demand, has proven difficult to obtain.¹

Further, it will not be enough for a prospective registrant to be confident that the HIF global incremental health impact assessment of its product will be reliable and reasonably accurate. The registrant must be confident that the HIF assessments of all products registered during its ten-year term will be reliable and reasonably accurate. A registrant's share of the HIF will be determined in proportion to the health impact of its registered product relative to all the products registered with the HIF. Under this model, mistakes or inaccuracies will be amplified. A significant error in one assessment will affect the reward of every product registered that year.

¹ See generally Center for Global Development, *A Risky Business: Saving money and improving global health through better demand forecasts* (2007).

In short, it will be an enormous challenge to ensure the HIF global health impact assessments are reliable and predictable. It may be an even larger challenge to convince potential registrants that it is so.

Even if potential registrants are convinced of the reliability of the health impact assessment process, rewards will remain difficult to predict. Global effective demand for many pharmaceutical products, particularly in developing countries, will be difficult to forecast. Even at the low manufacturing cost prices required by HIF, there will be wide variation in public and private healthcare infrastructure, regulatory authorities, pricing, and procurement systems across countries. Even if the registrant manages to accurately forecast demand, the amount of that reward is not entirely in that registrant's control. Rewards will vary, perhaps significantly, by the number of registrants and the nature of their products in any given year. Registrants may exit the HIF before the end of their ten-year term. During a Registrant's term with the HIF, other products may register to the HIF as well. There is no maximum or minimum number of products that may be registered with the HIF. Thus, the reward that HIF provides for a registered product one year may be significantly different from the next.²

The costs for Suppliers and Developers to participate in the HIF will be potentially significant.

Registrant Suppliers are required to pay an annual fee to cover the average cost of health impact assessment, which may be expensive.³

HIF will only determine and issue its reward payments annually. Accordingly, Suppliers would need to participate in the HIF for at least year before it would be able to learn its reward, foregoing patent-based prices in every country and market during that time. Given the limited effective patent term for most pharmaceutical products, this cost is significant.

As a condition of participation in the HIF, a registrant must agree to numerous intellectual property access conditions, which would require the registrant to grant non-exclusive, royalty-free licenses at the end of its ten-year reward term and whenever it does not seek regulatory approval or adequately supply its product to a country in which there is demand.

² The HIF proposes some design options to address these competitive risks. *See* HIF Book, at 18-20 (proposing a minimum, maximum or fixed reward per Quality-Adjusted Life Year (QALY)). These design options are policy determinations beyond the scope of this paper, but could usefully reduce the uncertainty related to the number and identity products and the reward given per QALY.

³ *See* HIF Book at 31 (“if the HIF had an annual budget of \$6 billion, it could spend about \$600 million on administration and assessment, with the bulk being devoted to assessment.”)

The latter two provisions will not be difficult to trigger. Manufacturing capacity requires years to develop and this investment is very costly and—particularly in such circumstances with uncertain demand—risky. Delivery of pharmaceutical products to developing countries necessitates managing clinical trials and regulatory approval processes in overlapping jurisdictions and under the often-inconsistent requirements of donor countries, multilateral institutions, and in-country authorities. Navigating the tangle of these regulatory requirements is costly and much delays the introduction of new lifesaving technologies. There is often a lack of clarity at country level regarding how regulatory decisions are made. Regimes change in unpredictable ways, imposing new manufacturing, intellectual property, and clinical trial requirements.

For Developers, the balance of internal risks and rewards are less favorable. The HIF rewards the supply of products (or more precisely, the effect of their supply), not their development. Accordingly, Developers will ultimately bear the aforementioned uncertainty and costs as Suppliers. Before supplying a product registered with HIF, however, a Developer must make a significant investment to research and develop it. If that investment would not be profitable without the HIF rewards, this will be a significant risk for Developers to undertake, particularly given the already uncertain nature of pharmaceutical research and development.

Ultimately, Developers will only undertake the investment necessary to develop a product if there is adequate assurance that, once successfully developed, the product will be eligible for the HIF and the reward payments will be sufficient to make that upfront investment and the costs of participating in the HIF profitable.

Challenges for HIF

There are at least four aspects of the HIF model that may pose significant challenges to HIF in the design of its relationships with registrants.

First, the health impact assessment-based reward system creates significant risks of registrant fraud and manipulation. The most likely source of the data available for the health impact assessment of a product will be the party with the greatest incentive to manipulate or falsify that data—the registrant. Registrants may engage in bribes or other unsavory tactics to increase the potential global health impact of their products.

Second, registrants could register one product on the HIF and sell a slightly different version of that product on the open market, in order to capture the HIF reward as well as patent-based prices.

Third, an unfettered ability to enter and exit the HIF, while necessary for registrant risk management, will create significant administrative challenges for the HIF and undermine its proposed intellectual property access conditions. The entry and exit of registrants at different times of the year will complicate the already difficult process of determining rewards based on an annual assessment of the incremental global health impact of registered products relative to each other. The HIF would need to adjust its calculations for partial year performance or compare registered products over different time periods.

Registrants will have an incentive to exit the HIF early in order to circumvent the requirement that, at the conclusion of the ten-year term, the registrant grant HIF a non-exclusive license of relevant patents, data, and other know-how used for the manufacture and sale of the registered pharmaceutical product.

Fourth, the complexity, high stakes involved, and competitive implications of HIF health impact assessments will lead to frequent disputes by and between registrants. Disputes may raise costs for registrants and the HIF alike and—if not fairly, expeditiously, and effectively resolved—undermine the credibility of the HIF. Audits alone are unlikely to assure registrants of the validity of these health assessments or resolve disputes.

Design Imperatives

Assessing the health impact of medicines is the central task and fundamental innovation of the HIF. The risks and potential uncertainty of this assessment and reward system, however, makes it imperative to design the commitments between HIF and its registrants in a manner that minimizes uncertainty for registrants and eliminates unnecessary risks in other areas of the relationship. HIF commitments must extend to Developers and Suppliers alike and be credible, legally binding, and enforceable. Procedures for eligibility, term and termination, control and access to intellectual property, and dispute resolution must be defined by clear, transparent rules rather than administrative discretion.

Likewise, the health impact-based reward model imposes significant risks on the HIF in terms of the potential for registrant abuse and gamesmanship. The HIF must have sufficient tools

and rights to ensure its proper operation and accountability. Those tools and rights, however, must be clearly defined and limited to avoid actual and perceived risks of mismanagement and abuse. Commitments must be carefully designed to minimize litigation and administration costs to the HIF.

These are not, of course, the only issues that will need to be addressed in regard to the HIF-registrant relationship. Other issues include determination of manufacturing cost plus price, liability, insurance, indemnification, recall of the product, payment, confidentiality, quality assurance, and coordination with regulatory and procurement systems, reference pricing models, and other government, intergovernmental, and philanthropic programs to fund the development and supply of drugs. The challenges and design imperatives identified above, however, provide a useful starting for considering the contractual structures and tools that could be used to address concerns at this early design phase.

The remainder of this section devotes itself to identifying approaches to key challenges in the currently proposed design: the need for a structure that engages Developers as well as Suppliers; product and registrant eligibility; entry, term, and termination; intellectual property and access conditions; and dispute resolution.

Structural Design

The HIF Book is unclear on whether the HIF-registrant relationship will involve some form of development agreement, in which a Developer would agree to develop a pharmaceutical product eligible for the HIF in return for some consideration. This is a critical issue. Many therapeutics with potential relevance to global health never make it to market because of financial and risk considerations undermining their development. A primary component of the HIF mission is to offer an economic incentive to change that dynamic.

At its core, the HIF-registrant relationship is a supply arrangement. A Supplier agrees to supply a pharmaceutical product in the manner prescribed by the HIF (an administratively determined low price) in exchange for consideration—in this case, a share of the Fund.

The HIF could limit itself to that supply arrangement with Suppliers and forego any contractual development arrangements with Developers. Once HIF had determined eligibility of

the product and Supplier,⁴ the Supplier would enter a supply agreement with HIF to provide the qualifying product at designated marginal price in return for a reward determined by health assessment-reward payment. The agreement would define, *inter alia*, its purpose and scope, the responsibilities of the parties, and the requirements for the product and its supply. The agreement would include attachments establishing the schedules, procedures, or formulae for calculating the marginal price, health assessment, and reward calculation.

Under this approach, the prospect of entering into a supply agreement would be the only incentive that HIF provides for Developers to undertake the investment necessary to develop products with high potential global health impact, but which otherwise would be insufficiently profitable. The HIF could increase the credibility of that incentive in the following ways.

- The HIF could issue a formal open offer for the supply agreement, complete with its terms and conditions, which any entity may accept if it has an eligible pharmaceutical product and is willing to commit to the binding terms. Upon acceptance, the offer would become a binding supply agreement.
- The HIF could establish a pre-registration consultation process in which a potential registrant Developer may seek a determination from HIF on the likely eligibility of its product for HIF registration. This process would have a similar purpose as the consultation that U.S. Food and Drug Administration offers to firms before they structure their clinical trials and prepare drug approval applications.
- The HIF could keep its eligibility requirements broad and flexible. The HIF will not be limited to treatments for a particular disease or certain type of product with technical and usability requirements.
- The HIF could ensure that funding commitments are credible, binding, and sufficiently long-term to provide an incentive for product research and development, which can require years to complete.

However, a significant drawback of this approach for developers is that HIF would be free to withdraw or change the terms of its offer and what would constitute acceptance may be a tricky issue, particularly in this context. This approach is likely to create too much uncertainty for most

⁴ Product and registrant eligibility and registration are discussed *infra* in greater detail.

Developers to make the large upfront investment that may be necessary and, thereby, dilute the incentives the HIF is meant to provide.

In order to foster development of products with high potential global health impact, HIF should extend its contractual arrangements to Developers as well as Suppliers of eligible pharmaceutical products. Such a structure could consist of two agreements:

- A Framework Agreement in which a Registrant Developer would agree to develop a pharmaceutical product eligible for the HIF in return for consideration from the HIF—the right, if successful, to enter into a second contract (a Supply Agreement) and compete for a share of the Fund. The Supply Agreement, complete with all its terms and conditions, would be attached and incorporated into, the Framework Agreement.
- A Supply Agreement in which the Registrant Supplier agrees to supply an eligible pharmaceutical product pursuant to the terms of the Supply Agreement (including an administratively determined low price) in exchange for consideration—an annual share of the Fund. This Supply Agreement would be identical to that which would be used for supply of eligible extant products.

Both agreements would be open and the Supply Agreement could operate as part of or independently of the Framework Agreement, depending on the circumstance. If a Developer were interested in pursuing the R&D of an eligible product, it could sign on to the Framework Agreement, creating a binding obligation on HIF to enter into the attached Supply Agreement with that Developer if the latter successfully develops an eligible product. If a Registrant Developer succeeds in developing a qualifying product, it should be entitled, but not required, to sign the Supply Agreement. Since the HIF would not directly invest or provide support to the development of products, the Framework Agreement should not require granting the HIF any rights, interests, or licenses to preexisting or developed intellectual property.

The HIF would have no obligations under the Framework Agreement unless the Registrant Developer successfully develops an eligible product and decides to enter into the Supply Agreement. Suppliers of existing eligible products could enter into the Supply Agreement without needing to enter into the Framework Agreement.

The benefit of this more developer-oriented approach is that the Framework Agreement, by attaching and incorporating the Supply Agreement, would provide credible, binding, and enforceable assurances of the availability and terms of the HIF. Moreover, the supplier-oriented and developer-oriented approaches are not mutually exclusive. The Supply Agreement could still be open to Suppliers of eligible products irrespective of whether they had entered into the Framework Agreement. The prospect of entering into that Supply Agreement would remain an incentive for research and development. HIF could still provide pre-registration consultations to Developers that may not wish to enter into a Framework Agreement.

The downside of this approach is that it could expose HIF to some risk. Changing the terms of the Supply Arrangement would be more difficult. Registrant Developers that successfully develop eligible products could pursue standard contract remedies, such as money damages and specific performance, against the HIF if it failed to enter into the Supply Agreement. These risks could be managed, however, with carefully crafted product and registrant eligibility requirements in the Supply Agreement and including sunset provisions that appropriately limit the duration of the Framework Agreement.

Finally, it is worth noting that, whichever approach is chosen, the structure and terms of the HIF contractual arrangements with Registrants will likely need to be standardized. Under the current HIF model, Registrant Suppliers will be competing against each other for their share of the HIF. They must be able to do so on equal footing. Accordingly, it will be difficult for the HIF to vary the material terms of the Framework or Supply Agreements to account for differences in any particular product or a Registrant Developer or Supplier's specific needs and objectives.

Product and Registrant Eligibility

To be successful in its aims, the HIF must determine its registrant and product eligibility requirements in advance and ensure those criteria are clear, public, and their application consistent. The HIF will only induce the development of medicines if potential Registrant Developers are able to understand and rely upon the specific requirements for registration. Further, since the HIF will reward registrants based on the health impact of their products relative to other registered products, potential registrants will likewise need to understand the criteria and be confident in its predictable, fair, and consistent application in order to assess the risks/rewards of competing in this system. Accordingly, wherever possible, the eligibility criteria

should be based on defined rules as opposed to standards or case-specific determinations in order to reduce concerns about unpredictability and potential discretionary abuse.

Registrant Eligibility

Prior to entering into Framework and/or Supply Agreements, the HIF should require a prospective registrant to submit information necessary to identify the legal status of the Developer registration/corporate incorporation information, and relevant data for conducting any necessary due diligence of the potential Registrant (e.g., to confirm that the Developer had not previously abused the HIF).

The HIF would reserve the right to refuse to enter into the Framework and Supply agreements with entities that have previously abused the HIF or entities that have no or poor record of manufacturing or supplying pharmaceutical products. These are discretionary criteria. The impact of that discretion, however, will be somewhat reduced since HIF would exercise it prior to entering into a Framework or Supply Agreement and before most of those prospective registrants made investments pursuant to their prospective participation in the HIF.

Product Eligibility

Product eligibility under the HIF will not be limited to a type of pharmaceutical product (such as a vaccine) for the treatment of a particular disease or condition in specific countries, with required technical and product specifications. Product eligibility criteria will be important, however, for the function and success of the Framework and Supply Agreements.

The HIF Book proposes four basic product eligibility requirements, which are examined below.

Pharmaceutical Product. HIF registration will be limited to pharmaceutical products that improve human health. The HIF Book suggests that eligible products would include drugs and vaccines, but not medical devices. The Supply Agreement must include a clear definition for “pharmaceutical product” which reflects the mission and objectives of the HIF.

Regulatory Approval. HIF registration should be limited to pharmaceutical products that have been authorized for use by a stringent national regulatory authority or accepted under the WHO Prequalification Program. Prior to entering into a Supply Agreement, HIF should require a prospective Registrant Supplier to submit supporting evidence such as a copy of registration certificate or marketing approval from a stringent regulatory authority and a copy of Good

Manufacturing Practice (GMP) certificate issued by a stringent national drug regulatory authority or WHO Prequalification letter certifying the compliance of the manufacturing site with WHO GMP requirements. The Supply Agreement should require the Registrant Supplier to obtain and maintain authorizations and approvals necessary to market and sell their registered products in any country in which they intend to do so.

Innovative. The HIF Book indicates that registration will be limited to pharmaceutical products that are “innovative.” This use of the term “innovative” is confusing as this eligibility requirement is meant to address two different HIF objectives. First, the HIF is intended to serve as an incentive for research and development of “innovative” products and uses of existing products (i.e., a technical advance in addressing the global burden of disease), but for which there is inadequate effective demand. Second, the HIF is intended to address the high prices that often put innovative (i.e., on-patent) drugs out of reach of most of the world’s population by providing an alternative to Registrant Suppliers charging high prices through the exercise of their patent rights.

The HIF Book proposes to use patent status as an eligibility requirement to address both concerns. Specifically, an eligible product would need to be under patent protection “in at least some set of major patent offices,” or have an indication that is under patent in those offices, at the time of its registration with HIF.

Patent status is an effective eligibility criterion for addressing the second of the HIF goals (reducing the high prices of innovative medicines), but an imperfect one for the first (providing an innovation incentive). Since the HIF is meant to act as an alternative to Registrant Suppliers charging high prices through the exercise of their patent rights, it is appropriate to restrict registration to products and uses which are on-patent at the time of registration and for a majority of the time for which the product is registered.

Patent status, however, is both under- and over-inclusive as a proxy for innovation. It is under-inclusive because there are technical advances with potential health impact that are difficult or impossible to patent that may not be eligible for the HIF.⁵ It is over-inclusive because the patent status of a product or its use does not guarantee that product or use represents a technical advance in terms of its potential health impact. There would be products or uses that

⁵ See Talha Syed, *Should a Prize System for Pharmaceuticals Require Patent Protection for Eligibility?* 3-4 (2009) (citing, for example, new uses for compounds on which product patent protection is either held by another or expired or not available and new safety and efficacy data on already-approved drugs).

are not innovative from the perspective of global health impact, but still eligible under an on-patent criterion.

An alternative approach, thoughtfully proposed by Talha Syed, would be to substitute regulatory approval of a “new drug application” (NDA)⁶ instead of patent status as an eligibility criterion. This approach has advantages and drawbacks. It would be more effective for addressing the first HIF goal (providing an innovation incentive), but less useful in achieving its second (reducing the high prices of innovative medicines).

An NDA requirement would cover some technical advances—in particular, new uses for compounds on which product patent protection is either held by another, expired, or not available and new safety and efficacy data on already-approved drugs—that would be excluded by a on-patent eligibility requirement. A concern, which Syed acknowledges, is that this approach may also reward uses that would be or are already discovered by doctors in the normal course of their practice or research and implemented off-label. Obtaining and rewarding an NDA for such applications would offer marginal new health value.

The NDA approach is an awkward fit with the second goal of HIF—providing an alternative to registrants charging high prices through the exercise of their patent rights. The potential problems are twofold.

First, this approach would reward some products and uses that are unpatented or off-patent and available at generic prices. Donor governments would have to pay more under the HIF for these uses and/or products than they do so now, undermining somewhat the argument that HIF will reduce those donors’ costs.

Second, this approach may raise fairness concerns and discourage the registration of on-patent products. Under the NDA approach, on-patent and off-patent products and uses would compete on equal footing for the HIF health impact-based rewards, but the conditions placed on on-patent products and uses would be significantly more onerous. Registrants would need to forego the ability to charge higher prices through the exercise of their patent rights as well as accept the access requirements that the HIF intends to place on on-patent registrants (such as granting a non-exclusive license at termination).

⁶ The U.S. Food and Drug Administration (FDA) approves NDAs based on the submission of full safety and efficacy data on the product, pursuant to either of the two types of “new drug applications” (“505(b)(1)” and “505(b)(2)” applications).

Ultimately, it will be a policy determination, to be decided in consultation with potential donors, whether the cost of stimulating and rewarding innovation that would not be covered by a patent eligibility requirement would justify their social value. If the answer is yes, the patent and NDA approaches need not be mutually exclusive. The Framework and Supply Agreement could simply define an eligibility requirement that includes on-patent products and specific innovations (such as the new uses discussed in Syed (2009)), which while unpatented, have achieved an NDA. This approach would address the concern about the under-inclusiveness of the patent eligibility criterion.

The concern about the over-inclusiveness of the patent eligibility criterion is mitigated by the annual administrative fee that registrants must pay and the health impact-based reward mechanism of the HIF. The registrant will be required to pay the average cost of health impact assessment as an annual fee for participating in the HIF, which may be expensive.⁷ The reward payment that HIF will provide to registrants is also proportional to their assessed health impact. Accordingly, products that have a modest health impact will receive a similarly modest payment, less the health assessment registration fee. This compromise approach, however, would not address the fairness and competitive concerns regarding the additional burdens that HIF will place on-patent products and uses.

If the eligibility criteria incorporate an on-patent requirement, a prospective Registrant Supplier would need to demonstrate patent status of the product or use and its remaining term. The HIF Book indicates that eligibility should be limited to products with patent protection (either on the product or method of use) that will not expire “soon” after registration. If a drug is about to become generically available, the HIF should not to pay for the global health impact of a bioequivalent version of that generic product.

This requirement could introduce administrative complications. The term of patent protection for a pharmaceutical product may vary in different countries; the scope of HIF is global. Patent protection for a product will also depend on the validity of those patents, which may be successfully challenged during the ten-year reward term of the HIF. The Supply Agreement should establish a clear, defined, and administratively simple requirement for the length of the remaining patent protection at registration.

⁷ See HIF Book at 31 (“if the HIF had an annual budget of \$6 billion, it could spend about \$600 million on administration and assessment, with the bulk being devoted to assessment.”)

One possible approach is that the Supply Agreement could require that Registrant Supplier warrant that it has at least a contractually defined duration of remaining patent protection—say, five years—in a country covered by the HIF. The HIF could require any prospective Registrant Supplier to identify the patent(s) on the pharmaceutical product or use being registered on which it is relying to make that warranty in the Supply Agreement. Under this approach, the HIF would not conduct its own analysis of the Registrant Suppliers’ claims or patents, but would have the right to terminate the Supply Agreement if the patents claimed by the prospective registrant are later proved invalid or of shorter duration.

Irrespective of whether the HIF is limited to on-patent products or uses, a prospective Registrant Supplier must warrant and represent in the Supply Agreement that it has and will maintain the intellectual property rights necessary, if any, to manufacture, market, and sell the registered medicine in any country in which that Registrant intends to do so. The HIF will not affect non-registrants’ patent rights or their ability to pursue legal recourse (including monetary and injunctive relief) against an infringing registrant. It will be important, however, for both potential registrants and funders that infringing products be excluded from the HIF. Further, as a deep pocket defendant and obvious target for lawsuits, the HIF should take reasonable measures to minimize the likelihood of such suits, whatever their merits may be.

Superiority. The HIF Book indicates registration should be limited to those products that offer a meaningful expected health impact compared to other products already registered with the HIF. The details of that requirement, however, are left undefined. A criterion that mandates a discretionary assessment by HIF of the clinical merits of a prospective product, relative to other registered products, would greatly undermine the predictability of HIF eligibility for prospective Registrant Developers and Suppliers.

There are at least three possible approaches to address this concern.

First, the Supply Agreement could include a requirement similar to the “clinical superiority” clause embodied in the US Orphan Drug Act.⁸

The Orphan Drug Act creates incentives, which the market might not otherwise provide, for the development of drugs for diseases and conditions that affect fewer than 200,000 people in the US. The primary incentive under the Act is the promise of seven years of market exclusivity

⁸ Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049 (1982) (codified as amended at 21 U.S.C. §§ 360aa-360ee (2000), 26 U.S.C. §45C, 42 U.S.C. §236.

for the indication for which the drug was approved—until a “clinically superior” follow-on product is approved. In subsequent regulations, the FDA defined three criteria for establishing clinical superiority as (1) more effective than an approved orphan drug; (2) safer than an approved orphan drug; or (3) in the absence of greater effectiveness or safety, the new drug must make a major contribution to safety care.⁹

This solution would be, at best, partial because a “clinical superiority” approach is useful only in addressing the issue of duplicative products being registered. The superiority clause in the Orphan Drug Act, for instance, only compares the superiority of a new drug to a drug that is otherwise the same. Moreover, its effectiveness has been debatable.¹⁰ A superiority clause that is not carefully drafted or applies across product types and indications would create undue uncertainty, discouraging potential Registrant Developers from entering into a Framework Agreement.

Second, the HIF could impose far stricter product eligibility criteria for the Supply Agreement, limiting registration to specific types of products with particular technical and usability criteria. This approach would be more similar to the advance market commitment for vaccines.

Last, HIF could rely on its health impact-reward mechanism coupled with the annual registration fee to discourage registration of products without meaningful health impact relative to other registered products. This last option should suffice and would be more consistent with the overall mission and objectives of HIF.

Entry, Term, and Termination

Carefully designed entry, term, and termination provisions in the Framework and Supply Agreements will be critical for creating incentives and managing risks for HIF and Registrant Developers and Suppliers.

For a Registrant Supplier, the terms under which it and potential competitors may enter and exit the Supply Agreement will be a principal factor in its decision to undertake the risks necessary to enter into that Agreement. The duration of the term will be closely tied to the size of

⁹ Orphan Drug Regulations, 21 CFR 316.3.

¹⁰ See, e.g., Robert A. Bohrer and John H. Prince, *The FDA's Uncertain Interpretation of the Orphan Drug Act*, 12 HARV. J. LAW & TECH. 365 (1999).

the potential rewards for registration and the incentives necessary for the pharmaceutical product development and supply that the HIF envisions. In general, entry, term, and termination provisions must be clearly defined and administrative discretion appropriately limited in order not to deter prospective and existing registrants.

For the HIF, entry, term, and termination provisions are equally important for its risk management and administrative needs. The term will establish and limit the extent of HIF's obligations to Registrant Developers and Suppliers. Termination provisions in the Supply Agreement will create a significant tool for HIF to prevent and eliminate abuse and fraud by Registrant Suppliers. Finally, the design of the entry and termination provisions of the Supply Agreement will be important for the ability of HIF to conduct an orderly health assessment process.

Entry

The HIF Book suggests a Registrant Supplier would be permitted to enter into a Supply Agreement for an eligible product at any time after HIF has confirmed its eligibility. The HIF health impact assessment system, however, must measure annually the incremental global health impact of all registered products and pay awards relative to the impact of all registered products. This design feature suggests that registered products should be measured over the same period time, which would make it difficult for Registrant Suppliers to enter the HIF at any time. It may be sensible, therefore, to establish a defined annual enrollment period for Registrant Suppliers to enter into the Supply Agreement.

Registrant Developers, on the other hand, should be permitted to enter into the Framework Agreement at any time during the development process. This approach maximizes the possibility that companies with promising technology or relevant expertise will participate in the HIF. There does not appear to be any obvious downside to permitting Registrant Developers to enter into the Framework Agreement in the later or even last stages of development.

Term

The HIF Book indicates that the term of the Supply Agreement will be ten years for eligible products and five years for eligible new indications. This length of this term would be independent of the patent status of the product or indication. Provided the product or indication is on-patent at registration, it would not be required to be so during the entire term. The duration of

the term of the Supply Agreement is a policy question, as it could be lengthened or shortened in order to reduce HIF costs or improve the incentives for registration.

It would also be necessary to define a term for the Framework Agreement. The duration of the Framework Agreement should be sufficient to allow Registrant Developers a reasonable opportunity to successfully develop an eligible product, but not so long to bind HIF to hopeless product development projects or commit donors beyond their willingness to support the HIF. This term should be determined in consultation with potential donors, prospective Registrant Developers, industry experts, and stakeholders.

Termination

Well-designed termination provisions can significantly affect the rights and risks of the parties of the Framework and Supply Agreements, defining the specific conditions that give rise to early termination of those Agreements and the obligations that remain after termination.

Framework Agreement. The Framework Agreement is designed to have no requirements or costs for the HIF until the Registrant Developer successfully develops an eligible product or use and enters into the Supply Agreement. Accordingly, if a Registrant Developer wishes to terminate that Agreement, it should be permitted to do so with written notice and no condition or penalty.

The Framework Agreement should also include a sunset provision that allows the HIF to exit after a defined period of time if the Registrant Developer has not entered into the Supply Agreement. The term of the Framework Agreement could also be linked to the Registrant Developer's achievement of defined development milestones by specified deadlines. Such provisions would grant the HIF an option to exit the Framework Agreement and devote its energies and donor resources elsewhere.

The Framework Agreement should also provide for early termination in the instance of a material breach of a term or condition of the agreement. If the Registrant Developer committed such a breach, the HIF could serve written notice to that Registrant and, unless the Registrant fully cured the breach within a contractually defined time after that notice, the HIF, at its option, could serve notice of cancellation on the Registrant Developer, and the Agreement would immediately terminate. The most likely examples of a material breach by the Registrant Developer would be failure to provide all the necessary information regarding its own eligibility

or demonstrate the achievement of any specific development milestones the Framework Agreement might impose. Possible HIF breaches of the Framework Agreement would include failure to enter into the Supply Agreement upon satisfaction of the condition precedent or a material change in the terms of the Supply Agreement. Allegations of material breaches under the Framework Agreement must be subject to dispute resolution to maintain the credibility of the Agreement.

The Framework Agreement for an early stage pharmaceutical product could be in force for a decade or more before the Registrant Developer successfully develops a candidate product and seeks to enter into a Supply Agreement. Accordingly, the Framework Agreement should provide another type of exit provision—a *force majeure* clause—should the HIF need to alter or exit the Framework Agreement as a result of extraordinary events. *Force majeure* literally means “greater force.” Such a clause would exclude parties from liability for early termination of the Framework Agreement if some unforeseen event beyond the control of that party prevents it from performing its obligations under the contract. This provision could apply to both parties, but only the HIF would be likely to use it in practice. The two most likely examples are (1) if some unforeseen event prevented the HIF from fulfilling its obligation to enter into a Supply Agreement upon fulfillment of the conditions precedent in the Framework Agreement and (2) if it were necessary to make changes in the eligibility terms of the Supply Agreement, which would be materially more burdensome to the Registrant Developers. To avoid the risk that a *force majeure* clause might be used by the HIF to renege on its commitments, it would be important to establish clear standards in the Framework Agreement for invoking that clause and make any decision to do so subject to dispute resolution.

Supply Agreement. If a Registrant Supplier wishes to exit early from the Supply Agreement, it should be permitted to do so after providing adequate written notice as defined in the Agreement. A Registrant Supplier would be most likely to enter into the Supply Agreement if its ability to exit the Agreement is unfettered. HIF, however, would have at least three interests in restricting the ability of Registrant Suppliers to exit the Supply Agreement before the end of its ten-year term.

First, a disproportionate amount of the cost of health assessment for a registered product is likely to be upfront. The costs for the assessment of a particular medicine would presumably

decrease over time, once HIF has established a baseline assessment and been evaluating the product for several years.

Possible approaches to address this concern are restricting Registrant Suppliers from exiting the HIF until a defined period after entry and/or imposing a particular penalty, in form of liquidated damages, for premature exit. Alternatively, the annual health impact assessment administration fee for Registrant Suppliers could be designed to start high and decrease over time in order to encourage longer participation in the HIF.

Second, an unfettered ability of Registrant Suppliers to exit the HIF could complicate an already difficult process of determining rewards based on the assessment of registered products relative to each other. The HIF would need to adjust its calculations for partial year performances and compare registered products over different time periods. It would be sensible to limit termination to a defined annual period. This period would be the same as the annual enrollment period discussed in relation to entry.

Third, a Registrant Supplier will have an incentive to exit the Supply Agreement early in order to circumvent the requirement that, at the conclusion of its ten-year term, the Registrant must grant HIF a non-exclusive, royalty-free license for all relevant patents, data, and other know-how needed to manufacture and sell of the registered product.

One solution, proposed in the HIF Book, is that Registered Supplier would be required to grant this license ten years from the effective date of the Agreement irrespective of when the Registrant Supplier exits the Agreement. This approach would be effective in preventing Registrant Suppliers from gaming the HIF through early departure. It would, however, also significantly reduce the utility of the early exit provision as a tool to manage the risks of Registrant Suppliers. Such a provision would discourage the participation of Registrant Suppliers with eligible products that have more than ten years of effective patent protection remaining and which otherwise would be willing to try the HIF.

A possible compromise approach is that Supply Agreement could be designed so that the requirement to grant the license ten years from the effective date of the Agreement would not attach until the Registrant Supplier had participated in the HIF for a contractually defined number of years—for example, 3 years. This approach would reduce of the risks for Registrant Suppliers to experiment with participation in the novel and unfamiliar HIF reward system while

reducing the risks for HIF of such Registrants exploiting the termination provisions to avoid granting the required licenses.

The termination provisions of the Supply Agreement must define the obligations that would remain for each party after termination. Early termination should not excuse the obligation of the HIF to pay the rewards earned by the Registrant Supplier prior to the effective date of that termination. In turn, the termination provisions should need to require that, even after termination, the Registrant Supplier must continue to supply the data necessary to assist the HIF in its health impact assessment of the product for the period of time on which it was on the HIF.

As with the Framework Agreement, the Supply Agreement should provide for termination as a result of a material breach by either party and *force majeure*. The Supply Agreement, however, would impose far more extensive requirements and obligations on the parties; the potential for material breaches and, to a lesser extent, *force majeure* would be greater.

The possibility of terminating the Supply Agreement for material breach is one of the primary tools that the HIF would have to control and reduce Registrant Supplier abuse of the HIF and its health impact assessment mechanism. Since it would apply to all terms and conditions of the Supply Agreement, this provision would allow HIF to address material failures of Registrant Suppliers to maintain the eligibility of registered products or perform their obligations under the Agreement. For example, if the Supply Agreement requires, as it should, that a Registrant Supplier comply with the U.S. Foreign Corrupt Practices Act and all other applicable laws in its marketing, distribution and sale of the registered product, evidence that Supplier has paid bribes in order to increase the potential health impact of its products would constitute a material breach of its obligations and be grounds for termination and potential damages.

The Supply Agreement should provide that if a Registrant Supplier does not cure its material breach upon written notice within a contractually defined period of time, the HIF could, at its option, serve notice of cancellation on that Registrant and the Agreement would terminate. The reverse of that circumstance, in which the HIF is in breach of the Agreement, would follow the same procedure.

The topic of addressing disputes arising from breaches of the Supply Agreement or *force majeure* is discussed *infra* in the dispute resolution section of this paper.

Intellectual Property and Access Conditions

In many technology pharmaceutical development and distribution partnerships, intellectual property is an important tool for achieving the objectives of the partnership, defining and structuring the relationship, and creating the ownership, control, incentives, and risks that move products through the value chain from discovery to delivery, bench to bedside. Such agreements may include clauses, for instance, that allow the funding partner to take ownership or appropriate licenses in intellectual property, preexisting as well as that which has been developed pursuant to the partnership, in order to complete the development of the target product and ensure its delivery. The inclusion and design of such clauses depends on necessary trade-offs between creating incentives for developers and suppliers to voluntarily participate in the partnership and the objectives of funders for the development and supply of the product.

Such intellectual property management tools, however, should play a less significant role under the HIF.

A Registrant Developer or Supplier will retain its ownership and interests in the technology, data, and know-how used for the manufacture and sale of the registered product or use.

In the Framework Agreement, there should be no access clauses. This is a given since the HIF will provide neither advance or interim development funding nor the guarantee of a prize payment for successfully developing the product. Under these circumstances, very few developers would enter into the Framework Agreement if it required them to cede control of their pre-existing or developed intellectual property.

The use of intellectual property management tools should likewise be limited under the Supply Agreement. The HIF Book proposes several such conditions that could apply under the Supply Agreement. Under this proposal, a Registrant Supplier must:

1. Provide whatever sales, clinical trial, and other proprietary data that HIF may require to conduct its audits and health impact assessments;
2. Authorize HIF, and provide any necessary data and know-how, to seek market approval for the registered product wherever the HIF has determined that the Registrant Supplier has failed to do so (the HIF would subtract the costs of this effort from the Registrant Supplier's next annual health impact reward payment);

3. If the Registrant Supplier fails to adequately supply the registered product, it must grant a HIF, or its designee, a non-exclusive, royalty-free license to make, have made, use, sell, offer for sale and import the registered product wherever the Registrant Supplier has failed to provide an adequate supply; and
4. Grant a nonexclusive, royalty-free license to the relevant intellectual property at the conclusion of the ten-year term of the Agreement.

The first requirement—to provide sales, clinical trial, and other proprietary data for the global health impact assessment—is unavoidable under the HIF model. HIF could not perform its assessment of a registered product without that data. The Supply Agreement should reduce, however, the risks imposed on Registrant Suppliers through provisions that ensure the confidentiality of submitted data.

The second and third requirements are counterproductive and duplicative of the incentives that the health impact based-reward system provides.

Under the HIF, a Registrant Supplier will achieve greater rewards each year by supplying its registered product to more people under conditions in which the product would have the most health impact. If under an incentive to expand access, a Registrant Supplier still does not seek regulatory approval or adequately supply a particular country, it will likely be because the additional rewards that the Registrant expects from HIF would not justify the costs of doing so. Under these circumstances, clauses in the Supply Agreement that require Registrant Suppliers to cede access or control over their intellectual property *and* pay for the costs of regulatory approval sought by HIF or another party only serve to deter Registrant participation.

Further, the potential risks imposed by such access provisions under the HIF would be great. The scope of the HIF mission and objectives are global. Registrant Suppliers will be required to provide their registered products in every country and market segment in which there is demand. A Registrant Supplier could be compelled to grant licenses in developed countries or markets in addition to developing countries, philanthropic program, or public sector markets.

A better way to achieve the objective of the second and third requirements would be to improve the certainty of HIF reward payments or provide larger rewards for difficult-to-serve countries and market segments.

The fourth requirement—the need to grant HIF a royalty-free nonexclusive license ten years after the effective date of the Supply Agreement—serves the HIF mission by encouraging long-term sustainable access to these products. It would undoubtedly deter some potential Registrant Suppliers with products for which the patent protection extends beyond ten years. In that instance, the predictable rewards offered by the HIF would need to exceed the returns that Registrant could earn globally through exercise of its patent rights for the product during its term with the HIF and the remainder of the effective patent term after those ten years.

The balance of private incentives and access considerations for this fourth requirement could be adjusted in two ways.

First, the Supply Agreement could limit the scope of the required license required to specified developing countries or public sector markets within those countries. This approach would reduce the burden of the license requirement for Registrant Suppliers by preserving its commercial interests in more remunerative markets. At the same, this approach would preserve access in countries and markets that are most ill equipped to pay new patent-fueled prices for the formerly-HIF registered product. It would be inconsistent, however, with the mission of HIF to provide sustainable access to such medicines at a single low price in developed and developing countries alike.

Second, the imposition of this fourth requirement could be limited to Registrant Suppliers that have participated in the HIF for a certain number of years—for example, 3 years. This approach would not address the cost of the license requirement, but would permit Registrant Suppliers to be more certain about the size of the potential reward. The HIF and its health impact-based reward system are novel; that novelty creates uncertainty for potential Registrant Suppliers. Delaying the imposition of this license requirement would reduce the costs for Registrant Suppliers to experiment with participation in the HIF.

Internal Adjudication and Dispute Settlement

The availability and procedures for dispute resolution and/or judicial review for disputes arising from the Framework and Supply Agreement will be important design issues for managing the risks of Registrants and the HIF.

Internal Adjudication

An adequate and carefully designed internal dispute resolution process will be necessary for the HIF health impact assessment and reward determination.

First, adequate due process would provide some essential assurance to prospective Registrant Suppliers that there will be adequate procedures to ensure the validity of health impact assessments and reward calculations. The global health impact assessment that HIF will conduct of registered products is difficult, complex and—for many diseases, types of products, and settings—unprecedented. The reward that HIF will provide will be entirely based on the outcome of the health impact assessment. The stakes for the Registrant Suppliers of that assessment could not be higher; the assurances of transparency and precision must be commensurate.

Second, the health impact assessment-based reward system is likely to generate a significant number of disputes given those high stakes, the complexity of the assessments, and competitive implications of assessments. Under the HIF model, a Registrant Supplier will not only have a vested interest in the validity and accuracy of the health impact assessment of its product, it will have a legitimate stake in the validity and accuracy of the health impact assessment of every other registered product. In light of the significant potential for disputes, the HIF should develop an internal dispute resolution process that will be efficient, reliable, and minimize administration costs and potential litigation.

The HIF should establish and fund an Independent Adjudication Body for resolving disputes arising from the health impact assessment process and reward calculation. The general procedure for resolving disputes under this approach could be as follows. Once the HIF assessment branch issues its determination of health impact assessment and calculates the rewards, Registrant Suppliers would be given a contractually defined number of days in which to file any complaints regarding that assessment or reward determination with the HIF audit branch. The audit branch would issue a formal written review of the assessment and the Registrant Supplier's complaint. The Registrant would again have a contractually defined number of days in which to seek review from the Independent Adjudication Body of the determination by the audit body. As a condition of the Supply Agreement, Registrant Suppliers would agree to be bound by the independent adjudication body's determinations. The independent adjudication body should have its own operational budget—to avoid the perception of undue HIF influence—and consist of a combination of legal specialists and global health, health assessment, and ex-industry

experts. The procedures and rules of the adjudication body should be written and available in advance to prospective and current Registrant Developers and Suppliers.

The downsides of this approach are twofold.

First, establishing and maintaining an independent adjudication body could be expensive, albeit likely cheaper than the arbitration and litigation alternatives, and would add to the already substantial administration costs of the HIF.

Second, the process for re-assessing health impact or reward calculations, when justified, would be complicated given the HIF model. The resolution of disputes would take time. The HIF cannot wait for resolution of all disputes regarding registered products' health impact assessments or rewards prior to issuing its annual payments. Once payments are made, however, it will not be feasible to recalculate and claw back over-paid rewards. Since Registrant Suppliers will free to terminate their Supply Agreements early, the HIF cannot rely on being able to adjust future reward payments.

Dispute Resolution

The Framework and Supply Agreements should indicate that other disputes arising from other terms of these Agreements, including eligibility and *force majeure*, will be resolved by arbitration. The Agreements should designate the law that would govern the agreement and the venue and procedures for the arbitration. Such disputes would involve allegations of material breach of the Agreements; HIF would be a party. It would not be prudent or acceptable to Registrants to resolve those disputes at the Internal Adjudication Body.

SUMMARY OF RECOMMENDATIONS

The goal of the HIF-registrant relationship must be to align registrant incentives with the sustainable public health outcomes that are root and standard of HIF's mission. Critical determinants of success will include the size of the reward, the clarity and predictability of the reward system, and the contractual obligations placed on registrants. It will be essential to convince registrants that the global health impact assessments are transparent and precise. The HIF plan, as currently envisioned, takes many innovative and positive steps in addressing these issues, but nonetheless poses significant structural and contractual challenges to its relationships with registrants.

Below is a summary of the critiques and recommendations this paper makes for the design of arrangements that HIF will offer to registrants.

1. The full power of the HIF model to transform the global health marketplace can only be harnessed by including both Developers as well as Suppliers within its contractual arrangements. Without credible, binding, and enforceable assurances of the availability and terms of the HIF, Developers are unlikely to make the significant and risky investment to develop a pharmaceutical product, which has high potential health impact, but would be unprofitable absent the HIF.

This paper proposes a structure for this potential relationship with Resident Developers consisting of two agreements:

- A Framework Agreement in which a Registrant Developer would agree to develop a pharmaceutical product eligible for the HIF in return for the right, if successful, to enter into a second contract (a Supply Agreement) and compete for a share of the Fund. The Supply Agreement, complete with all its terms and conditions, would be attached and incorporated into, the Framework Agreement.
- A Supply Agreement in which the Registrant Supplier agrees to supply an eligible pharmaceutical product pursuant to the terms of the Supply Agreement (including an administratively determined low price) in exchange for an annual share of the Fund.

This Supply Agreement would be identical to that which would be used for supply of eligible extant products. Suppliers of existing eligible products could enter into the Supply Agreement without needing to enter into the Framework Agreement.

2. The HIF must include carefully defined, non-discretionary product eligibility criteria, designed to promote the registration of the best products.

This paper proposes that eligible products should be limited to:

- pharmaceutical products, as defined in the Supply Agreement, or uses thereof, that improve human health that
- have been authorized for use by a stringent national regulatory authority or accepted under the WHO Prequalification Program, and
- are on-patent, or have a use that is on-patent, at the effective date when the Registrant Supplier enters into the Supply Agreement.

HIF should consider including two other product eligibility requirements. First, the HIF should consider including in the eligibility criteria defined, specific types of innovations, which while unpatented, that have achieved an NDA. Second, the HIF should consider including a clinical superiority clause, akin to that which is in the U.S. Orphan Drug Act, which would exclude duplicative products from registration on the HIF.

3. The health impact-based reward system creates uncertainty for Registrants and risks of fraud and manipulation for the HIF.

The HIF should include carefully design the entry, term, and exit provisions of the Framework and Supply Agreements to create constructive incentives and manage the risks for registrants and the HIF alike. Accordingly, the HIF should:

- Permit Registrant Developers to enter or exit the Framework Agreement at any time during the development process.
 - Include a sunset provision in the Framework Agreement which allows the HIF to exit if the Registrant Developer has not entered into the Supply Agreement by a contractually defined date.
 - Permit Registrant Suppliers to enter and exit the Supply Agreement, but only during contractually defined annual enrollment periods.
 - Ensure that early termination does not excuse: (1) the HIF from paying rewards earned prior to termination; (2) the Registrant Supplier from supplying the data necessary for the health impact assessment; and (3) the obligation to grant a royalty-free, nonexclusive license for the product ten years from the effective date of the Supply Agreement.
 - Provide for termination for material breach and *force majeure* in the Framework and Supply Agreements.
4. The intellectual property access conditions proposed in the HIF Book will unnecessarily deter potential registrant involvement.

The Framework Agreement should include no provisions granting access to the preexisting or developed intellectual property of the Registrant Developer.

The Supply Agreement should:

- Include an obligation for Registrant Suppliers to provide sales, clinical trial, and other proprietary data for the global health impact assessment, but also include provisions requiring the HIF to maintain its confidentiality.

- Include an obligation to grant HIF a royalty-free nonexclusive license ten years after the effective date of the Supply Agreement, but limit its application to Registrant Suppliers that have participated in the HIF for a contractually defined number of years (i.e., 3 years).
 - Not include an obligation to authorize and provide HIF with any necessary data and know-how to seek market authorization in whichever countries the Registrant Supplier has failed to do so.
 - Not include an obligation to grant HIF, or its designee, a non-exclusive license to make and sell the registered product in whichever countries the Registrant Supplier has failed to adequately supply.
5. Given the stakes, complexity, and competitive implications of the HIF health impact assessments, this reward system will generate disputes by and between registrants and deter some potential registrants with its novelty.

The HIF should establish an independent adjudication body to hear disputes arising from the health impact assessment and reward determination. The Supply Agreement should require Registrant Suppliers to agree to be bound by this body's determinations on issues within its jurisdiction.

Disputes arising from other terms of the Framework and Supply Agreements, including eligibility and *force majeure*, should be resolved by arbitration.

NEXT STEPS

Significant work remains. This paper is not intended to provide an exhaustive analysis of the relationship of HIF with its registrants. Among the topics that this paper has not covered are: alternative mechanisms for achieving manufacturing cost plus price; quality assurance; inspection and testing of products; liability; insurance; indemnification; recall of products; confidentiality; choice of law; and payment and timely performance. This paper has also not considered external factors that will affect the design of the contractual arrangements between the HIF and its registrants, including: global regulatory architecture; international reference pricing for pharmaceuticals; and coordination with foreign aid programs and other government, intergovernmental, and philanthropic initiatives to create incentives for commercial investment for sustainable access to drugs. These topics and factors must be considered.

In the interim, the analysis in this paper will help enable IGH to have substantive and more productive consultations with potential funders, registrants, and stakeholders. It is the feedback from those consultations that will ultimately drive the legal and policy work necessary to structure and draft the contractual arrangements between HIF and its registrants.