Global Challenges Report

Strategic Review of WIPO Re:Search

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Including: Response from the WIPO Secretariat

WIPO
WORLD
INTELLECTUAL PROPERTY
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Prologue

This report summarizes the insights of one consultant, contracted to assess events occurring over nearly a decade. I do not claim data comprehensiveness nor do I believe that another consultant listening to what I heard, interpreting the documents I read, and assessing the meaning of events described to me would draw the same conclusions. I recognize that each individual involved in WIPO Re:Search will have a unique set of experiences and reactions to events from which they will draw their own conclusions. While I am quite experienced in this type of organizational assessment and have academic publications on subject matter relevant to my investigation, I do not assert that my account is scientifically rigorous nor do I see it as an "objectively written report." Thus there is no need for meticulous and exhaustive documentation. In fact, I cannot conceive of any exposition so comprehensive that it could over-ride what the principals involved have experienced and are personally disposed to believe. The very good news is that (subject to geographical and travel constraints) I have had sufficient access to constituency leaders to feel very solid about what I've concluded – and what is in this report. My hope is that readers will find this document, including its sometimes blunt assessments and recommendations, a useful prompt to additional thinking and mutual discussion.

My views are intended as a prologue for subsequent face-to-face discussions and are presented in the spirit of assisting readers in fulfilling their personal commitment to address some of the greatest needs in the world.

I would like to express my gratitude to Prof. Samuel Culbert of the Anderson School of Management at The University of California, Los Angeles (UCLA) for helping me over many years to learn a few things about organizations, people and the requirements for success.

Richard T. Mahoney, PhD

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Section 1:
Executive Summary

WIPO Re:Search was established in 2011 and has enjoyed more than three years of progress and success. The current report explores ways to secure the longer-term success and sustainability of WIPO Re:Search through the expansion of its programs and additional support. The Consortium, an initiative of the World Intellectual Property Organization (WIPO), which hosts the WIPO Re:Search secretariat is managed jointly with BIO Ventures for Global Health (BVGH) (Seattle, USA) which operates the WIPO Re:Search Partnership Hub.

The report was prepared on the basis of a study of the published and unpublished literature, websites, and other documents provided to the author by WIPO and BVGH, and 30 interviews with key stakeholders as recommended by WIPO and BVGH. Interactions with staff at WIPO and BVGH have been invaluable. The report includes various annexes:

- Annex 1: Terms of Reference;
- Annex 2: A list of interviewees;
- Annex 3: The questionnaires used;
- Annex 4: Summary of changes to the WIPO Re:Search operating environment;
- Annex 5: A description of other organizations and their research work; and
- Annex 6: Description of selected potential donors.

WIPO Re:Search operates in an environment involving intellectual property and research that has fundamentally changed over the last decades. There is unanimous agreement that WIPO Re:Search is a valuable addition to the global endeavor to reduce the impact of neglected tropical diseases (NTDs), malaria, and tuberculosis (TB), and should be sustained. WIPO Re:Search has demonstrated that intellectual property is not a barrier to research for products to diagnose and treat NTDs, malaria and TB in least developed countries. The report outlines the Consortium's successes and also identifies areas in which it has been less successful (Section 3.1).

A key strength of the WIPO Re:Search Consortium is its ability to attract the collaboration and support of several of the world's largest pharmaceutical companies. It has also assembled a large database of technology assets, created an effective Partnership Hub, fostered the formation of a large number of partnerships, and supported capacity building in developing countries.

It has seen less success in expanding the number of participating companies, catalyzing agreements with developing country institutions, responding to requests for financial and technical support from developing country partners, attracting new donors, and demonstrating that partnerships can lead to product development. It has also had some difficulty in creating and operating a structure that is widely understood, and in shaping a clear long-term vision.

In terms of funding, WIPO covers the costs of running the WIPO Re:Search secretariat and the private sector supports the costs of operating the Partnership Hub.

The report draws a number of additional conclusions (Section 4) as follows:

1. WIPO Re:Search should be judged, in the near term, on its ability to catalyze the discovery of new leads for exploitation by others and not on progress in product development.

2. WIPO Re:Search emerged at a time when intellectual property was a central contention. While it remains important, intellectual property to a large extent is no longer the source of such heated debate.

3. WIPO Re:Search is creating a new market for underutilized assets.

4. In the near term, WIPO Re:Search is adding value through its active formation of a global network of companies, academia, research centers, and government agencies. This is facilitating the exchange of valuable assets in the form of technologies and research that could be a potent means to accelerate progress in the field.

5. To achieve its potential, WIPO Re:Search needs to attract additional financial resources and broader support.

The most important recommendations (from the viewpoint of this author) are summarized here. More detailed recommendations are provided in Section 5.

1. WIPO Re:Search is the only international mechanism operating under the aegis of a specialized agency of the United Nations (UN), with policies that

successfully address IP issues and facilitate private sector activities to accelerate early-stage research by public and private institutions for disease control in developing countries.

2. Consideration should be given to the expansion of financial support by the private sector in the form of small grants (either pooled or individual) to WIPO Re:Search users to support research resulting from collaborative agreements. Such support would have two benefits. First, it would help ensure that collaborative agreements result in more than the provision of compounds and limited technical assistance through Material Transfer Agreements (MTAs). Second, it would establish a mechanism to channel new donor funding, giving priority to supporting universities and developing country research centers.

3. Formalizing the role of the private sector in WIPO Re:Search's operations should be considered. For example, contributing companies could become members of an Advisory Committee that would meet at least every year for a day, to review WIPO Re:Search operations and provide advice on priorities, resource allocation, and management. Such an Advisory Committee would demonstrate the important role of the private sector and would provide an opportunity for more extensive sharing of expertise and knowledge in this complex area. It could also give company representatives an opportunity to assure their management that the views and needs of companies are being expressed and met in WIPO Re:Search.

4. WIPO Re:Search's objectives should be modified to emphasize that it facilitates "early stage" research and effectively addresses possible barriers to products moving into PDPs, if the PDPs wish to develop them further. Such a description will clarify the role of WIPO Re:Search vis-á-vis PDPs, potentially leading to more product development.

5. There is an immediate need to substantially upgrade the operation of the web-based Database. As currently constructed, it is difficult to use. The goal would be to make it as easy to use as, for example, the accommodation database of Airbnb.

6. Establishing two levels of company membership should be considered. One level would encompass companies that contribute technologies and that financially support the Partnership Hub. These companies would be eligible to become members of the proposed Advisory Committee. A second tier would include companies that contribute products to the WIPO Re:Search database but do not offer any financial support. These companies would be eligible to attend annual meetings of WIPO Re:Search members but would not qualify for membership of the proposed Advisory Board. This would eliminate any risk of free-riding.

A set of metrics need to be developed to measure the performance of WIPO Re:Search. These should include:

- An assessment of in-kind and direct contributions (e.g. full time equivalents, financing, monetized value of intellectual property) made by companies to WIPO Re:Search.

- Publication of the minutes of the proposed Advisory Committee to illustrate the leadership and intellectual contributions made by industry.

- Publications of the proceedings of a consultation between PDPs and WIPO Re:Search including conclusions highlighting the complementary relationship between them, and recommendations for future action.

- The number of capacity-building activities undertaken with other organizations such as the Special Programme for Research and Training in Tropical Diseases at WHO (TDR) and the Tres Cantos Open Lab Foundation supported by GlaxoSmithKline (GSK).

The two most critical recommendations, however, remain the adoption of a value-added contribution statement and the formation of a WIPO Re:Search Advisory Committee. We recognize that the exact value-added contribution statement and the exact form of the Advisory Committee will be the result of further deliberations of the stakeholders, but the outcome should retain the fundamental concepts.

The implementation of these recommendations (and others described in the main text) will provide a basis for attracting donor funding to, *inter alia:*

- expand the partnering program,

- support partner research especially in developing countries, and

- support capacity building.

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Response from the WIPO Secretariat

WIPO Re:Search – Sharing Innovation in the Fight Against Neglected Tropical Diseases, was launched in October 2011 by the World Intellectual Property Organization (WIPO), BIO Ventures for Global Health (BVGH), and 31 original "Members," including eight pharmaceutical companies* and six "Supporters." The Consortium, as WIPO Re:Search was originally characterized, reflected a certain leap of faith by WIPO, BVGH, and its partners that a public-private sector partnership under the aegis of a United Nations agency could provide a valuable and concrete contribution to improving R&D landscape for neglected tropical diseases, malaria and tuberculosis. As of October 2015, WIPO Re:Search comprised 100 Members, including 17 Supporters, with BVGH having facilitated over 90 collaborations among Members.

Targeted financial support from the Governments of Australia and Japan enabled WIPO and BVGH to organize and support research sabbaticals for six developing country scientists at Member facilities, to produce essential promotional materials (such as videos), and to convene meetings and workshops that resulted in the expansion of WIPO Re:Search membership from developing countries.

In its initial phase of operations, WIPO Re:Search has established a robust track record. Most notably, it has demonstrated that "intellectual property does not have to be a barrier to research, development, and availability of new technologies for NTDs, malaria and TB in LDCs" as noted in the Review (Section 3.1).

At the current stage, WIPO and its partners face a number of strategic questions, namely:

- What is the longer-term vision of WIPO Re:Search?
- What are the next steps to ensure that WIPO Re:Search is able to build on its success?
- What resources are required, especially for WIPO and BVGH as the administrator of the Partnership Hub, to support the ongoing expansion of WIPO Re:Search?

To explore these questions and to provide some guidance, if not answers, WIPO engaged the services of an external expert, Dr. Richard T. Mahoney, to conduct an independent external review of WIPO Re:Search. The report of Dr. Mahoney's review drew from interviews with WIPO, BVGH, many Members, and other knowledgeable figures in the field of global

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health. It should be noted that Dr. Mahoney himself has decades of invaluable experience in global health, product development, institution-building and international development, having worked for many years with the International Vaccine Institute (IVI) in Korea.

The views expressed in the Report are those of Dr. Mahoney. Where inferences or conclusions were made resulting from any factual misunderstanding, WIPO and BVGH pointed them out and they were corrected. Otherwise, the value of an external review is precisely that it is external. A qualified, independent, yet knowledgeable observer offers a fresh and unique perspective that usually escapes those involved in the day-to-day management of a project.

There is much in the report with which we agree and will be implemented over the coming months. Other observations or recommendations are less clear-cut and while they may prove valuable they are not considered priorities for either the WIPO Re:Search Secretariat or its Partnership Hub. In some cases, specific recommendations are challenging and require further discussion by the wider Membership, or may not be acted upon. The presence of these recommendations in the Report is a reflection of the Reviewer's independence, but should not be understood as an endorsement.

In this context, the response by the WIPO Re:Search Secretariat identifies and comments on a number of the Report's key findings. Going forward, we see the report as a strategic tool for promoting the Consortium to a wider and broader range of potential financial donors. As noted in the report, this is critical to WIPO Re:Search's future success.

These comments, however, are in no way a substitute for careful – and critical – reading of the Report itself.

Comments on Key Findings

1. High level findings:

The Report makes numerous references to **the success of WIPO Re:Search *to date***. These include references to the success :

- in proving that intellectual property does not have to be a barrier to research on NTD technologies (Section 3.1);
- in demonstrating that pharmaceutical companies will and do make valuable intellectual property assets available for early-stage research without significant IP constraints (Section 5.1.2);
- in operating the BVGH-administered Partnership Hub, which is widely recognized as capable, energetic and productive (Section 3.1); and
- in facilitating the transfer of under-used IP assets to qualified researchers at no cost to them. One Member estimated the "in-kind" donation value of a material transfer agreement negotiated under WIPO Re:Search at between US$100,000 and US$1,000,000 (Section 3.1).

As noted in the report, "WIPO Re:Search was an experiment, and no one was sure it would succeed. Now, we can see that it was a great idea. It should continue and expand."

(Section 3.1) The Secretariat, on behalf of all WIPO Re:Search Members, welcomes these findings.

2. Key areas for action:

The Review points to **a number of areas where improvements can and should be made**. It recommends that:

- there should be an immediate and overriding need to upgrade the database. (Section 5.1.2; emphasis in the original).

  The Secretariat fully agrees with this recommendation and is already taking action in this regard. Financial resources for this purpose have been proposed in WIPO's 2016/2017 budget.

- The Reviewer also notes the importance of upgrading and improving the user-friendliness and appeal of the WIPO Re:Search web site pointing to its under-used potential and the need to appeal to new donors and partners (Section 5.1.2).

  The Secretariat takes note of these recommendations and will use resources ear-marked for this purpose to further improve the re-designed WIPO Re:Search web-site, launched shortly after Dr. Mahoney began his work in late 2014.

- The report notes that a certain amount of confusion exists among many Members regarding the relative roles of BVGH and the Partnership Hub, and the Secretariat, WIPO. (Section 4.2).

  This valuable insight is partly explained by the growth in the number of WIPO Re:search Members. Membership has more than tripled since launch, and many new Members are unfamiliar with the Consortium's structure and the respective roles of WIPO and BVGH. It is, however, also the case that more can be done by the Secretariat to keep Members better informed and engaged in the WIPO Re:Search operations. This observation may also be attributed to the fact that Dr. Mahoney interviewed a number of individuals who are not part of WIPO Re:Search (See Annex 2).

- The Reviewer notes (Section 5.2) that the Guiding Principles governing WIPO Re:Search provide for the eventual establishment of an Advisory Committee (or "Governance Committee").

  In its initial phase, given the relatively small number of Members, governance issues were secondary to achieving tangible results. The main focus was on facilitating col-laborations through the Partnership Hub, expanding membership, and other capacity building activities, such as research visits and intellectual property workshops to demonstrate the Consortium's value proposition. The Secretariat will continue to consult with Members and BVGH to prepare an appropriate recommendation on this governance issue, for consideration and action at the 2015 WIPO Re:Search Annual Meeting (October 29).

3. Recommendations relating to funding and membership:

The report also makes a number of observations and/or recommendations that relate directly to **the way WIPO Re:Search is promoted and its ability to attract** new donors.

- It notes that the "Value Added Contribution" of WIPO Re:Search, as measured by the value of the assets available for licensing and the work involved in establishing the collaborations, should be defined and measured, in financial terms (from the view-point of Providers) to the extent possible (Section 5.1.1).

  The WIPO Re:Search Secretariat agrees with this and also believes it is important to measure the value of WIPO Re:Search to developing countries.

- It recommends that high-level descriptions of WIPO Re:Search should emphasize private sector contributions (Section 5.1.2).

  The Secretariat agrees.

- It also recommends that WIPO Re:Search's financial model should be expanded to enable the private sector to grant funds in support of follow-on work by Users flowing from WIPO Re:Search collaborations (Section 5.1.2).

  This recommendation has some merit but the Secretariat feels it is a priority to encourage companies to engage with WIPO Re:Search collaborations and licensing activities and that some caution should be exercised to ensure they are not burdened with bureaucratic funding procedures. The Secretariat will discuss this further with Member companies at some future date.

- The report notes that WIPO should more actively engage with the Product Development Partnership (PDP) community to highlight the complementary nature of WIPO Re:Search and to underline the fact that it is not competing with PDPs for the same pool of donor funding (Section 5.1.2).

  The Secretariat agrees that it is important to strengthen relations with the PDP community which plays a key role in moving products along the development pipeline. An initial dialogue with those PDPs that are WIPO Re:Search Members is being initiated and an appropriate strategy to strengthen relations is under development. An initial consultation is scheduled for October 29-30, 2015, immediately after the WIPO Re:Search Annual Meeting, and the proceedings of that meeting will be published.

- The report recommends that WIPO makes WIPO Re:Search capacity building activities a priority. Such activities could include encouraging companies to donate used research equipment, expanding the number of workshops and opportunities for sabbaticals, by for example, making it possible for private sector scientists to take sabbaticals at developing country institutions (Section 5.1.2).

  The Secretariat takes note of these recommendations, but does not assign them the same level of priority as others, for example, upgrading the data base. The primary focus of WIPO Re:Search is to facilitate collaborations through the Partnership Hub. The capacity building activities, undertaken to date, have proven successful and popular with many Members, but our ability to run them hinges on the availability of additional resources. The continuation and expansion of these activities will require more funding from existing donors and/or recruitment of new donors.

4. Recommendations on which the Secretariat does not intend to take action:

The Reviewer made a number of observations and/or recommendations that are **unlikely to be acted upon, at least in the foreseeable future because, for example, they** are impractical or fall outside the competence or capacity of the Secretariat and/or BVGH. Some of these recommendations include:

- Changing the policy that currently requires all for-profit private sector Members to contribute financially to the Partnership Hub (Section 5.2).

  WIPO Re:Search's funding model requires all private sector for-profit Members to support the Partnership Hub. This model is essential to operations of the Consortium, and, in the absence of other revenue/funding streams, is non-negotiable. A longer-term funding strategy for WIPO Re:Search should envision a financial model that evolves, so that BVGH's operations are not overly dependent on a few "paying" Members of the Consortium.

- The report also suggests that WIPO Re:Search should consider allowing private sector companies to list assets for licensing on the database, but to opt out of providing financial support to the Partnership Hub (Section 5.2).

  WIPO Re:Search confronted this situation when one of its Members, a private company, left the Consortium due to internal cost-cutting and re-structuring, but requested that its assets continue to be listed in the database. As noted above, the present structure of WIPO Re:Search does not allow for this. To do so would present problems for the Partnership Hub's budget and would create a "free rider" problem with respect to the other private sector Members. At present, the Secretariat sees no alternative to the current model but, in future, an alternative policy relating to the participation of private sector Members may be considered, provided the essential services of the Partnership Hub are fully met and expanded by other sources of financial support.

- The report recommends a more direct role for WIPO in WIPO Re:Search and suggests a formal role on any advisory committee and/or representation on the BVGH board of directors.

  Regarding the advisory committee, the guiding principles specifically notes that WIPO would be only an observer on such a committee.

  WIPO and BVGH work closely together on WIPO Re:Search, and BVGH engages in other global health work as well. WIPO does not see any need or value in a formal reconfiguration of their roles at this stage.

5. Potential Funding Strategies.

The Reviewer recommends that, after implementing the Report's recommendations, as appropriate, potential donors such as philanthropies, government aid agencies, etc., should be approached as potential contributors (Section 5.3). This is seen as a means to fund:

- ongoing R&D resulting from WIPO Re:Search collaborations;

- capacity building, especially research visits by developing country scientists to the laboratories of WIPO Re:Search Members; and,

- the operations of the Partnership Hub and costs of running and maintaining the data base.

The Secretariat agrees with the general thrust of the Reviewer's recommendations on this point, and will use the Report, and input from the Members, as a basis for developing a comprehensive funding strategy.

Conclusion

The Report is an important first step in moving WIPO Re:Search to its next, more mature phase. The first three years of the project have focused, correctly, on achieving certain measurable deliverables, such as growth and diversity of Membership and collaborations. These have clearly been achieved and the challenge now remains to identify ways of maintaining the project's success while simultaneously supporting its future evolution

The Secretariat hopes that the Members and other readers agree that this Review contributes positively to that goal.

Geneva, October 21, 2015

* The eight pharmaceutical companies were: Alnylam, AstraZeneca, Eisai, GlaxoSmithKline, MSD, Novartis, Pfizer, and Sanofi. Since 2011, AstraZeneca left WIPO Re:Search, and Merck KGaA and Takeda Pharmaceuticals joined. Supporters are entities that are not involved in NTD research, but express their support for the Consortium's goals.

Section 2:
Background and Context

2.1 OBJECTIVES OF THE REPORT

This is a report to the World Intellectual Property Organization (WIPO) on WIPO Re:Search. The report provides the information, conclusions and recommendations emerging from a process dictated by the Terms of Reference (see Annex 1) which were developed by WIPO and benefitted from inputs by BIO Ventures for Global Health (BVGH) which serves as the Partnership Hub for WIPO Re:Search. The objectives of the assignment are stated in detail in the Terms of Reference and are summarized as follows:

The primary challenges now facing WIPO and BVGH, are:

- What should the medium to long-term strategic plan look like?
- What are the next steps the Consortium must take if it is to build on its success?
- How can the Partnership Hub have a sustainable and solid budget in order to achieve the new goals in collaboration with WIPO?

This report addresses each of these questions.

2.2 THE EVOLUTION OF UNDERSTANDING OF INTELLECTUAL PROPERTY

Before presenting the substance of the Review's findings, it may be useful to set the context in which WIPO Re:Search established. An expanded version of this Section is found in Annex 4.

As readers are well aware, the pharmaceutical industry allocates large resources to R&D which generates what are referred to as product "leads." Some of these leads are relevant to the diseases to which the company accords priority and some, such as for neglected tropical diseases (NTDs), are not. As a matter of routine practice, companies will seek patent protection for almost all leads but will not pursue those of low priority. These low priority leads, the associated know-how, and technical data may be "put on the shelf" and no further research will be undertaken.

During the 1990s and 2000s, in parallel with the creation of PDPs, a debate concerning the role of intellectual property in health took place. On one side, it was argued that patents allowed companies to develop monopolies allowing them to charge high prices not affordable by the poor. In this view, intellectual property (IP) was a barrier to improved health in developing countries. On the other side, it was argued that patents provided an essential foundation to make possible the costly investments required to develop new medicines. In other words, a product that was not developed could not be accessible to anyone, regardless of intellectual property. In this view, intellectual property was a facilitator of product development and the issue of access in developing countries was a (largely) separate matter.

Those who saw patents as 'bad' aimed a great deal of their advocacy toward the World Trade Organization (WTO) because the WTO was the forum for the negotiation of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), codifying minimum standards for protecting intellectual property, including for pharmaceutical products. Critics of WTO believed that the extension of IP enforcement to developing countries could only make the situation worse, i.e. products more expensive, while those on the other side believed that this extension would foster the development of innovative capabilities in developing countries allowing those countries to develop their own biomedical products.

As controversies around intellectual property and access ensued in the 1990s and 2000s (see, the discussion of South Africa in Annex 4), some attention turned to WIPO as well because WIPO was seen by some as an unflinching advocate for intellectual property with little if any interest in the needs of developing countries. In this view, WIPO was seen as perpetuating a bad situation.

Over time, and as progress on access to life-saving therapies, particularly for HIV/AIDS, was made, the arguments of both sides became more nuanced.

Advocacy groups that were critical of patents came to realize, inter alia that it was not so much who owned the patents but the mechanisms by which ownership was generated that could determine access. They realized that those who paid for research and development would obtain the patents on potential products. Because industry paid for the very large bulk of research and development in health technologies, industry became the owners of the resulting intellectual property. The advocacy groups therefore began lobbying for the establishment of global research and development funds that would shift the burden of

R&D investment from the private to the public sector. To date, although alternative funding mechanisms have been recommended by WHO advisory committees, a fund of sufficient size and scope has not been established.

Industry, for its part, realized that they could do more to address the "access" side of the "innovation – access continuum." One opportunity to do more would be to expand avenues for licensing their compound libraries and other assets to qualified researchers working on neglected tropical diseases (NTDs), malaria and tuberculosis (TB. These diseases represent a non-competitive space for the companies' commercial interests, where there is a large human need for new and improved treatments, vaccines and cures. WIPO, given its expertise in intellectual property, and its long-standing relations with private sector innovators through its many technical and normative functions (e.g., the Patent Cooperation Treaty) was a natural venue to establish the multi-sectoral platform known as WIPO Re:Search.

The evolution of the understanding of intellectual property in the global health context is a large and complex issue. The above summary only identifies a few key themes that illuminate, hopefully, why the original Members of WIPO Re:Search were willing to engage with WIPO, which is neither a global health nor a global development agency, per se, in a project focused on catalyzing more R&D for NTDs, malaria, and TB.

2.3 WIPO RE:SEARCH AND ITS CURRENT CHALLENGES

WIPO Re:Search was launched in 2011. The aims and objectives of WIPO Re:Search can be found in the Guiding Principles.

The Consortium aims to accelerate the discovery and product development of medicines, vaccines, and diagnostics to create new solutions for people affected by neglected tropical diseases (NTDs), malaria, and tuberculosis by making intellectual property and know-how available to the global health research community.

The objective of the Consortium is to encourage and support research and development of Products for NTDs. In particular, WIPO Re:Search will benefit patients in Least Developed Countries (LDCs) by creating an open innovation platform through which public and private sector entities can share, for this purpose, Intellectual Property.

The primary objective of WIPO Re:Search is to catalyze new research and development for NTDs, with a particular focus on the needs of patients in LDCs, by making Intellectual Property available on concessionary terms to researchers everywhere.

As further stated in the Guiding Principles, WIPO Re:Search has three major components:

1. A **Database**, hosted by WIPO, providing details of Intellectual Property available for licensing from a Provider (as defined below), as well as services and other technology or materials not necessarily protected by intellectual property rights which can be accessed by Users (as defined below).

2. A **Partnership Hub**, managed by a Partnership Hub Administrator, which shall be BVGH or any subsequent competent entity, in cooperation with WIPO, where Members (defined below) and other interested parties that support or are considering supporting these Guiding Principles can learn about the Consortium, available licensing and research collaboration opportunities, networking possibilities, and funding options.

3. A range of specific **Supporting Activities**, led by WIPO in cooperation with BVGH, to facilitate negotiation of licensing agreements and to address technical matters such as identifying research needs and opportunities, among others, with technical advice from the World Health Organization (WHO).

Three categories of members are defined as:

- "Providers" are Members that contribute Intellectual Property, materials or services to *WIPO Re:Search* for license or use.

- "Users" are Members that have entered into license agreements with Providers to use *Re:Search* in accordance with, and in furtherance of, the Principles and Objectives.

- "Supporters" are Members that encourage the facilitation of research and development of Products for NTDs. Supporters may voluntarily offer to provide support, services or assistance of any kind to the Consortium or its members in order to facilitate achievement of the Principles and Objectives.

In October 2014, the Global Challenges Division of WIPO commissioned a review of WIPO Re:Search. The objectives as stated in the Terms of Reference are reproduced here for ease of reference:

"The primary challenges now facing WIPO and BVGH, are:

- What should the medium to long-term strategic plan look like?

- What are the next steps the Consortium must take if it is to build on its success?

- How can the Partnership Hub have a sustainable and solid budget in order to achieve the new goals in collaboration with WIPO?

Thus three broad categories of inquiry should be considered:

a. Membership: With almost 90 Members,[1] the administrative capacity of WIPO and BVGH is stretched to the limit. Yet, as noted above, the Consortium requires more private sector members in order to support financially the Partnership Hub. How and what can WIPO and BVGH do to increase private sector Membership?

Active involvement of Current Members: Different members will have different reasons for joining and participating in WIPO Re:Search. Some Members have uploaded data in the database, participated in the hosting arrangements, and entered into collaborations. Others have been more passive, often despite repeated outreach efforts to, for example, upload data in the database. The Reviewer will interview the principal points of contact at a range of Members, including those who have been very active, selectively involved, or with very little activity, to ascertain whether WIPO Re:Search is meeting their needs and expectations, and if not why not.[2]

b. Collaborations: WIPO Re:Search's most important goal is to facilitate collaborations between Members. The purpose of the collaborations is to advance R&D in the field of NTDs, malaria and TB. With over 65 collaborations in less than three years,[3] it is clearly achieving this important first goal. However, important questions for the future of the Consortium include:

    - Is the type of collaboration facilitated by WIPO Re:Search enough? In other words, once initial collaborations are established, is there a further role for WIPO Re:Search/Partnership Hub to facilitate further development of a collaboration?

    - What types of future services (by WIPO and/or BVGH) may be required in order to advance the collaborations?

    - What specific untapped resources are "embedded" in WIPO Re:Search's important group of Supporters?

    - As part of a future funding strategy should WIPO Re:Search assume responsibility for helping institutions raise funds to move projects from pre-clinical to clinical stages? Put differently, what, if anything, is the role of the Consortium in facilitating the move from 'R' to 'D''? Note that BVGH has developed the BVGH Funders Database which is intended to support Members gaining access to funding.

c. Funding base of WIPO Re:Search: As WIPO Re:Search moves from its early post-launch stage to a more mature phase, a growing imperative is broadening and deepening sources of financial support, specifically for the Partnership Hub. While some modest progress has been made, such as the addition of two small and two major company Members, this must be measured against both the goals of three new paying members per year, and the loss of one of the original Members, AstraZeneca. (It should also be noted that WIPO Re:Search has benefitted from Funds-in-Trust contributions from both the Governments of Australia and Japan.)

The Reviewer will engage current funding Members, a point of contact at AstraZeneca, and companies that have declined to join, to develop information as to how WIPO Re:Search provides value to a company, or, conversely, why a company has not agreed to join the Consortium. WIPO and BVGH will supply the consultant with relevant contacts."

This report seeks to fulfill the Terms of Reference (Annex 1).

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1 This number is current at the time of the Review. By October 2015, the Consortium counted 100 Members.

2 The specific list of Members to be interviewed will be determined by WIPO, BVGH and the consultant.

3 This number was current at the time of the Review. By October 2015, there were over 90 collaborations.

Section 3:
Evaluation

3.1 OVERVIEW

Thirty interviews were conducted with stakeholders of WIPO Re:Search spanning all categories of Members plus individuals who had participated in sabbaticals at developed country laboratories. See Annex 2 for a list of the interviewees. See Annex 3 for the questionnaires that were sent to the interviewees prior to the interview.

There has been profound change in the world of intellectual property and research on NTDs, malaria and TB over the last two decades, and these changes have led to the environment in which WIPO Re:Search was founded and currently operates. A discussion of intellectual property can be found in Annex 4 (summarized in Box 1). A description of other organizations and their research can be found in Annex 5.

Some of the more important conclusions that emerged from the interviews are summarized here.

Perhaps the most important conclusion reached is that there is unanimous agreement that WIPO Re:Search is a valuable addition to the global endeavor to reduce the impact of NTDs, malaria, and TB, and it should be sustained. As one interviewee stated, "WIPO Re:Search was an experiment, and no one was sure it would succeed. Now, we can see that it was a great idea. It should continue and expand."

Since its launch in 2011, **WIPO Re:Search has achieved a number of important successes.**

- It has attracted the support of several of the world's largest pharmaceutical companies that have contributed resources for the operation of WIPO Re:Search and have made available proprietary technologies, supportive technical information, research compounds, and know-how.
- It has assembled a large database of potentially valuable assets that might be useful in the development of products for NTDs, malaria, and TB.
- The Partnership Hub created and administered by BVGH is widely recognized as capable, energetic, and productive.
- It has identified a significant number of research centers and university laboratories in both developed and developing countries that are interested in participating in the WIPO Re:Search platform.
- It has fostered the formation of a significant number of partnerships between the pharmaceutical companies and the research centers and university laboratories.
- It has supported capacity building in developing countries by providing opportunities for developing country scientists to work in laboratories of the pharmaceutical companies and developed country research centers. Furthermore, it has facilitated visits by pharmaceutical company scientists to developing country centers to provide training in product development.

WIPO Re:Search has had less success in other areas. These include:

- Expanding substantially the number of supporting companies.
- Catalyzing agreements between companies and developing country institutions.
- Responding to developed and developing country research centers' requests for financial and technical support to complement the provision of technologies through Material Transfer Agreements (MTAs). (It should be noted that such support is not an objective of WIPO Re:Search. The point here is that almost unanimously, developing country Members felt there should be assistance of this type.)
- Obtaining support from foundations and other public sector donors such as additional bilateral aid agencies for core operating costs and to support projects initiated through WIPO Re:Search.
- Demonstrating that the partnerships formed through WIPO Re:Search are leading to new products.
- Demonstrating that product development for developing countries can be accelerated by reducing IP constraints.
- Creating an operating structure that is understood by stakeholders (see also below for further discussion of this matter).
- Creating a clear long-term vision of WIPO Re:Search's value added contribution to the effort to reduce the burden of NTDs, malaria and TB in LDCs.

In addition, Members are asking questions. These include:

- Production of products will likely not take place in LDCs. Will the WIPO Re:Search IP policies be able to ensure access in LDCs?

- A valuable set of partnerships has been formed. Are they sustainable?

- Although not currently an objective of WIPO Re:Search, capacity building is seen as one of WIPO Re:Search's most important potential contributions. How can or should it make this contribution?

- The potential in terms of number of agreements and partnerships is very large. Will WIPO Re:Search be able to provide effective management?

- Doing good and obtaining favorable publicity are valuable for companies. Are they enough to ensure a long-term commitment?

WIPO Re:Search Members believe (based on the interviews conducted for this report) that the three major components and the categories of members were conceived correctly and continue to be valid features of the structure of WIPO Re:Search. However, some additional objectives of the establishment and operation of WIPO Re:Search were identified by Members. They believe that these objectives have been achieved, which could be summarized as:

1. The demonstration that intellectual property does not have to be a barrier to research, development, and availability of new technologies for NTDs, malaria and TB in LDCs.

2. The demonstration that the pharmaceutical industry is willing and able to contribute to the development of these new technologies especially for the LDCs.

3. The realization, in a tangible manner, of the WIPO Development Agenda which included a specific call to address the needs of the public sector and of developing countries.

Based on discussions with Members of WIPO Re:Search, and for purposes of this report, the objective of WIPO Re:Search (as currently established and operated) could be defined as:

- To catalyze new research and development of drugs, vaccines, and diagnostics for NTDs, malaria and TB for the benefit of individuals in LDCs.

- It seeks to accomplish this objective by:

- Making intellectual property and other industry assets such as know-how and samples available to researchers on concessionary terms,

Catalyzing the formation of partnerships and networks of public and private sector organizations to facilitate the conduct of research and development,

Building capacity, particularly in developing countries, for the conduct of research and development.

Box 1:

KEY POINTS IN THE EVOLUTION OF IP AND R&D (SEE ALSO ANNEXES 4 AND 5)

- The public sector has greatly enlarged its participation, and in many areas, its leadership in development of products needed in developing country. This enlargement was based on the understanding that the private sector could not be expected to devote large resources to the development of products for poor countries. The creation and successful functioning of PDPs is the embodiment of this enlarged role. A key aspect of PDPs is their strong reliance on collaboration with the private sector.

- The large pharmaceutical industry has fundamentally changed its approach to IP and product development for developing countries. Previously it used IP as a means to protect investments for large markets in developed countries. Today, industry has many initiatives where it deploys IP and undertakes research (or collaborates with PDPs) to accelerate product development for developing countries.

- As the lead UN agency for IP, WIPO has also changed. Previously, many argued that WIPO was largely an unflinching advocate for IP with little interest in the needs of developing countries. However, WIPO has adapted to the changes in IP and R&D by adopting a Development Agenda specifically addressing the needs of developing countries.

- With its goal of marshalling the capabilities of industry and its IP to address the needs of developing countries for health technologies through public-private collaboration, WIPO Re:Search can be seen as a natural and appropriate response to the evolution of the last several decades.

3.2 GOVERNANCE AND STRUCTURE

The governance and structure of WIPO Re:Search are somewhat unusual. The name "WIPO Re:Search" leads to the impression that the organization is a part of WIPO or, at the least, operating in some way under its supervision. In reality, WIPO Re:Search has two functioning parts. One is the Partnership Hub administered by BVGH, a non-profit organization based in Seattle, USA. The funding for BVGH to operate WIPO Re:Search comes from the Sponsoring Members which have signed MoUs with BVGH under which they make their contributions. The second part is the Secretariat based at WIPO in Geneva and funded by the internal budget of WIPO.

WIPO Re:Search as a whole is referred to as the Consortium.

The responsibilities of WIPO and BVGH are laid out in the Guiding Principles.

> The Guiding Principles provide for a Governance Committee whose principal duties and responsibilities "shall include inputs on and guidance of the general activities and operations of WIPO Re:Search, including its effectiveness at realizing its stated aims."
>
> This Committee has not been put into operation.

WIPO Re:Search could be described as a two-headed organization comprised of WIPO and BVGH. The activities where one party has the lead (one party can support the other in executing a lead responsibility) could be summarized as follows:

WIPO

- Manage a web based database that provides information on available intellectual property, materials and services.
- Access technical assistance from WHO.
- Organize annual or biennial meetings of Members.
- Lead discussions of policy.
- Provide supportive services to Members including:
- Model licensing clauses
- Capacity-building activities in licensing
- Mobilize resources for the Secretariat.

BVGH

- Provide information about licensing and collaborative research opportunities, networking possibilities, and funding options.
- Disseminate information about WIPO Re:Search.
- Recruit additional Supporters, Providers, and Users.
- Catalyze collaborations between Providers and Users.
- Mobilize resources for the Partnership Hub.

There is no detailed specification of how WIPO and BVGH will formally coordinate their activities. Also, there is no precise specification of who has ultimate responsibility for WIPO Re:Search. These two facets of WIPO Re:Search naturally can lead to both external and internal misunderstandings as cited by many of the individuals interviewed for this report.

Box 2:

A REVIEWER'S COMMENT

A reviewer of an earlier version of this report suggested that BVGH's responsibilities be stated as follows:

- Facilitate collaborations between Members.
- Communicate, via articles, presentations at meetings, seminars, etc. information about licensing and collaborative research opportunities, networking possibilities,a and funding options.
- Disseminate more broadly information about WIPO Re:Search.
- Recruit additional Supporters, Providers and Users.
- Catalyze collaborations between Providers and Users.

This may provide an opportunity for discussing the revision of the responsibilities of BVGH as stated in the Guiding Principles.

Still there is a third major stakeholder in WIPO Re:Search that is not formally established – the group of Funding Members that provide financial support to BVGH through annual contributions. This group is regularly consulted and informed through conference calls and meetings. It has no legal standing and thus has no mandated control over management or budgets except to the extent that each individual company can withhold, maintain or increase funding.

From the interviews, it is clear that the structure and governance of WIPO Re:Search is not well understood by all members. Interviewees stated that it was not clear whom they should approach for what services or matters. There was more clarity about the role of BVGH which was seen as the primary mechanism for day-to-day operations. Interviewees saw WIPO in less clear terms and expressed a strong desire for the database to be made more user friendly.

3.3 FUNDING

Funding for the Partnership Hub comes from the private sector, for-profit members of WIPO Re:Search (Funding Members) whereas the WIPO Secretariat is funded directly from the budget of WIPO. To date, additional support for the Partnership Hub has not been obtained from other sources such as philanthropic foundations and European and North American bilateral donors. The annual budget of the Partnership Hub is approximately USD800,000 and covers the costs of BVGH staff, travel, and overheads.

In addition, with support from the governments of Japan and Australia, the Partnership Hub, with the support of the WIPO Secretariat, has been able to arrange research sabbaticals by developing country scientists to Providers' laboratories.

A major purpose of this review is to assess how WIPO Re:Search might be able to approach additional donors successfully for additional funding. See Annex 6 for a discussion of some donors programs and activities.

Section 4:
Analysis

4.1 PROGRAMMATIC ANALYSIS

The following findings emerge from the interviews and the foregoing context analysis.

- WIPO Re:Search should not be judged in the near-term on progress in product development because:
    - It does not have grant resources to push product development.
    - It does not have the staff resources to manage product development like a PDP.
    - The technologies it is working with are mostly very early stage candidates that could enter Phase 1 trials only in several years.
    - The User partners (university and research institutes) are not product developers.
    - Those PDPs already working in this space could cast doubt on claims of progress in product development.
- While WIPO Re:Search emerged from an environment in which intellectual property was a focal point, intellectual property is to a great extent no longer a main issue of contention (but it is still important):
    - WIPO Re:Search has demonstrated that large commercial pharmaceutical companies are willing to overcome intellectual property considerations in order to facilitate NTD, malaria and TB disease research by sharing valuable technologies, know-how and documentation.
    - IP issues relating to access are not a focal concern for the program because the development of the candidates will require moving the candidates through additional stages of development and the entry of additional parties such as PDPs which will have well-established IP policies that will be directed to ensuring access.
    - To discuss IP issues with respect to access opens WIPO Re:Search to criticism because it cannot be proven now that the current policies will, in the long term, ensure access to products. There are too many actors, events (e.g. failed clinical trials leading to product reformulation with other intellectual property), and issues that will emerge in the future to say that WIPO Re:Search policies will ensure access.
    - On the other hand, WIPO Re:Search can claim a great achievement. It has demonstrated unequivocally that intellectual property is not a barrier to the launch of research by third parties of products developed by industry. As one interviewee said, “The proposition that intellectual property does not have to be a barrier for research on NTD technologies has been proven.”
- WIPO Re:Search is creating a new market. As the assets provided by the companies are otherwise under-used, the corporations can make them available to researchers at no cost while obtaining other benefits such as fulfillment of corporate responsibility policies and favorable public relations. Operation of this “marketplace” is made possible by the creation of an open source database on the web containing detailed descriptions of the assets which are available. Potentially interested scientist can access and use those resources to meet their needs. Based on interviews with the companies providing the assets and the researchers utilizing the assets, it seems clear that the values of the exchanges are significant. One company estimated that a single Material Transfer Agreement imposed in-kind costs between USD100,000 and USD1 million.
- In the near-term, an important value-added contribution of WIPO Re:Search is the active formation of a global network of companies, academia, research centers, and government agencies facilitating the exchange of valuable assets in the form of technologies and research that could be a potent means to accelerate progress in the field.
    - It has demonstrated that companies are willing to participate in these networks.
    - It provides an invaluable intermediary to facilitate collaboration between industry and academia in developing countries and between academia in developed countries with counterparts in developing countries.
    - It provides a means to contribute to capacity building in developing countries. As one developing country academic said, “In the past, if I wrote to a company or a developed country professor to ask for help, I got no answer. WIPO Re:Search made it possible for me to access wonderful resources that I could not get on my own. And these relationships are continuing.”

- Through the Internet it provides a highly cost-effective means for access to the WIPO Re:Search database. As one interviewee commented, “WIPO Re:Search created a market where one didn’t exist before.”[4]

To achieve its potential, WIPO Re:Search needs to find additional resources and additional sources of support:

- Because there is no exchange of funds between the partners in the agreements, it is not possible to extract fees from the transactions.

- There is a high priority need to enhance the database website for it to function at a higher level of ease of use.

    - To take advantage of the foundation that has been constructed, additional companies and other Members should be added implying a need for additional technical and administrative staff, particularly at BVGH.

    - A diversified funding base including foundations and government donors will help ensure sustainability and acceptability among the multi-sectoral stakeholders of WIPO Re:Search.

    - Developing country research centers and academic centers in developed countries that have participated in WIPO Re:Search projects uniformly express a desire to obtain small scale around USD100,000 support for the work they do in the partnerships formed under WIPO Re:Search.

We have also sought to define what makes WIPO Re:Search unique or distinguishable from the other programs and organizations in the space of NTDs, malaria and TB. We state that uniqueness as follows: WIPO Re:Search is the only international mechanism, with policies that successfully address intellectual property issues, operating under the aegis of a UN specialized agency and facilitating private sector activities to accelerate early-stage research by public and private sector institutions for disease control in developing countries. We will discuss this further in the following sections.

4.2 STRUCTURE AND GOVERNANCE ANALYSIS

The current lack of clarity in the roles of WIPO and BVGH and lack of effective coordination leads to some confusion, both inside and outside WIPO Re:Search.

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4 Another interviewee noted that exchange between companies and academia takes place continuously and that many agreements for collaboration have been formed. In our view, what makes WIPO Re:Search different is that it provides a web-accessed database that makes it possible for scientists anywhere in the world, particularly the developing countries, to identify technologies that may be of interest to them. At the same time, WIPO Re:Search provides a technically credible and mutually trusted intermediary to bring the parties together. This is the new marketplace.

Section 5:
Recommendations

WIPO Re:Search has been, to date, a very successful undertaking and has many individual successes to its credit. The recommendations made here are, therefore, forward-looking and seek to provide a basis for the continued successful operation and expansion of WIPO Re:Search in the years to come. The objective of these recommendations is primarily to provide a coherent and logical framework for raising additional support to sustain WIPO Re:Search and secondarily to enhance its operations to improve clarity, efficiency and productivity.

5.1 PROGRAMMATIC RECOMMENDATIONS

5.1.1 VALUE-ADDED CONTRIBUTION

To obtain additional and continuing support for WIPO Re:Search, it will be necessary to define clearly its value-added contribution to global efforts to control NTDs, malaria and TB. The statement on value-added contribution should be credible and should meet the needs of the members of WIPO Re:Search. The value-added contribution of WIPO Re:Search has three components:

- It is the only international mechanism, under the aegis of a UN specialized agency, in which pharmaceutical companies working together provide leadership, technology and financial resources to accelerate early stage research for disease control in poor countries.

- It is a proven mechanism in which intellectual property associated with early-stage technologies are managed to provide a framework in which:

    - laboratories can pursue research on technologies in direct collaboration with the IP owners, and

    - there are no IP constraints to negatively affect access to any products that may result either directly or indirectly from the research.

- It is the only international mechanism that employs the power of the internet to provide a new and highly cost-efficient trusted intermediary (BVGH) for researchers in developed and developing countries leading to high value research and new opportunities for highly leveraged capacity building.

5.1.2 MAXIMIZING THE VALUE-ADDED CONTRIBUTION

There are opportunities to enhance each of the three components of the value-added contribution of WIPO Re:Search.

- The only international mechanism in which pharmaceutical companies working together provide leadership, technology and financial resources to accelerate early stage research for disease control in poor countries.

    - The high-level description of WIPO Re:Search should further emphasize the leadership of the pharmaceutical companies in WIPO Re:Search.

    - Consideration should be given to the expansion of company financial support in the form of small grants (either through a pool or one-to-one) to Users to support their research resulting from collaborative agreements.[5] Such support would have two benefits. It would help ensure that collaborative agreements result in more than the provision of compounds and limited technical assistance through MTAs. It would also establish a mechanism to channel funding of other donors who would give priority to support of universities and developing country research centers. (This was a specific recommendation of a senior official of one of the Supporting Members.)

    - Consideration should be given to formalizing the role of the companies in the operation of WIPO Re:Search. For example, the contributing companies could be members of an Advisory Committee that would meet at least once per year for a day to review in detail the operations of WIPO Re:Search and provide advice on priorities, resource allocation, and management. Such an Advisory Committee would tangibly demonstrate the important role played by the companies and would provide them with greater opportunity for sharing their expertise and knowledge in this complex area. It could also provide the company representatives with an opportunity to assure their management that the views and needs of companies are being expressed and met in WIPO Re:Search.

- A proven mechanism in which intellectual property associated with early-stage technologies are managed to provide a framework in which a) laboratories can pursue research on technologies in direct collaboration with the IP owners, and b) there are

no IP constraints to negatively affect access to any products that may result either directly or indirectly from the research.

- It should be emphasized that WIPO Re:Search's great success with respect to IP is in demonstrating that pharmaceutical companies will make available valuable assets for early-stage research without significant IP constraints. In addition, WIPO Re:Search policies are designed to ensure that IP considerations are not a barrier to further product development by other groups including PDPs and developing country manufacturers. The two key points here (and what is different from what has been done in the past) is to highlight "early stage" research and the lack of barriers to products moving into PDPs, if the PDPs wish to develop them further.

- The high level description of WIPO Re:Search should also be modified to emphasize that WIPO is a UN specialized agency composed of Member States, with most Members being developing countries. Thus, WIPO Re:Search is a reflection of the policies and needs of those countries.

- WIPO Re:Search should seek means to generate a consensus between WIPO Re:Search and PDPs on their relative and complementary roles with respect to intellectual property. The goal would be to assure PDPs that WIPO Re:Search projects and IP policies are being conducted in such a manner as to complement and integrate with the activities and policies of PDPs. A further goal would be to assure PDPs that a goal of WIPO Re:Search is to "help fill the pipeline" for the PDPs and not to undertake product development such as is done by the PDPs. Such assurances could help relieve PDP concerns, expressed in the interviews, that WIPO Re:Search is attempting to operate in the same space as the PDPs and compete for limited donor funds in that space. While PDPs represent only one possible mechanism for further advancement of products, attempts by WIPO Re:Search to obtain funding from donors who support PDPs (which is true for almost all potential donors for WIPO Re:Search) will face great obstacles if the PDPs are not supportive, or worse, oppose such funding.

- It is the only international mechanism that is based on the power of the internet to provide a new and highly cost-efficient trusted intermediary (BVGH) for researchers in developed and developing countries to directly access technologies and their owners leading to high value research and new opportunities for highly leveraged capacity building.

  - The value of the work of WIPO Re:Search has not been monetized. It would be valuable to undertake a monetization exercise. For example, one company interviewee indicated that the company invested, in-kind, between USD100,000 and USD1 million for each product it put in the database. This exercise will be important because many donors ask what they are getting for their investment.

  - There is an immediate need to substantially upgrade the operation of the web-based database. As currently constructed, the database is difficult to use. The goal would be to make the database as easy to use as, for example, the accommodation database of Airbnb. **The importance of this upgrading cannot be over emphasized.**

    1. As demonstrated by other organizations and companies seeking to use the internet as a key tool in their business, success and failure is determined in large part by the ease of use of the web-based database of available resources.

    2. A substantially upgraded database should lead to a rapid increase in interest in working with WIPO Re:Search especially among developing country laboratories and research centers. This should be appealing to many donors.

    3. A substantially upgraded database (including semi-automated means for negotiating agreements) make it possible for the Partnership Hub to facilitate a greatly expanded number of partnerships without requiring substantial additional resources, and allow the Partnership Hub to provide more effort to ensure that the resulting partnerships are productive and sustainable. This will be important in mobilizing additional resources because potential donors will naturally want to know the outcomes of the partnerships.

    4. Upgrades would also include, where possible, direct functional linkage of the WIPO Re:Search database with among others: .

       ✔ The BVGH Pipelines web page[6]

✔ The Emory University web site "Global Health Primer"[7] which was prepared by BVGH.

✔ The Medicines for Malaria Venture (MMV) website[8] with information about the Malaria Box and the Pathogen Box.

- In some cases a functional linkage would not be possible, but a simple link would still be useful.

- All the web components of WIPO Re:Search should be consolidated in a unified new web site. This will greatly facilitate access to and use of the WIPO Re:Search resources. We note that WIPO owns the website name "wiporesearch.org."

- The high-level description of WIPO Re:Search should be modified to include description of it as a part or an example of the Sharing Economy. This will help to differentiate it and show its uniqueness.

- Priority should be accorded to expanding the capacity-building activities of WIPO Re:Search. (WIPO Re:Search is undertaking some capacity building with the sabbaticals of developing country professionals. If necessary, the objectives or functions of WIPO Re:Search could be modified to include capacity building.) These expansions would require additional financial and human resources and thus provide an opportunity for fund raising.

    - There is an opportunity to collaborate with the Special Programme for Research and Training in Tropical Diseases at WHO (TDR) in this area. TDR has expressed a willingness to work with WIPO Re:Search to support capacity building.

    - Such an opportunity may also exist at the Tres Cantos Open Lab Foundation research facility operated by GlaxoSmithKline (GSK) in Spain.

    - As noted above, a role of WIPO in WIPO Re:Search is to provide capacity-building opportunities such as short-term training courses. This needs to be emphasized and expanded in the work of WIPO Re:Search.

    - Several of the companies involved in WIPO Re:Search have opportunities for their staff to spend sabbaticals at academic or other research centers in developing countries. WIPO Re:Search should assess whether it could identify placements for such company staff.

    - Companies often retire working research equipment. It has been suggested that WIPO Re:Search could be a mechanism for transferring this equipment to collaborating centers in the WIPO Re:Search network.

5.2 STRUCTURE AND GOVERNANCE RECOMMENDATIONS

There are two significant issues with respect to structure and governance to be addressed with respect to WIPO Re:Search. The first issue involves the possible roles and responsibilities of pharmaceutical companies in WIPO Re:Search. The second issue involves the relative roles and responsibilities of the BVGH Partnership Hub and the WIPO Secretariat.

- Possible roles and responsibilities of pharmaceutical companies:

    - Current policies provide that companies can only be members if they also contribute financially to WIPO Re:Search. This is unfortunate since some companies are very sympathetic to the goals of WIPO Re:Search and would like to show their support but either do not have sufficient products to place in the database or do not have sufficient support from upper management to obtain the financial resources necessary to contribute. The goal of the membership policies should not be directed towards generating financial support but rather towards establishing the widest possible institutional support for WIPO Re:Search. Thus, consideration should be given to the establishment of two levels of company membership. One level would be those companies that have not only contributed technologies to the database but also provide financial support for the Partnership Hub. In return for their financial support, these companies would be eligible for membership in the Advisory Committee (recommended above) thereby providing them with greater assurance that their views and needs will be met by WIPO Re:Search. Those companies not providing financial support would be eligible to attend WIPO Re:Search Annual Meetings and could put products in the database for potential partnerships but (to address the free rider problem) would not have Advisory Committee membership.

- Relative roles and responsibilities of the BVGH Partnership Hub and the WIPO Secretariat.

    - At this point, it is possible to identify some points for consideration when reconfiguring the relationship between the Hub and the Secretariat.

- Because its name is included in the name of the program, WIPO clearly has reputational risks with respect to WIPO Re:Search. Thus it should have clear opportunities to influence the management and operation of the Hub. Further, there is wide agreement that WIPO should receive visibility and credit for its leadership in the founding and continuation of WIPO Re:Search. It is important to show further that intellectual property is not a barrier to health innovation and that WIPO is a positive force for this innovation. One option for WIPO would be for it to be the Chair of the proposed Advisory Committee. Another would be for WIPO to have a seat on the Board of BVGH or, at the least, be an official Observer on the Board.

5.3 RECOMMENDATIONS AS TO POTENTIAL FUNDING STRATEGIES, INCLUDING FOUNDATIONS, BILATERAL AND MULTILATERAL DONORS

Once thorough consideration on the above recommendations has been provided and action taken, as appropriate; there should be a clear presentation to donors why they should support WIPO Re:Search. From the above discussion and other considerations, it is this Reviewer's opinion that potential donors will be most interested in the following opportunities:

- Contributing to an expansion of the partnering activities especially to involve more developing country investigators.

- Contributing to a pool of funds to support research projects resulting from the collaboration agreements, particularly in developing countries.

- Contributing to capacity-building activities particularly involving developing country scientists being trained in companies abroad or receiving training in their countries from company scientists and others.

If they are willing to contribute to these three items, they most likely would be willing to contribute to core costs for operation of the Partnership Hub including the maintenance of the web-based database.

5.4 FUTURE TARGETS AND PERFORMANCE INDICATORS

The following targets and performance indicators (metrics) of success for WIPO Re:Search are derived from this report's preceding recommendations on Program, Structure and Governance. (The lists include some metrics that are already being reported.)

5.4.1 PROGRAMMATIC METRICS

Short term metrics (1 – 2 years):

- A measure of the in-kind and directly measurable contribution (e.g. full- time equivalents, financing, monetized value of intellectual property) made by the companies to the workings of WIPO Re:Search.

- Number of partnerships formed with a breakdown between developed and developing country partners and a graphical presentation of the growth of each.

- A metric (e.g. self-reporting by partners with evidence to support claim) enumerating the partnerships that would not have occurred without the existence of WIPO Re:Search

- Publication of the minutes of the proposed Advisory Committee to illustrate the leadership and intellectual contributions made by industry.

- Publications of the proceedings of a consultation between PDPs and WIPO Re:Search including conclusions and recommendations of the participants recognizing the mutually reinforcing activities of each.

- Completion of a major upgrade of the WIPO Re:Search database and website. A metric would be the number of links to other websites and reports on the extent to which the database and subsidiary links had been exploited by users.

- Publication of a paper, preferably in a peer-reviewed journal, demonstrating how WIPO Re:Search operates as an organization in the Sharing Economy.

- Number of capacity-building activities carried out in collaboration with other organizations such as TDR and the Tres Cantos Open Lab Foundation.

- Number of capacity-building activities (and number of benefiting developing country individuals) carried out by WIPO in direct connection with WIPO Re:Search.

- Number of company staff serving in sabbaticals to research centers in developing countries catalyzed by WIPO Re:Search.

- Equipment donated by WIPO Re:Search companies to developing country centers.

- Number of developing country scientists trained at research institutes in developed countries.

Long term metrics (5 years):

- A composite metric of the first three short term metrics above.
- A report on the overall success and productivity of the Advisory Committee emphasizing its programmatic contributions.
- A report on how WIPO has continued to support and endorse the operation of WIPO Re:Search.
- A report summarizing the interactions between PDPs and WIPO Re:Search illustrating a growing number of ways in which WIPO Re:Search has supported the work of PDPs and vice versa.
- An overall evaluation of the WIPO Re:Search website and database demonstrating the extent to which it has become a valued source of information and a catalyst for formation of partnerships.
- A detailed report on capacity-building activities demonstrating the tangible benefits of these activities for developing country partners.

5.4.2 STRUCTURE AND GOVERNANCE METRICS

Short-term metrics (1 – 2 years):

- An increase in the number of private sector members both of those providing financial support for the Partnership Hub and of those not providing financial support.
- A report on the formation of the proposed Advisory Committee.
- A transparent report on progress in enhancing the profile of WIPO in WIPO Re:Search such as is recommended above.

Long-term metrics (5 years):

- An external third-party technical and administrative evaluation of WIPO Re:Search lauding its structure and governance.

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5 The Japanese companies participating in the Global Health Innovative Technology Fund (GHIT) each contribute USD1 million per year. An increase in the current level of company support for WIPO Re:Search would, therefore, appear to be reasonable.

6 http://ow.ly/SWb4h

7 http://ow.ly/TItn5

8 http://ow.ly/SWb8l

Annex 1:

Terms of Reference for the External Strategic Review of WIPO Re:Search

Title of Assignment: Strategic Review of WIPO Re:Search

Name of unit/sector: Global Challenges Division Global Issues Sector

Place of Assignment: n/a

Expected places of travel (if applicable): Seattle, Washington, New York City, New York, USA, and possibly Geneva, Switzerland

Expected duration of assignment: Around 60 working days over a period of approximately 6 months

INTRODUCTION

WIPO Re:Search is an initiative launched in October 2011 by the World Intellectual Property Organization (WIPO) and BIO Ventures for Global Health (BVGH, a US-based non-profit, non-governmental organization) together with a number of private and public sector partners. Its purpose is to catalyze increased R&D in the field of neglected tropical diseases (NTDs), malaria, and tuberculosis (TB) through the sharing of intellectual property, including know-how, proprietary data, services, compounds, compound libraries and other assets between Members.[9] The policy context for the creation of WIPO Re:Search includes the fact that R&D investment in these neglected diseases lags behind that in other fields for a variety of reasons. For example, because the burden of NTDs falls disproportionately on the world's poorest populations, there is a lack of economic incentive to invest the large sums necessary to develop new and better drugs, vaccines and diagnostics ('market failure').[10]

Yet, the private sector, in particular pharmaceutical companies, have significant resources and knowledge that could be useful to others working on NTDs, malaria and TB. Through WIPO Re:Search, participating pharmaceutical companies, among other Members, provide intellectual property assets to academic and nonprofit researchers anywhere in the world on a royalty-free basis, to help scientists work on NTDs, malaria and TB. WIPO Re:Search collaborations include the sharing of drug compounds, compound libraries, computational chemistry, data, clinical samples, reagents, general drug development expertise and will eventually include patent licenses.

WIPO, based in Geneva, Switzerland, serves as the Secretariat of WIPO Re:Search, while BVGH, based in Seattle, USA, is the administrator of the 'Partnership Hub' which is the mechanism to connect the Providers and Users and thereby facilitate collaborations.

WIPO acts as the Secretariat of the Consortium and finances its activities through its own resources. BVGH, however, requires a financial contribution, US$106,250/year from the large pharma companies, US$50,000/year from medium-sized enterprises and US$25,000/year from small companies or start-ups. In practice, this has meant that of the current 87 Members, nine pharmaceutical/biotech companies provide BVGH with the necessary operational budget of which three fall into the start-up category.

BACKGROUND

As noted above, WIPO Re:Search was launched in October 2011, and thus is approaching the completion of its third year of operations. The initial metrics to measure progress and success were focused on increasing Membership, including the geographical diversity of Members, and through the Partnership Hub, facilitating active collaborations (such as the sharing of IP assets) between Members.[11]

Key successes of the Consortium include:

- Membership: Significantly exceeding targets for Membership.[12] At launch, WIPO Re:Search had 31 Members, as of August 2014 there are 87 Members. Annual membership targets were approximately five-to-eight new Members per year which would require around 50 Members to have met the objective.

- Collaborations: Over 90 collaborations between Members have been facilitated since the beginning of 2012, an average of over 20 per year, compared to the initial targets of three to five in year one, five to 10 in year two and 15 collaborations in year three (for a total of around 26). From January to July 2014 alone, 21 collaborations have been concluded. Collaborations cover almost all NTDs, as well as malaria and TB.[13]

- "Hosting" Arrangements: An additional accomplishment of WIPO Re:Search in its first two years, and not originally planned, has been the "hosting" of developing country scientists by developed country

Members of WIPO Re:Search. Thanks to a grant (Funds in Trust) contribution from the Government of Australia, WIPO Re:Search has financed research sabbaticals for six African scientists at research facilities of two pharmaceutical companies, AstraZeneca and Novartis, and three US universities, Stanford, University of California, San Francisco and University of California, San Diego.

One area where WIPO Re:Search has fallen short of its goals is in the recruitment of more private sector, for-profit companies to the Consortium. Targets in 2012 were six new Providers and in 2013 two new paying private sector company members. In the event, two small biotech companies (Kineta and 60 Degree Pharma, both based in the USA and recruited by BVGH) joined the Consortium, and one major pharmaceutical company, AstraZeneca, left WIPO Re:Search upon restructuring. However, in 2014, the combined efforts of WIPO and BVGH resulted the first new large pharmaceutical company joining, Merck KGaA, based in Germany.[14]

In order for the Consortium to continue to be successful, one key objective is to broaden financial support, specifically for the Partnership Hub. Various attempts since 2012 at obtaining grants from funders such as the Bill & Melinda Gates Foundation and the Ministry of Foreign Affairs of Japan were unsuccessful.

OBJECTIVE OF THE ASSIGNMENT

The Strategic Review is commissioned at the end of the third year of operations of WIPO Re:Search. As noted above, during these first three years, the principal measurable goals were increasing membership and facilitating collaborations. These goals have been exceeded (except in its goal to enlist 1-3 new large pharma, or other for-profit private sector companies).

The primary challenges now facing WIPO and BVGH, are:

- What should the medium to long-term strategic plan look like?
- What are the next steps the Consortium must take if it is to build on its success?
- How can the Partnership Hub have a sustainable and solid budget in order to achieve the new goals in collaboration with WIPO?

Thus three broad categories of inquiry should be considered:

a. Membership: With almost 90 Members, the administrative capacity of WIPO and BVGH is stretched to the limit. Yet, as noted above, the Consortium requires more private sector members in order to support financially the Partnership Hub. How and what can WIPO and BVGH do to increase private sector Membership?

   Active involvement of Current Members: Different members will have different reasons for joining and participating in WIPO Re:Search. Some Members have uploaded data in the database, participated in the hosting arrangements, and entered into collaborations. Others have been more passive, often despite repeated outreach efforts to, for example, upload data in the database. The Reviewer will interview the principal points of contact and a range of Members, including those who have been very active, selectively involved, or with very little activity, to ascertain whether WIPO Re:Search is meeting their needs and expectations, and if not why not.[15]

b. Collaborations: WIPO Re:Search's most important goal is to facilitate collaborations between Members. The purpose of the collaborations is to advance R&D in the field of NTDs, malaria and TB. With over 90 collaborations three years, it is clearly achieving this important first goal. However, important questions for the future of the Consortium include:

   - Is the type of collaboration facilitated by WIPO Re:Search enough? In other words, once initial collaborations are established, is there a further role for WIPO Re:Search/Partnership Hub to facilitate further development of a collaboration?
   - What types of future services (by WIPO and/or BVGH) may be required in order to advance the collaborations?
   - What specific untapped resources are "embedded" in WIPO Re:Search's important group of Supporters?
   - As part of a future funding strategy should WIPO Re:Search assume responsibility for helping institutions raise funds to move projects from pre-clinical to clinical stages? Put differently, what, if anything, is the role of the Consortium in facilitating the move from 'R' to 'D'? Note that BVGH has developed the BVGH Funders Database which is intended to support Members gaining access to funding.

c. Funding base of WIPO Re:Search: As WIPO Re:Search moves from its early post-launch stage to a more mature phase, a growing imperative is broadening and deepening sources of financial support, specifically for the Partnership Hub. While some modest progress has been made, such as the addition of two small and one major company Members, this must be measured against both the

goals of three new paying members per year, and the loss of one original Members, AstraZeneca. (It should also be noted that WIPO Re:Search has benefitted from Funds-in-Trust contributions from both the Governments of Australia and Japan.)

The Reviewer will engage current funding Members, a point of contact at AstraZeneca, and companies that have declined to join, to develop information as to how WIPO Re:Search provides value to the company, or, conversely, why a company has not agreed to join the Consortium. WIPO and BVGH will supply the consultant with relevant contacts.

REVIEW METHODOLOGY

The Strategic Review will be conducted through desk reviews, telephone, and limited in-person interviews, questionnaire survey(s)s, and a limited number of on-site visits with selected (in consultation with WIPO and BVGH) existing, former, and prospective Members and financial donors.

WIPO will be available to assist the Reviewer in formulating questions to interviewees, but the Reviewer is also expected to be knowledgeable and experienced in the field of global health research, public-private sector partnerships, PDPs, and strategic planning to develop appropriate questions and follow-up lines of inquiry.

To assist the Reviewer in preparing for the interview, WIPO will make available (and guide the Reviewer through):

1. Core documents such as the Guiding Principles, the MOU between WIPO and BVGH, the MOU between BVGH and funding Members, personnel and organizations (WIPO, BVGH, companies, NGOs, other partners) involved in its creation. These include governance, core policies, operating principles, and practices.

2. The WIPO Re:Search Strategic Plans for 2012 and 2013 (as these are internal documents, they will be made available to the Reviewer once s/he has been selected). This includes the results framework (i.e. objectives, targets, performance indicators, etc.).

3. The financial and resource mobilization plans, particularly those relating to the services of the Partnership Hub.

4. Select collaboration agreements.

The consultant is expected to consult via telephone in the first phase with BVGH, as well as a few active Members, selected by WIPO and BVGH. Overall, the majority of the interviews of Members in Africa, the Americas, Asia, and Europe, will be conducted by phone. A questionnaire may also be circulated to Members.

Further, and in consultation with WIPO and BVGH, the consultant is also expected to meet select donor agencies (foundations, bilateral, others) to assess possibilities of financial support for WIPO Re:Search, particularly the Partnership Hub.

DELIVERABLES/SERVICES

A draft review report shall be submitted to WIPO and BVGH for comments. Such report should include:

1. An executive summary with principal findings, conclusions and recommendations, including, but not limited, to:

    - The overall program
    - The results framework
    - Governance, structure and processes
    - Relations with Members
    - Strategies to enhance the product portfolio
    - Future targets and performance indicators (specific, measurable, achievable, realistic, and time scaled, or SMART)
    - Strategies to increase funding, including donor relations, and
    - Other recommendations to improve efficiencies and future activities.

2. A description of WIPO Re:Search's strengths and weaknesses, as perceived by the Members and benchmarked also against the stated objectives with special emphasis on the strategy and operating practices, as well as the level of involvement of various groups of Members (private sector, public sector, developing country institutions, etc.).

3. An evaluation of the portfolio of collaborations, the product pipeline (e.g., from early stage discovery to screening of compounds to pre-clinical trials) and the mix of NTDs, malaria and TB projects, specifically with a view to enhancing the likelihood of supporting the progress of initial, pre-clinical, collaborations "review" into the drug development process, (e.g., Phase 1, 2, and 3, clinical trials).

4. An assessment of the institutional structure of WIPO Re:Search and its appropriateness and effectiveness for achieving the objectives of the Consortium in a cost-efficient way, including an assessment of staff resources and Consortium communications.

5. Recommendations as to potential funding strategies, including foundations, bilateral and multilateral donors.

6. Options on strategies to more strongly engage Supporters to better leverage their extensive networks.

7. A framework proposal with principal elements for adaptation to different donors should also be delivered to WIPO.

Preliminary initial findings should be presented orally to WIPO and BVGH and may be presented with a few Power Point slides, at the Annual Meeting on November 6, 2014, in New York City, USA. The occasion of the meeting will also allow the consultant to meet many Members and talk to a wider audience, particularly at the margins of the IFPMA General Assembly taking place in New York on November 5 and 6, 2014.

A draft report should be submitted to WIPO by the end of 2014. Prior to issuing the final report, the Reviewer should take into consideration comments to be provided by WIPO and BVGH.

It is anticipated that WIPO will provide a written response to the recommendations and publish the Strategic Review, together with the response, for distribution primarily to WIPO Re:Search Members, prospective donors and Member States where there are WIPO Re:Search member institutions. It is intended that a suitable version of the Strategic Review will also be published as a WIPO Global Challenges Report.

Reporting Anatole Krattiger, Director, and Thomas Bombelles, Head, Global Health, Global Challenges Division. For elements 5.5, 5.6, and 5.7 of the Deliverables (i.e., those relating to mobilization of external resources) Mr. Joe Bradley, Head, Intergovernmental Organizations and Partnerships Section, Department of External Relations, will also be part of the reporting chain in WIPO.

Profile (e.g. area of specialization/expertise, specific knowledge/skills/experience)

At least 20 years of experience in building and leading global health consortia, in participating in and evaluating the operations of public-private partnerships in health product development, institution building, program funding, health products development, technology transfer to developing countries, and developing country access issues.

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9 Members include Providers (who provide IP for licensing), Users (who use the licensed IP; Users can also be Providers), and an important group of Supporters.

10 For additional background, see, the World Health Organization's First (WHO/HTM/NTD/2010.1) and Second (http://ow.ly/SWaYB) WHO Reports on NTDs.

11 Source documents, such as the 2012, 2013 and 2014 strategic plans with specific goals and deliverables, and mid-year and year-end reports summarizing achievements measured against those goals, will be provided to the Reviewer at the beginning of the assignment.

12 For a current list of Members, see http://www.wipo.int/research/en/about/members.html

13 See http://www.wipo.int/research/en/collaborations/ for a list of all collaborations.

14 Subsequent to the Review, in mid-2015, Takeda Pharmaceutical Company Limited, of Japan became a Member.

15 The specific list of Members to be interviewed will be determined by WIPO, BVGH and the consultant.

Annex 2:
List of Interviewees

Agyare, Christian, University of Accra, Ghana

Ano, Susan, National Institutes of Health, United States of America

Asada, Makoto, Eisai, Japan

Bernhardt, Martin, Sanofi Aventis, France

Bhagwandin, Niresh, Medical Research Centre, South Africa

Caffrey, Conor, University of California San Francisco, United States of America

Cho-Ngwa, Fidelis, University of Buea, Cameroon

Deberardine, Robert, Sanofi Aventis, France

Denys, Luc , Johson&Johnson, Switzerland

Fine, Jackie, MSD, United States of America

Hammam, Olfat, Theodor Bilharz Research Institute, Egypt

Hayward, Tara, Sabin Vaccine Institute, United States of America

Hsieh, Michael, Biomedical Research Institute, United States of America

Keil, Petra, Novartis, Switzerland

Liotta, Dennis, Emory University, United States of America

Millward, Rick, Walter Reed Army Institute of Research, United States of America

Notegan, Eric, Roche, Switzerland

Olsen, David, MSD, United States of America

Owuso Dabo, Ellis, Kumasi Center, Cameroon

Oyibo, Wellington, Centre for Malaria Diagnostics, University of Lagos, Nigeria

Paccaud, Jean-Pierre, Drugs for Neglected Diseases initiative (DNDi), Switzerland

Pritchard, Kevin, formerly of Astra Zeneca, United Kingdom

Rohrbaugh, Mark, National Institutes of Health, United States of America Rosenberg, David, GSK

Terry, Robert, Special Programme for Research and Training in Tropical Diseases (TDR), WHO, Switzerland

Vessotskie, Janet, MSD, United States of America

Waldron, Roy, Pfizer, United States of America

Watanabe, Lisa, Program for Appropriate Technology in Health (PATH), United States of America

Welch, Larry, Eli Lilly and company, Switzerland

Annex 3:
Questions for Various Stakeholders

QUESTIONS FOR FUNDING MEMBERS

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search is addressing?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

What are the most important reasons your company is a contributing member?

Please give one or two examples WIPO Re:Search has done that you are especially pleased with.

In what ways do you think WIPO Re:Search could be strengthened?

How could WIPO contribute more?

How could BVGH contribute more?

In your view, what should WIPO Re:Search be like in five years?

COMPANIES WITH INTEREST BUT NOT JOINING

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search could address?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

What are the most important reasons your company is not a member and supporter?

In what ways do you think WIPO Re:Search could be strengthened?

In your view, what should WIPO Re:Search be like in five years?

COMPANIES THAT DROPPED OUT

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search is addressing?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

What are the most important reasons your company withdrew?

Please give one or two examples WIPO Re:Search has done that you are especially pleased with.

In what ways do you think WIPO Re:Search could be strengthened?

In your view, what should WIPO Re:Search be like in five years?

DEVELOPING COUNTRY|INSTITUTIONS THAT BENEFITTED FROM SABBATICALS

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search is addressing?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

How do you see WIPO Re:Search contributing in tangible ways to health in developing countries?

Please give one or two examples WIPO Re:Search has done that you are especially pleased with.

In what ways do you think WIPO Re:Search could be strengthened?

In your view, what should WIPO Re:Search be like in five years?

INSTITUTIONS THAT HOSTED SCIENTISTS

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search is addressing?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

What is WIPO Re:Search's value added for a group like yours?

Please give one or two examples WIPO Re:Search, has done that you are especially pleased with.

In what ways do you think WIPO Re:Search could be strengthened?

How could WIPO contribute more?

How could BVGH contribute more?

OTHER DEVELOPING COUNTRY INSTITUTIONS

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search is addressing?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

How do you see WIPO Re:Search contributing in tangible ways to health in developing countries?

Please give one or two examples WIPO Re:Search, particularly, BVGH has done that you are especially pleased with.

In what ways do you think WIPO Re:Search, particularly, BVGH could be strengthened?

In your view, what should WIPO Re:Search be like in five years?

PDPs (MEMBER AND NON-MEMBER) AND OTHERS

How would you state the objectives of WIPO Re:Search?

What needs do you think WIPO Re:Search is addressing?

How do WIPO Re:Search objectives fit with the big picture of technology development for health in developing countries? What is its value added? Think of NIH, Gates, PDPs, pharmaceutical companies, et al.

How do you see WIPO Re:Search complementing the work of your group?

Please give one or two examples WIPO Re:Search has done that you are especially pleased with.

In what ways do you think WIPO Re:Search could be strengthened?

In your view, what should WIPO Re:Search be like in five years?

For each interview, I informed the interviewees that their comments would be kept confidential and only summaries would be provided to WIPO. Any specific quotes provided in the report will not be attributed to the speaker. I also told them that my report would become public, again maintaining confidentiality of comments by interviewees, and WIPO would prepare a response.

Annex 4:

Changes in the World of Intellectual Property in the last two Decades

To analyze the performance of WIPO Re:Search and to clarify its potential contribution, it is important to understand the larger context in which WIPO Re:Search operates.

THE EVOLUTION OF PRODUCT DEVELOPMENT PARTNERSHIPS (PDPS)

Efforts to develop health technologies needed in developing countries have gone through a great change over the last several decades. Starting with the Population Council in the 1950s and 1960s, followed by various programs at WHO in the early-1970s, and leading to the founding of the Program for Appropriate Technology in Health (PATH) in 1977, the public sector understanding of how to develop products and, of great importance, how to work successfully with the private sector grew enormously. The founding of these organizations was driven by a realization that the private sector health industry did not accord priority to the development of products for the poor in developing countries and that if such products were to be developed, the public sector would have to assume some level of leadership. The successful experience of these organizations set the stage for the tremendous expansion that occurred throughout the 2000s with the establishment and generous funding of PDPs most prominently by the Bill and Melinda Gates Foundation,[16] and by others such as European bilateral donors and Médecins sans Frontires (for the Drugs for Neglected Diseases initiative, DNDi).

For a time during the 2000s there was some skepticism about the efficacy of PDPs to achieve their goals of developing new products. The lack of success in vaccines for HIV/AIDS and TB cast a pall on these efforts. For example, Dr. Trevor Mundel, after assuming the position of President for Global Health at the Bill & Melinda Gates Foundation in 2011 (from a position in the pharmaceutical industry), questioned the usefulness of PDPs. He felt that perhaps the most efficient way for the Foundation to proceed would be to work directly with large pharmaceutical companies, and he assigned some of his staff to try to construct a world without PDPs. At the Gates Foundation annual PDP meeting in the spring of 2013, Mundel reported on the outcome of this work. He said that the staff had been unable to create a scenario for product development for developing countries that did not involve PDPs. The Foundation recommitted itself to support of PDPs.

For much of the 2000s European bilateral aid agencies hesitated to support PDPs but starting after 2010, the United Kingdom, Germany, and the Netherlands provided generous support.

Resounding successes by MMV (e.g. Eurartesim – a fixed dose combination for treatment of uncomplicated malaria), DNDi (artesunate and amodiaquine fixed-dose combination therapy (ASAQ) for malaria), the Meningitis Vaccine Program (developer of MenAfriVac which has had a profound impact on meningitis A in Africa), the Malaria Vaccine Initiative (developed with GSK through Phase 3 of a malaria vaccine), the International Vaccine Initiative (IVI; developer of a low cost cholera vaccine used in Haiti and elsewhere) and others have clearly demonstrated the efficacy of these initiatives.

PDPs operate within certain constraints. Product development may cost up to USD3 billion for a single product[17] and even the largest PDP has a budget of less than USD100 million per year for all its portfolio, which usually includes multiple candidates. Within these constraints, PDPs need to focus on advanced leads that are either in or through Phase 1 testing. In recent years, they have come to appreciate the need to replenish their portfolios and PDPs like DNDi and MMV have active programs to screen for new leads.

PDPs have innovated in a number ways. They have:

- Developed methods for identifying product leads to assemble rational portfolios coupled with product development programs (often called Virtual R&D) through partnerships with public and private entities.
- Developed collaboration frameworks for working with the private sector that meet the needs of both.
- Developed IP policies that both protect the private sector while ensuring access in developing countries.
- Found ways to work through the national regulatory process to accelerate the licensing of safe and effective products.
- Developed ways to transfer technology to developing countries to take advantage of lower cost production in those countries.

- Established approaches for working with national health systems to foster the introduction and use of new technologies.

- Worked with developing countries research centers to build capability in product development, disease surveillance, clinical evaluation and other areas.

One area where PDPs have been criticized is a lack of support for laboratory and preclinical studies conducted in developing countries. The PDPs explain that their mission is to develop new products in the most cost effective and expeditious manner and not to undertake long-term capacity building.

THE EVOLUTION OF THE VIEWS AND PRACTICES OF INDUSTRY

The South Africa AIDS Story

A critical series of events transpired in South Africa beginning in 1998 that led, in part, to a fundamental change in the position of large pharmaceutical organizations vis-à-vis markets in developing countries.[18] (There are differing views as to the details of this matter, but the overview by Fisher and Rigamonti summarized here is generally accurate and supports the conclusion (in the Reviewer's view) of the impact on the pharmaceutical industry and the relevance of that impact for WIPO Re:Search.)

Faced with a rapidly expanding need for anti-retroviral drugs to treat HIV/AIDS, the Ministry of Health explored various options for obtaining these drugs. Drugs available to the Ministry were priced at levels beyond the means of the Ministry to purchase. However, the same drugs were being manufactured and sold at much reduced prices in countries such as India where patents had not been applied for for those drugs by the original developers. The government of South Africa amended its Medicines and Related Substances Control Act (MRSCA) to allow the minister of health to undertake parallel import of pharmaceuticals from generic producers. To block the Act, in February 1998, several US pharmaceutical companies challenged the constitutionality of the amended MRSCA before the High Court of South Africa. The US government supported industry's efforts by adding the issue to trade negotiations. It added South Africa to the Special 301 watch list.

This court action set off an international fire storm of criticism of the US pharmaceutical industry and indirectly of all large pharmaceutical companies that relied, in part, on patents to manage markets. The US government was also heavily criticized and eventually changed its policy and no longer opposed South Africa's efforts to access lower cost anti-retrovirals. Eventually, in April 2001, the pharmaceutical companies dropped their challenge.

The impact on the pharmaceutical industry of this series of events was perhaps best summarized by the Wall Street Journal. It said, "Can the pharmaceutical industry inflict any more damage upon its ailing public image? Well, how about suing Nelson Mandela?"[19]

Changing Markets

In some ways, a much larger change in the pharmaceutical industry took place throughout the 2000s. A number of developing countries experienced rapid economic growth led by the BRICS (Brazil, Russia, India, China and South Africa) and their populations represented nearly half the world's population. Benefiting from this economic growth, these countries rapidly increased funding for science and industry. Demand for high value products by the population increased dramatically. While these markets were still small on a global scale, it did not take much mathematics to conclude that the markets were likely to be large in the not-to-distant future. Most, if not all, large pharmaceutical companies realized that they needed to position themselves to enter these markets.

Impacts of the South Africa AIDS Story and Changing Markets[20]

The pharmaceutical industry realized that it needed to take actions that would improve its image in developing and developed countries and would position it to enter expanding markets in developing countries. These actions were also the result of a sincere commitment by all the companies and their staff to make positive contributions to human health throughout the world.[21] These actions included:

- GSK's collaboration with the Malaria Vaccine Initiative (MVI) to develop a malaria vaccine, promising that the price of the vaccine would be "cost plus 5%."

- Sanofi Pasteur's recommitment to (after a major setback) and dramatic expansion of its dengue vaccine development program.

- Novartis's establishment of research institutes in Singapore (Novartis Institute for Tropical Diseases), Shanghai, and Siena addressed to the needs of developing countries.

- Many companies' efforts to buy or merge with pharmaceutical companies in developing countries as exemplified by GSK's purchases in China and India, and Sanofi Pasteur's purchase of Shantha Biotechnologies in India.

- GSK's establishment of the Tres Cantos Open Lab Foundation, a research center in Spain devoted to tropical disease research.

- Entry-into-collaboration agreements by almost all pharmaceutical companies with PDPs.

- MSD's MECTIZAN Donation Program, African Comprehensive HIV/AIDS Partnerships, China-MSD HIV/AIDS Partnership, the GARDASIL Access program, and the Hilleman Vaccine Institute in India in collaboration with the Wellcome Trust.

- Pfizer's Global Health Fellows, International Trachoma Initiative, Diflucan Partnership, Infectious Diseases Institute in Uganda, and Malaria Efforts.

- Eisai's commitment to the Global Health Innovative Technology Fund (GHIT).

- The joint effort of many companies to establish and support WIPO Re:Search.

THE EVOLUTION OF UNDERSTANDING OF INTELLECTUAL PROPERTY

The pharmaceutical industry allocates large resources to R&D which generates product leads. Some of these leads are relevant to the diseases to which the company accords priority and some may also be of potential use against diseases to which they do not accord priority such as NTDs. As a matter of routine practice, industry will seek patent protection for almost all leads but will not pursue those of low priority. These low priority leads, the associated know-how, and technical data may be "put on the shelf" and no further research will be undertaken.

During the 1990s and 2000s, in parallel with the founding and maturation of PDPs, a debate concerning the role of intellectual property took place. On one side, it was argued that patents allowed companies to develop monopolies allowing them to charge high prices not affordable by the poor. In this view, intellectual property was a barrier to improved health in developing countries. On the other side, it was argued that patents provided an essential foundation to make possible the costly investments required to develop new safe and effective technologies. A product that was not developed could not be provided to the poor no matter what the situation with intellectual property. In this view, intellectual property was a facilitator of product development and the issue of access in developing countries was a (largely) separate matter.

Those who saw patents as 'bad' aimed a great deal of their efforts toward the WTO because it was the mechanism for the formulation and implementation of the TRIPS Agreement which sought to make IP policies more uniform among developed and developing countries. These critics of WTO believed that the extension of IP enforcement to developing countries could only make the situation worse, i.e. products becoming more expensive, while those on the other side believed that this extension would foster the development of innovative capabilities in developing countries allowing those countries to develop affordable products. The WTO is concerned with trade and the treaties associated with trade, and it does not address the technical issues of intellectual property. Because of this, attention turned to WIPO once the TRIPS Agreement went fully into effect. WIPO was seen by some as an unflinching advocate for intellectual property with little if any interest in the needs of developing countries. WIPO was seen as perpetuating a bad situation.

In 2007, WIPO adopted a Development Agenda which included 45 recommendations many of which called for addressing the needs of developing countries and, in particular, LDCs.[22] Subsequently, WIPO staff evaluated possible actions to implement the recommendations of the Development Agenda. One of the fruits of this work was the establishment of WIPO Re:Search and its launch in 2011. The objectives of WIPO Re:Search are stated above.

During this time of debate about intellectual property, progress in crystallizing the technical issues was achieved. From a time when intellectual property was seen as the focal issue, thinking evolved to the realization that intellectual property is only one factor that affects availability of new health technologies. This is well illustrated by developments in three sectors: advocacy groups, PDPs and academia.

Advocacy groups include those who have been most critical of patents as limiting access to health technologies by the poor. However, it seems they came to realize that it was not so much who owned the patents but the mechanisms by which ownership was generated. They realized that it was those who paid for research and development that would obtain the patents that emerged. In general, because individual companies paid for the very large bulk of research and development for a particular health technology, that company owned the resulting intellectual property. The advocacy groups therefore began lobbying for the establishment of global research and development funds that would basically take away the responsibility for research and development from industry and transfer it to the public sector. To date, although such a fund has been recommended by a WHO Advisory Committee, a fund of sufficient size and scope has not been established.
In the early 2000s, there was debate about the extent to which PDPs would be affected by and could manage intellectual property in their product development efforts. Some felt that PDPs would be hamstrung because they would not be able to obtain necessary licenses to push forward product development.
As the 2000s wore on, it became clear that, although

intellectual property was an important factor in influencing the strategies for product development, in almost all cases PDPs were able to obtain access to the intellectual property they needed to push forward the products they felt most likely to have an impact in developing countries. PDPs came to realize that perhaps the most significant barrier to progress was the lack of sufficient funding to finance advanced clinical trials of promising candidates. At one point, the Gates Foundation even announced that it would not support Phase 3 studies because of their cost (in fact the Gates Foundation has funded Phase 3 studies, but only in limited cases). Through the sharing of information and mutual learning, the PDPs developed robust IP management strategies and policies which are effectively executed today. Academic researchers also looked carefully at the impact of intellectual property on health technology development. One study of PDP programs published by this author concluded that intellectual property was only one of six factors that influenced progress in the product development of health technologies.[23] The other five are 1) support for research and development, 2) development of national markets, 3) development of international markets, 4) creation of high-quality manufacturing facilities, and 5) the implementation of high-quality regulatory systems to ensure safety and efficacy.

Another insight that emerged was the different IP issues depending on the stage of development of the technology. In the early stages, patents might be used to control who could undertake product development research on a new candidate through the use of Material Transfer Agreements. These Agreements often had a clause that prohibited the use of the patented products in humans. When a product reached the clinical trials stage, patents were often the tool used to regulate the formation of partnerships between product developers and organizations capable of undertaking clinical trials. Finally, as a product approached licensure, patents and other intellectual property were used in the formation of partnerships between those who had contributed to the product development and those who would manufacture and distribute a product.[24] This analysis is important for understanding WIPO Re:Search, because WIPO Re:Search deals almost exclusively with products in the early stages, and with Material Transfer Agreements. There are at least two major stages through which products must pass, involving additional IP issues, before those products can enter a market.

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16 The first advisor in health to Bill and Melinda Gates was Gordon Perkin who was then the President of PATH. He later became the first leader of Global Health at the Foundation and made many of the grants that launched PDPs.

17 http://ow.ly/SWaQV

18 Fisher WW, Rigamonti C. The South African AIDS Controversy: A Case Study in Patent Law and Policy. The Law and Business of Patents. Harvard Law School. February 10, 2005 (http://ow.ly/SWaLT).

19 Helene Cooper et al., AIDS Epidemic Puts Drug Firms In a Vise: Treatment vs. Profits. Wall Street Journal. March 2, 2001.

20 Many other factors led to these changes but the South Africa AIDS Story and the Changing Markets encapsulate many of the others.

21 T. Bombelles of WIPO makes the following insightful observation: "The companies and their staff have understood and been motivated by a sincere commitment to make positive contributions to human health throughout the world. The challenge has been, and became more acute in the context of the AIDS crisis, to be understood as doing so. The business model of developing new treatments for patients in developed and middle-income countries did nothing to address the access issues regarding poor patients in poor countries. This was the challenge the industry had to address."

22 http://www.wipo.int/ip-development/en/agenda/recommendations.html

23 Mahoney RT. Product Development Partnerships: Case studies of a new mechanism for health technology innovation. Health Res Policy Syst, 9, 2011.

24 This is admittedly an oversimplified description of the very complex process.

Annex 5:

PDPs and Other Organizations Involved in NTDs, Malaria and TB

There are a number of organizations working in areas of concern to WIPO Re:Search. These include, with a listing of their priority disease targets:

Aeras
- TB vaccines

Drugs for Neglected Diseases initiative (DNDi)
- Human African Trypanosomiasis
- Leishmaniasis
- Chagas
- Malaria
- Paediatric HIV
- Onchocerciasis
- Lymphatic filariasis

Global Health Innovative Technology Fund (GHIT)
- NTDs
- Malaria
- TB

Malaria Vaccine Initiative (MVI)

Medicines for Malaria Venture (MMV)

Novartis Institute for Tropical Diseases (NITD
- Dengue drugs
- Human African Trypanosomiasis drugs
- Malaria drugs

Sabin Vaccine Institute Product Development
- Partnership (Sabin PDP)
- Hookworm vaccine
- Schistosomiasis vaccine
- Chagas Disease/Leishmaniasis vaccine
- SARS vaccine

Special Programme for Research and Training in
- Tropical Diseases at WHO (TDR)
- Malaria
- HIV/AIDS
- Tuberculosis
- NTDs and sexually transmitted diseases

TB Alliance
- TB drugs

Tres Cantos Open Lab Foundation
- NTDs
- Malaria
- TB

AERAS FOUNDATION

Disease: TB vaccines
Legal status: Non-profit organization
Location: Rockville, MD, USA with offices in Beijing, China, and Cape Town, South Africa
Staff: 11 (senior leadership team only)
Annual budget: USD48 million
Link: http://www.aeras.org/

What it does relevant to WIPO Re:Search:
Aeras has a portfolio composed of vaccines in clinical trials or vaccines candidates in preclinical study. In addition, "Aeras is pursuing a novel antigen selection strategy, identifying new antigen targets for potential inclusion in ongoing TB vaccine development."[25]

DRUGS FOR NEGLECTED DISEASES INITIATIVE (DND*i*)

Diseases
Human African Trypanosomiasis
Leishmaniasis
Chagas
Malaria
Paediatric HIV
Onchocerciasis
Lymphatic filariasis

Legal status: Independent non-profit
Location: Geneva, Switzerland, with offices in New York, USA, Nairobi, Kenya, New Delhi, India, Tokyo, Japan, Rio de Janeiro, Brazil, Pulau Pinang, Malaysia and Kinshasa, Democratic Republic of Congo
Staff: ~100
Annual budget: €24.4 million (2013)
Link: http://www.dndi.org/

What it does relevant to WIPO Re:Search.[26]
DNDi's primary objective is to deliver 11 to 13 new treatments by 2018 (five to seven more than the six already in implementation phase in 2011) for leishmaniasis, human African trypanosomiasis (sleeping sickness), Chagas disease, malaria, paediatric HIV, and specific helminth infections and to establish a strong R&D portfolio that addresses patients' treatment needs and supports long-term objectives.

Highlights of the Business Plan

- Although the R&D landscape for NTDs has improved from 2000, sustainable public funding remains a critical issue to support these R&D efforts.

- DND*i* will concentrate its efforts on the three primary diseases (leishmaniasis, Chagas disease, and human African trypanosomiasis). It will complete its malaria activities and launch two 'mini-portfolios': paediatric HIV and specific helminth infections.

- With its pipeline maturing, DND*i* will increasingly focus on access, with the ultimate aim of facilitating maximum impact via appropriate use of treatments, assuring their effective transition to relevant access partners and implementers, and leveraging success for future steps.

- A critical component of the updated strategy is the further empowerment of Regional Offices, aiming at their transition from a support role to a more active contribution to all DND*i* activities.

In particular, its research program focuses on screening and lead optimization.[27]

Screening process

Compounds

Targets: Chagas, Human African Trypanosomiasis (HAT), leishmaniasis, and specific filarial infections. Extensive investigation of advanced candidates and small series of compounds; identification of promising chemical classes from libraries of private companies; access to chemical diversity essential to identifying potent and selective hits with acceptable drug-like characteristics; identification of novel compounds via high-throughput screening; and screening compounds and assessing their activity against a specific target

Partners: AbbVie (formerly Abbott), USA; Actelion, Switzerland; Anacor, USA; Astellas, Japan; AstraZeneca, Sweden; Bayer, Germany; Bristol-Myers Squibb, USA; Celgene, USA; E.I. du Pont de Nemours, USA; Eisai Co. Ltd, Japan; Genomics Institute of the Novartis Research Foundation, USA; GSK, Tres Cantos, Spain; Institute of Medical Microbiology, Immunology, and Parasitology, Hospital University of Bonn, Germany; Medicines for Malaria Venture, Switzerland; MSD, USA; Northwick Park Institute for Medical Research, UK; Novartis Institute for Tropical Diseases, Singapore; Pfizer, USA; Pfizer Animal Health, USA; Sanofi, France; Sigma-Tau, Italy; Special Programme for Research and Training in Tropical Diseases (WHO-TDR); TB Alliance, USA; TI Pharma, Netherlands; Vertex, USA

Screening

Identification of new active compounds via low- to high-throughput screening assays in dedicated centres:

- *High-throughput screening*. High-throughput screening of large-size libraries for Leishmania, T. cruzi, and T.b. brucei (Institut Pasteur Korea), and for Leishmania (Drug Discovery Unit at the University of Dundee)

  Partners: Institut Pasteur Korea (IPK), South Korea; Drug Discovery Unit at the University of Dundee, UK

- *Reference Screening Centres*. Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland; Laboratory of Microbiology, Parasitology, and Hygiene (LMPH), University of Antwerp, Belgium; and London School of Hygiene & Tropical Medicine (LSHTM), UK

Lead optimization

- *Objective*: Obtain optimized leads by progressing 'hits' with a good safety profile and activity against all target diseases (Chagas, HAT, and leishmaniasis)

  Partners: Centre for Drug Candidate Optimisation (CDCO)/Monash University, Australia; Epichem, Australia; Federal University of Ouro Preto (UFOP), Brazil; Institut Pasteur Korea (IPK), Korea; iThemba, South Africa; LMPH, University of Antwerp, Belgium; LSHTM, UK; Murdoch University, Australia; SCYNEXIS Inc., USA; TB Alliance, USA; University of Auckland, New Zealand; Pace University, USA; Pfizer, USA; Wuxi AppTech, China

Nitroimidazole backup – HAT

- *Objective*: Profile potential backup candidates for fexinidazole for the treatment of HAT

- *Partners*: TB Alliance, USA; Swiss TPH, Switzerland; Suwinski, Poland; Pace University, USA; WuXi AppTec, China

Oxaborole backup – HAT

- *Objective*: Profile potential backup candidates for SCYX-7158 for the treatment of HAT

  Partners: Anacor, USA; SCYNEXIS, USA; Pace University, USA; WuXi AppTec, China

Nitroimidazole backup – Visceral Leishmaniasis (VL)

- *Objective*: Profile potential backup candidates for VL-2098 for the treatment of VL

- *Partners*: TB Alliance, USA; Advinus Therapeutics, India; Central Drug Research Institute, India; LMPH, Belgium; LSHTM, UK; Auckland University, New Zealand

Nitroimidazole – Chagas disease

- *Objective*: Investigate the potential of a nitroimidazole compound that is safer and more efficacious than the current Chagas disease standard of care (benznidazole and/or nifurtimox)

- *Partners*: TB Alliance, USA; Centre for Drug Candidate Optimisation (CDCO)/ Monash University, Australia; Epichem, Australia; Murdoch University, Australia; Federal University of Ouro Preto (UFOP), Brazil; Institut Pasteur Korea (IPK), South Korea

GLOBAL HEALTH INNOVATIVE TECHNOLOGY FUND (GHIT)

Diseases: HIV/AIDS, Tuberculosis, Malaria, and other NTD
Legal status: Non-profit organization
Location: Tokyo, Japan
Staff: Small administrative group
Annual budget: ~USD20 million (2014)
Link: https://www.ghitfund.org/general/top

What it does relevant to WIPO Re:Search
Two ministries of the Japanese government (Health and Foreign Affairs) have supported the founding of the Global Health Innovative Technology (GHIT) Fund whose mission is "to facilitate international partnerships that enable Japanese technology, innovations, and insights to play a more direct role in reducing disparities in health between the rich and the poor of the world." The GHIT Fund involves five Japanese pharmaceutical companies (Astellas, Daiichi-Sankyo, Eisai, Shionogi, and Takeda), the Bill & Melinda Gates Foundation, and UNDP, in addition to the two Japanese ministries.[28] In 2013, the Gates Foundation made grants totaling USD15,110,000 to support the GHIT and became active in the oversight and operation of the GHIT through membership on its Board of Directors and Scientific Advisory Committee. The Japanese government has pledged over USD14 million a year to the fund and the participating companies have committed USD1 million each per year.[29] The objectives of GHIT are similar to those of WIPO Re:Search in that they call for mobilizing dormant technologies that Japanese pharmaceutical companies own for research and development on neglected diseases particularly in less developed countries. By November 2014, the GHIT had made grants totaling more than USD30 million including more than USD12 million for neglected tropical diseases. Organizations partnering in the 9 neglected tropical diseases projects were Eisai, the Broad Institute, DND*i* (4 projects), Astellas, Merck KGaA, Swiss Tropical and Public Health Institute, Top Institute Pharma, University of Liverpool, Liverpool School of Tropical Medicine, Takeda, Institute of Microbial Chemistry,

The Chemo-Sero-Therapeutic Research Institute (KAKETSUKEN), Mahidol University, Baylor College of Medicine, Aeras, and the Sabin Vaccine Institute.

GHIT IP policy

Licenses
In the case of licensing-out data or products funded by GHIT Fund, grantees and/or participants will grant royalty-free licenses in Low-Income Countries (LICs) categorized by the World Bank classification. In Lower-Middle-Income Countries (LMICs) and Upper-Middle-Income Countries (UMICs), grantees and/or participants will grant licenses that can improve access to the product for low-income patients and populations.

Pricing
In Low-Income Countries (LICs), Lower-Middle-Income Countries (LMICs), and Upper-Middle- Income Countries (UMICs) categorized by the World Bank classification, participants and/or grantees will set prices for products on the basis of a no gains/no loss policy that can improve access to the product for low-income patients and populations.

MALARIA VACCINE INITIATIVE (MVI)

Disease: Malaria
Legal status: A program of PATH, a non-profit organization
Location: Washington, DC with office in Seattle, USA
Staff: ~35
Annual budget: USD63 million (2013)
Link: http://malariavaccine.org/index.php

What it does relevant to WIPO Re:Search[30]

Feasibility studies
New initiatives aim to combine several approaches to developing highly efficacious clinical and transmission-blocking vaccines

MVI is working with a range of partners to evaluate antigens and delivery systems using specialized assays and animal models. These preclinical feasibility studies represent the early stages in vaccine development. Feasibility studies are generally short (typically 6 to 18 months) and require lower levels of investment. Successful outcomes of some of these programs will lead to their advancement to translational programs. By supporting these studies, MVI ensures that any projects that make transition into the portfolio are effectively aligned with our long-term strategic goals.

CSP RI conjugates

Partners: New York University (NYU), MSD

Type of project: Pre-erythrocytic antigen evaluation

Description: CSP Region I is a highly conserved, subdominant epitope in the N-terminal region of CSP, and is hypothesized to play a critical role in initiation of liver stage infection by Plasmodium species.1 Cleavage at this site via parasite cysteine protease(s) exposes a C-terminal TSR adhesive domain, facilitating invasion of hepatocytes.2 Investigators at NYU and MSD designed and synthesized several peptide based vaccine candidates based upon this epitope, and tested their capacity to induce functional immune responses in rodents. The first stage of this work was completed in 2014, and discussions regarding next steps are ongoing.

Duration: 2010 – 2015

MEDICINES FOR MALARIA VENTURE (MMV)

Disease: Malaria
Legal status: Non-profit organization
Location: Geneva, Switzerland
Staff: ~70
Annual budget: >USD20 million (2013 est.)
Link: http://www.mmv.org/

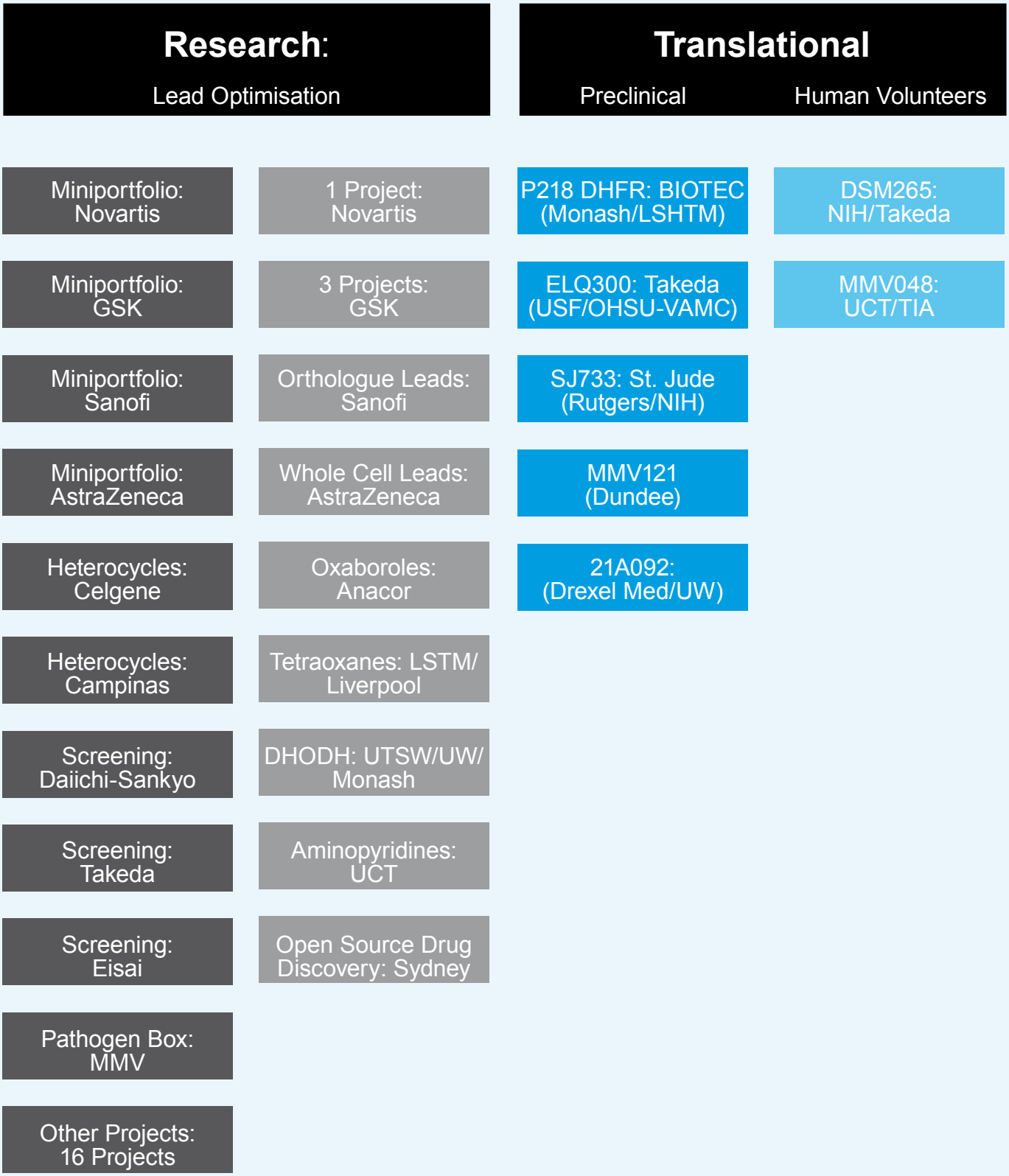
What it does relevant to WIPO Re:Search
Historically, one of the key problems in neglected disease drug discovery has been identifying new and interesting chemotypes. Phenotypic screening of the malaria parasite, Plasmodium falciparum has yielded almost 30,000 submicromolar hits in recent years. To make this collection more accessible, a collection of 400 chemotypes has been assembled, termed the Malaria Box (Figure 1). Half of these compounds were selected based on their drug-like properties and the others as molecular probes. These can now be requested as a pharmacological test set by malaria biologists, but importantly by groups working on related parasites, as part of a program to make both data and compounds readily available. In this paper, the analysis and selection methodology and characteristics of the compounds are described.

MMV Supported Projects in Research and Translational 3Q 2014[31]

(See Figure 1: MMV's Malaria Box on the next page.)

Figure 1:

MMV'S MALARIA BOX[32]



NOVARTIS INSTITUTE FOR TROPICAL DISEASES (NITD)

Diseases: Dengue drugs, Human African Trypanosomiasis drugs, Malaria drugs
Legal status: Not-for-profit organizations supported by Novartis
Location: Singapore
Staff: ~100
Annual budget: Not determined
Link: http://www.nibr.com/cs/www.nibr.com/downloads/research/NITD/NITD-FactSheet.pdf

What it does relevant to WIPO Re:Search[33]
NITD has state-of-the-art screening labs equipped with automated screening platforms that can screen our extensive Novartis compound library against both target and cell-based assays including the pathogens that cause the diseases we are working on.

To address this unmet global health need, NITD has led the formation of a research consortium that brings together cutting-edge drug discovery at Novartis with world-class malaria biology expertise. Armed with support from

- *The Wellcome Trust,*
- *Medicines for Malaria Venture,*
- *and the Singapore Economic Development Board, the consortium has the ambitious goal of identifying new drugs with a potential for a single-dose treatment for P. falciparum malaria and a therapy for P. vivax malaria.*

The NITD dengue team has worked with many of Singapore local and international collaborators to establish novel research tools and approaches, characterizing NS4B target to enable drug discovery, establishing dengue animal models for antiviral testing, defining structure and function of dengue viral proteins, and developing screening assays which have been used to identify several candidate compounds in the fight against dengue.

SABIN VACCINE INSTITUTE PRODUCT DEVELOPMENT PARTNERSHIP (SABIN PDP)

Diseases: Hookworm vaccine, Schistosomiasis vaccine, Chagas Disease/Leishmaniasis vaccine, SARS vaccine
Legal status: Independent non-profit
Location: Washington, DC, USA with offices in Houston, USA and London, UK
Staff: ~45
Annual budget: USD22.6 million (2013)
Link: http://www.sabin.org/

What it does relevant to WIPO Re:Search

Human Hookworm[34]
The Human Hookworm Vaccine Initiative (HHVI) has identified and produced several candidates for potential use as a vaccine. HHVI is focused on developing and testing a vaccine to prevent moderate to severe hookworm infection in children younger than 10 years old living in endemic areas. The goal is to reduce the anemia, delayed physical growth and impaired cognitive development caused by hookworm infection.

Currently, two lead candidate antigens are being developed to stimulate the human immune system to produce antibodies that inhibit parasite blood feeding: Na-GST-1 and Na-APR-1.

Na-GST-1: Phase 1 clinical testing of the Na-GST-1 hookworm vaccine began in January 2012. Currently, clinical trials are being carried out in Minas Gerais, Brazil and Washington, DC, USA.

Na-APR-1: Na-APR-1 has also shown protection against adult hookworm in preclinical studies. Clinical testing began in September 2013.

Because hookworm affects only the world's poorest people, Sabin PDP's approach is filling an important market gap by developing an inexpensive vaccine with little or no traditional market value. Sabin partners with private, academic and public institutions in low- and middle-income countries (LMIC), Australia, the United States and Europe to collaborate on preclinical studies, vaccine manufacturing and clinical testing.

The Sabin PDP is a member of the HOOKVAC Consortium, led by the Academic Medical Center (AMC) at the University of Amsterdam, which has been awarded a grant from the European Commission to expand the development and testing of this vaccine. Under this grant, the HOOKVAC Consortium will begin the first clinical testing of the human hookworm vaccine in sub-Saharan Africa in the nation of Gabon. The Consortium will also engage European small- and medium-sized enterprises (SMEs) to manufacture and co-formulate the two vaccine antigens, Na-GST-1 and Na-APR-1, into a single bivalent product for use in future Phase II/III clinical testing.

Schistosomiasis[35]
In collaboration with researchers at the James Cook University and The George Washington University, a promising new antigen, Sm-TSP-2 (Schistosoma

mansoni Tetraspanin-2), was selected for development as a schistosomiasis vaccine. Then at Texas Children's Hospital and Baylor College of Medicine, Sabin and its partners developed the process for manufacture of the vaccine under cGMP, and was followed by technology transfer to Sabin's manufacturing partner, Aeras. Following final lot release, a toxicology study and subsequent regulatory filing for the vaccine are scheduled to take place in 2013 with a Phase 1 clinical trial slated to begin in late 2013/2014.

Chagas Disease/Leishmaniasis[36]
The Sabin PDP is currently engaged in collaboration for early research and development for a bivalent therapeutic vaccine for the treatment of chronic Chagas disease (American trypanosomiasis).
It would be the first therapeutic vaccine for this disease. The vaccine is comprised of two Trypanosoma cruzi recombinant proteins formulated on alum.
One of the antigens is a unique T. cruzi 24 kDa antigen (Tc24) and the other is a unique T. cruzi surface transialidase (TSA-1). Pre-clinical work includes initial expression and characterization of the antigens in preparation for advancing the pre-clinical process development.

SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES AT WHO (TDR)

Diseases: Malaria, HIV/AIDS, Tuberculosis, NTD, and sexually transmitted diseases
Legal status: A program operating under the legal auspices of WHO with co-sponsorship by UNICEF, UNDP, the World Bank and WHO
Location: Geneva, Switzerland
Staff: ~35
Annual budget: ~USD45 million
Link: http://www.who.int/tdr

What it does relevant to WIPO Re:Search
For many years, TDR conducted a robust R&D program however in recent years, it has focused on policy, delivery, epidemiology and information sharing. Of particular importance, it has continued a capacity-building program to support research and development.

As stated on its Web page[37]

> Strengthening research capacity where it's needed most

EXPANDING RESEARCH GRANT SUPPORT

Both early and late career grants are being planned, including:

- 15 post graduate training and research grants
- 5 post-doctoral training and research grants
- 25 impact grants

The highly regarded Career Development Fellowship is now collaborating with EDCTP, the European & Developing Countries Clinical Trials Partnership. An evaluation of the fellowship recommends further expansion, and the fifth round of applications will go out in October 2015.

There are also plans to identify two regional training centers in the African and Eastern Mediterranean regions, adding to the four TDR centers already established on good health research practices in Colombia, Kazakhstan, Indonesia and the Philippines.

TB ALLIANCE

Disease: TB drugs
Legal status: Non-profit organization
Location: New York, USA, with offices in Brussels, Belgium, and Pretoria, South Africa
Staff: ~35
Annual budget: USD43 million (2012)
Link: http://www.tballiance.org/

What it does relevant to WIPO Re:Search
Box 3[38] summarizes TB drug discovery research by the TB Alliance and other groups.

TRES CANTOS OPEN LAB FOUNDATION

Diseases: NTDs, Malaria, Tuberculosis
Legal status: Not-for-profit organization supported by GSK
Location: Near Madrid, Spain
Staff: >100
Annual budget: Not determined
Link: http://www.openlabfoundation.org/about.html

What it does relevant to WIPO Re:Search
It provides a venue for the conduct of research.[39]

"Open lab projects are designed to explore new ideas that may lead to finding new medicines for diseases of the developing world. Projects are focused on early stage drug discovery and could involve research into new targets, tools, screening, lead identification and optimization. To be considered for support, there should be added value for the project in operating within the collaborative principles of the Open Lab, and it must align with the strategic objectives of the Foundation:

- *To develop novel classes of medicines for malaria.*
- *To develop new medicines that reduce treatment time and improve activity against multiple drug resistant (MDR) and extensively drug resistant (XDR) TB.*
- *To develop novel approaches to tackle other neglected diseases of the developing world, such as leishmaniasis and trypanosomiasis."*

The Foundation selects visiting scientists from universities, not-for-profit partnerships and other research institutes to work at the Tres Cantos campus for a dedicated period of time, accessing GSK drug discovery expertise as part of an integrated team to develop new medicines for diseases of the developing world.

A review of the Web page[40] reveals that the partnerships are with organizations in Spain, United States, United Kingdom, Italy, and Finland.

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25 http://www.aeras.org/annualreport2013

26 http://www.dndi.org/about-us/business-model.html

27 http://ow.ly/SWaHe

28 https://www.ghitfund.org/general/top

29 http://ow.ly/SWa8C

30 http://malariavaccine.org/rd-collaborations.php

31 http://www.mmv.org/research-development/rd-portfolio

32 http://ow.ly/SWarZ

33 http://ow.ly/TIrFR

34 http://ow.ly/SWaEv

35 http://ow.ly/SWaA5

36 http://ow.ly/SWavX

37 http://www.who.int/tdr/about/ar2013_beyond_4p.pdf?ua=1

38 www.newtbdrugs.org/pipeline.php

39 http://www.openlabfoundation.org/about.html

40 http://www.openlabfoundation.org/about/partners.html

Box 3:

GLOBAL TB DRUG DISCOVERY PIPELINE

Hit to Lead

Phenotype Hit-to-Lead (Vertex Pharmaceuticals)
Actinomycete Metabolites (U ILL Chicago, Myongii U)
Novel Hit-to-Lead Programs (Lilly DDi) GATB
Adamantanids (U ILL Chicago)
Whole-Cell Hit-to-Lead (GSK, GATB)
Malate Synthase Inhibitors (GSK, TAMU, GATB)
Menaquinone Synthase Inhibitors (CSU)
M. tb Energy Metabolism Inhibitors (UPenn, GATB)
Isoprenoid Biosynthesis Inhibitors (Lilly DDi)
Whole-Cell Hit-to-Lead (GATB, Sanofi)
RNA Polymerase Inhibitors (GATB, Rutgers U)
ATP Synthesis Inhibitors (GATB, Calibr)

Lead Optimization

Diarylquinolines (GATB, U Auckland, Janssen)
InhA Inhibitors (GSK)
LeuRS Inhibitors (Anacor Pharmaceuticals, GSK)
Pyrazinamide Analogs (GATB, Yonsei U)
Translocase-1 Inhibitors (Sequella)
DprE Inhibitors Azaindoles (GATB, Calibr)
Ureas (Sanofi, GATB)
Ruthenium(II)phosphine/picolinate Complexes (FAPESP/Brazil)
Spectinamides (St. Jude, U Tenn, CSU, UZ, Microbiotix)
Indazoles (GATB, GSK)
Macrolides (GATB, Sanofi)
Cyclopeptides (GATB, Sanofi)
DrpE Inhibitros (GATB)
SPR-113 (Gates Foundation)

Abbreviations of developers: CSU- Colorado State University; FAPESP-Sao Paulo Research Foundation; GATB-Global Alliance for TB Drug Development (TB Alliance); GSK-GlaxoSmithKline; Lilly DDi-Lilly TB Drug Discovery Initiative; RI-Research Institute; St. Jude-St. Jude Children's Research Hospital; TAMU-Texas A&M University; U-University; U ILL-University of Illinois; UPenn-University of Pennsylvia; UTenn-University of Tennessee; UZ-University of Zurich

Annex 6:
Description of some Potential Donors for WIPO Re:Search

The British, Dutch, German and US governments and the EU have funded PDPs in the last several years and have accorded priority to NTDs, malaria and TB. At this time, there are no Request for Proposals (RFPs) issued by the bilateral donors or the EU.

The British, Dutch and German governments are understood to be reviewing their past support of PDPs and are expected to issue RFPs in late 2015. It is likely that WIPO Re:Search including its European institutions will be able to compete for funding.

The US government, through USAID, has major programs in NTDs, malaria and TB. The NTD program accords priority to provision of drugs and collaborates with GSK, Johnson & Johnson, MSD, Pfizer, Inc., and Merck KGaA. In addition to supporting malaria control programs, USAID supports discovery and development of new antimalarial drugs, malaria vaccines and TB drugs. In the financial year 2012, it provided grants to PATH, Global Alliance for TB Drug Development, the Medicines for Malaria Initiative and others. As of the end of 2014, there are no open RFPs at the United States Agency for International Development (USAID) for these disease areas.

The EU is conducting the EU Horizon 2020 program.[41]

Horizon 2020 is the biggest EU Research and Innovation Program ever with nearly €80 billion of funding available over 7 years (2014 to 2020) – in addition to the private investment that this money will attract. It promises more breakthroughs, discoveries and world-firsts by taking great ideas from the lab to the market.

It is expected that the EU will issue additional RFPs (or Calls) under this program including for health. The rules for participation in Horizon 2020 indicated that non-European institutions can participate but based on previous experience, it clearly would be beneficial for WIPO Re:Search to emphasize the many European institutions involved in its activities.

The two most important foundations concerned with NTDs, malaria and TB (although they fund many other areas) are the Bill and Melinda Gates Foundation (BMGF) and the Wellcome Trust.

With the exception of the Response by the Secretariat, this report was prepared by Richard T. Mahoney (richardtmahoney@gmail.com), Consultant, Sedona, USA.

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www.wipo.int/globalchallenges

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