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By Dr. Minna Allarakhia
Editor, CanBiotech Inc.
Director, BioEndeavor Network

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Introduction

Increased technological and market complexities associated with new drug development are drivers in the formation of a health commons. Used originally to describe the sharing of natural resources including the interactions that occur to manage such natural resources, in this paper, the health commons refers to knowledge-based assets that are shared or owned in common by stakeholders found across the health value chain. This health commons offers several advantages including knowledge sharing, knowledge verification, joint and efficient knowledge creation. The Human Genome Project is perhaps a turning point in the creation of the health commons—with both varied resources such as information, biological materials, research-based tools and models, and even chemical compounds deposited into the commons; further, stakeholders from both the public as well as private sectors appear to be participating in its construction. The need for verification in the post genome era given the uncertainty of knowledge associated with disease processes and hence value creation, has become paramount. Further, the scale and cost of research is no longer manageable by isolated laboratories or firms.

Moving from early biological research, to compound development and then clinical testing, the notion of openness changes: beginning with open access to information, materials, tools, and compounds including public sector entities, private sector stakeholders, and uniquely, patients in the commons; evolving to dissemination of newly created resources via open licensing strategies including stakeholders functioning within and outside the health commons; and emerging as open collaboration between stakeholders acting on the periphery of the health commons. Worth noting is that upon approval and market entry, open access strategies may be used to distribute medical products to those at the bottom of the pyramid. In this article, the initial focus is on the role of public private partnerships for malaria as enabling for open innovation and the engagement of stakeholders either within or on the periphery of the health commons.

The incentive to engage in R&D targeting neglected diseases has typically been carefully managed through public-private partnerships (PPP). These partnerships have the objectives to encourage the creation of new technology and to ensure its availability to as many patients in disease-endemic countries. Taubman (2010) discusses that the World Health Organization has distinguished PPPs for product development for neglected diseases from PPPs focused on access to existing drugs (Merz, 1995). Product development PPPs are non-profit organizations that sponsor others to conduct R&D—be it discovery, preclinical, clinical, or manufacturing based activities. Access PPPs are instead non-profit organizations primarily concerned with expanding access to health-based technologies in existence, by collaborating with manufacturers and funding agencies, as well as developing countries. Through such collaborations, access PPPs play a role in the purchase and distribution of existing drugs, vaccines and other medical technology in developing countries (Merz, 1995; Taubman, 2010).

Product development PPPs carefully craft out agreements pertaining to both the rights to and exercise of background intellectual property (that is, IP that both or either parties bring to the partnership from the outset) and

research or project based IP (that is, IP generated from funded research and development). PPPs as such, must balance the need to encourage their private sector partners to engage in the necessary R&D including resource commitment where such R&D generally would not occur without sponsorship and the need to ensure broad access to the final products to patients in neglected markets. IP management in this case, may involve IP exercise rights segregated by market, with the private sector player maintaining ownership and/or exercise rights in developed markets while ceding rights for developing markets; access to IP beyond the scope of the sponsored research such as background technology required for final product development; march-in-rights that ensure that IP will be transferred to the non-profit organization in the event that the private sector partner fails to meet its commitment; and access to necessary IP (including to test data, background technology, manufacturing know-how) provided for third parties in the event that the original private sector partner fails to meet the agreed upon criteria for dissemination of the new product in neglected markets (Taubman, 2004; Taubman, 2010).

Access PPPs may alternatively consider the optimal downstream distribution of a finished product and not give priority to ownership of IP. As a consequence, IP ownership can be traded in exchange for meeting specified distribution targets. In this case, ownership rights to IP generated through funded research, access to background IP, and provisions pertaining to licensing new technology particularly for developed markets, can be used as part of the trade-off for fair and broad technology distribution to neglected markets. The trade-off will include distinct requirements for how the technology is to be distributed in target markets such as volume of distribution, preferential pricing, or access provided on the basis of non-market mechanisms (Merz, 1995; Taubman, 2004; Taubman, 2010; DNDi, 2011; IAVI, 2011).

While the literature is filled with discussions of PPP IP ownership and exercise rights provisions, further analysis reveals a multitude of other mechanisms employed by public sector and private sector stakeholders to promote openness including: the development of disease specific commons; open collaboration; humanitarian or preferential licensing; patent pools under a joint licensing scheme; patent commons with non-assertion pledges; and donation programs providing access to final products.

Public-Private Partnerships for Malaria: Medicines for Malaria Venture (MMV)

The discussion of strategies to develop technologies for the treatment of malaria typically begins with the Medicines for Malaria Venture (MMV) and Malaria Vaccines Initiative (MVI). MMV was launched in 1999. As a virtual organization, all of MMV's R&D, access and delivery activities are undertaken in collaboration with partner organizations across the world (MMV, 2011). MMV has worked in partnership with more than 130 research institutions and companies. Pharmaceutical and biotech partners bring expertise and facilities in drug discovery and development, including access to cutting-edge technologies to speed up discovery by compound screening, as well as manufacturing capability. In the public sector, academic research institutions bring scientific research expertise and facilities in areas ranging from basic biology to clinical medicine and field expertise (MMV, 2011).

When MMV enters into contractual relationships with its partners, its primary goal is to make certain that the malaria drugs it develops and launches will be accessible to those most in need in malaria-endemic countries. To facilitate this goal, MMV requires special treatment of the intellectual

property (IP) that is brought to and developed under a research program. Specifically, MMV and its partners decide on an appropriate strategy for managing existing and newly generated IP. Such a strategy includes whether IP generated under the program should be the subject of a patent application or should be dedicated to the public domain. (Table 1) This requires MMV and its partners to determine whether the IP has value as an incentive for the partners or others in later-stage commercialization of the resulting products—providing evidence of the saliency of determining the correct transition point given the characteristics and structure of the associated knowledge. The decision is a matter of deposit then into the health commons or the decision to appropriate technology and move to the periphery of the health commons. If IP is generated during a given research program, it is not essential that MMV will take an ownership position in it to accomplish its mission. If, however, ownership of IP does not vest in MMV, MMV will insist on appropriate license rights to any compound(s) being developed under its portfolio (MMV and Intellectual Property Rights, 2011). Particularly in the event that partners cannot follow through with their original commitment, agreement provisions permit MMV to take ownership or appropriate licenses to both program and background intellectual property rights (IPR) to allow the project to be completed and the resultant drug to be launched in malaria-endemic countries. The provisions address exclusivity, royalties, and transferability rights (MMV and Intellectual Property Rights, 2011).

If MMV does not own the necessary IPR outright, it would insist on being granted an exclusive license to use the program IPR and any necessary background IPR. That license should be worldwide, to ensure maximum flexibility for later-stage activities such as manufacturing and distribution. Any such licenses are preferably royalty-free, at least in malaria-endemic countries, to help keep costs to a minimum and ensure that the drug will be sold at the lowest price possible in these countries (MMV and Intellectual Property Rights, 2011). The exclusive right enables MMV to control the broad dissemination of final products. Moreover, MMV does not conduct any R&D in-house or any manufacturing and, therefore, requires IPR that can be transferred to other partners – especially manufacturing partners as necessary. With respect to final products, MMV will negotiate for delivery to the poor in developing countries to be on a "no profit, no loss" basis (MMV and Intellectual Property Rights, 2011).

The PATH Malaria Vaccine Initiative (MVI)

The PATH Malaria Vaccine Initiative (MVI) also established in 1999 is a global program of the international non-profit organization PATH. MVI seeks to accelerate vaccine development through multiple approaches including partnering and the funding of promising projects. MVI has several partnerships in vaccine projects worldwide (Shotwell, 2007). The Initiative establishes product development partnerships around promising malaria vaccine approaches through the application of PATH's Guiding Principles for Private-Sector Collaboration. In openness with respect to participants or proposed private sector collaborations, PATH considers three issues: Availability, Accessibility and Affordability (PATH's Guiding Principles for Private-Sector Collaboration, 2011). In terms of availability, PATH ensures that the organization as well any associated collaborators can create a product-development program that will be sufficiently rigorous, funded, and prioritized to provide a reasonable opportunity for success. With respect to accessibility, PATH and any collaborators must develop a manufacturing and distribution plan that can lead to sufficient quantities of the product

made available through appropriate channels to meet clearly defined public-sector demand in developing countries. Finally, affordability involves an open discussion and then agreement upon a product pricing approach that can result in widespread adoption in public-sector programs of developing countries over a reasonable time (PATH's Guiding Principles for Private-Sector Collaboration, 2011). The Initiative in parallel has outlined several rules-in-use for partner selection and management including assessment criteria, and the definition of roles, responsibilities and expectations respectively. Any agreement for example must include a clearly defined management, and decision-making structure for the collaboration and a clearly stated process for monitoring, evaluating, and terminating the collaboration (PATH's Guiding Principles for Private-Sector Collaboration, 2011).

As a publicly funded organization, PATH has an obligation to ensure dissemination of the results of its private-sector collaborations. PATH explores a variety of approaches, incentives, and mechanisms to fulfill both public and private sector goals (PATH's Guiding Principles for Private-Sector Collaboration, 2011). The management of intellectual property appears to be defined within the guidelines principally in terms of types of collaborations: technology transfer, product development support, and product introduction. The first two collaboration types are relevant to the discussion of technology and IP management. Transfer of a technology developed or owned by PATH may occur to a private sector collaborator including intellectual property for further development, manufacturing, and distribution. Ultimately then PATH supports collaborators by providing significant resources or expertise (such as funding, management, co-development, and assistance with clinical studies) to a private-sector collaborator. Here, the interactions occur on the periphery of the open access health commons. In this case, IPR are utilized by PATH to ensure that a collaborator seeks to increase the availability, accessibility, and affordability of the technology in developing-country public health programs. PATH recognizes that commercial benefits are necessary in order to ensure a sustainable commitment to the collaboration (PATH's Guiding Principles for Private-Sector Collaboration, 2011). (Table 1)

The Drugs for Neglected Diseases Initiative

The Drugs for Neglected Diseases Initiative (DNDi) is similarly, a not-for-profit product development partnership working to research and develop new treatments for neglected diseases, in particular human African trypanosomiasis, leishmaniasis, Chagas disease, malaria, paediatric HIV, and specific helminth-related infections. Since 2007, DNDi has delivered four products including a two fixed-dose anti-malarials (ASAQ developed with Sanofi and ASMQ) (DNDi, 2011). In the development of ASAQ with DNDi, Sanofi used differential pricing tailored to local conditions alongside discretionary IP enforcement. The company decided to forego its patent rights to the new formulation, while pricing was tailored for different distribution channels (Sanofi-aventis, 2007; Mansell, 2010). For example, in public sector markets, the new formulation is sold as ASAQ Winthrop at a no profit/no loss price, equivalent to less than $0.5 per day for children under five years of age and less than $1 per day for adults. A branded version, Coarsucam, is sold through private pharmacies at a regular price, and the combination product is also available under the Impact Malaria brand at a no profit/no loss price (Sanofi-aventis, 2007; Mansell, 2010).

As a move toward further open collaboration is the recent announcement by Sanofi and DNDi of a three-year research collaboration agreement for the research of new treatments

for nine neglected tropical diseases (NTDs) to treat patients in endemic countries. The open collaboration will involve Sanofi bringing molecules from its libraries into the partnership, while DNDi and Sanofi will collaborate on research activities. Noteworthy is the agreed upon management of intellectual property generated through the collaboration (DNDi, 2011). The rights to results produced by this partnership will be co-owned by Sanofi and DNDi. Further, the partners will facilitate publication of the results (and hence deposit into the open access health commons) to ensure access to the wider community of researchers focusing on NTDs. The public sector will benefit from the drugs developed through this agreement with ease of access for patients in all endemic countries, irrespective of their level of economic development (DNDi, 2011). We see therefore, that the differential management of knowledge generated through the collaboration is a function of its form and structure. Technology generated through the partnership will be managed through the open collaboration partnership with research results deposited and managed through the health commons. (Table 1)

The discussion must however extend to the governance of varied knowledge types such as sequencing information, chemical compounds, and other materials. The increased use and participation in the health commons to manage these knowledge types is likely a result of several factors namely: changing paradigms with an increased focus on the underlying and upstream biological processes of a disease; an increase in the knowledge of such biological processes with the completion of the Human Genome Project; and the increased complexities associated with technology development that require broad access to upstream knowledge from multiple sources and providers.

Initiative	Participation in the Health Commons	Participation in Open Collaboration
MMV	Possible IP donation to the Health Commons.	Technology based partnership; IP management and IP transfer as necessary.
MVI		Technology based partnership; IP transfer as necessary.
DNDi	Research results deposited into the Health Commons.	Technology based partnership; Co-ownership of resulting IP.

Table 1: PPP Participation in the Commons and on the Periphery of the Commons

The attention surrounding malaria given its fatal impact in neglected markets should reveal the usage of unexpected mechanisms promoting openness—moving beyond the sole consideration of IP ownership and exercise, to the openness of resources across the product value chain.

References:

1. Mansell, P. Why patient access means market access, December 8 2010.
2. Merz, F.J., 2005. Intellectual Property and Product Development Public/Private Partnerships Final Report. World Health Organization, Commission on Intellectual Property Rights, Innovation and Public Health.
3. MMV and Intellectual Property Rights, http://www.mmv.org/sites/default/files/uploads/docs/policy_documents/

MMV_and_Intellectual_Property_Rights.pdf, accessed 9/2011.
4. PATH's Guiding Principles for Private-Sector Collaboration, http://www.path.org/files/ER_gp_collab.pdf, accessed 9/2011.
5. Sanofi and DNDi - Drugs for Neglected Diseases initiative - Sign an Innovative Agreement to Generate New Drugs for Neglected Tropical Diseases, May 30 2011.
6. Shotwell S.L., 2007. Patent Consolidation and Equitable Access: PATH's Malaria Vaccines, Chapter 17.21 in IP Handbook of Best Practices, Concept Foundation.
7. Taubman, A., 2004. Public-Private Management of Intellectual Property for Public Health Outcomes in the Developing World: The Lessons of Access Conditions in Research and Development Agreements, Initiative on Public-Private Partnerships for Health Geneva.
8. Taubman, A., 2010. A Typology of Intellectual Property Management for Public Health Innovation and Access: Design Considerations for Policymakers, The Open AIDS Journal, 4, 4-24.
9. www.dndi.org, accessed 9/2011.
10. www.iavi.org, accessed 9/2011.
11. www.malariavaccine.org, accessed 9/2011.
12. www.mmv.org, accessed 9/2011.