

Robert Reinhard
425 Market Street, 32nd floor
San Francisco, CA 94105
September 24, 2007

Secretariat for
Public Health, Innovation and Intellectual Property (PHIIP),
World Health Organization (WHO)
20 avenue Appia
CH-1211 Geneva 27
Switzerland
E-mail: PublicHearings@who.int

RE: Draft global strategy and plan of action on public health, innovation and intellectual property - A/PHI/IGWG/2/2 (Draft Global Strategy)¹

To the WHO Secretariat, PHIIP:

Brief Summary:

Thank you for the opportunity to comment on the Draft Global Strategy, A/PHI/IGWG/2/2. I am a member of civil society groups and community advisory boards working with clinical investigators to prevent or treat HIV/AIDS.

These comments explain why additional means to facilitate research and development for vaccines to prevent or treat HIV infection (the complex large molecule biologic products made from living materials) must be separate from the means pertaining to therapeutic, small molecule HIV/AIDS drugs. The important work in WHO's Draft Global Strategy and in the Commission on Intellectual Property Rights, Innovation and Public Health Report in 2006 takes the circumstances of therapeutic drugs as their exemplary focus in order to evaluate effects of intellectual property on innovation and access to care.² That work resulted in several useful ideas to negotiate interlocking issues for innovation, production, licensing, low cost global access, and delivery of products in a somewhat mature market. In that market, several chemical compound therapies (and some preventives) have already been proven safe and effective since HIV was identified over 25 years ago. They can be copied generically with relative ease, skill and know-how, are subject to a variety of payment subsidies or policies, can move across borders in multiple ways and rely on relatively few patents or other property rights. Hopefully consensus on the WHO ideas will be forthcoming.

But this focus can be inapposite to the unique differences affecting the innovation needs for HIV/AIDS vaccines. These biologics require the appreciation of many more rights - not only numerous patents or patent thickets but also specialized know-how, private data, diagnostics, ownership of samples and other factors. The world is years away from the prospect of approving even the first safe and efficacious HIV vaccine, prime-boost regimen or adjuvanted products. It

¹ http://www.who.int/gb/phi/pdf/igwg2/PHI_IGWG2_2-en.pdf

² <http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf>

is unlikely one vaccine could be copied as a biosimilar or follow on biologic and shown to retain its safety, purity and potency in a quality manufacturing environment, let alone the variety of vaccines and combinations that may be needed. For the reasons articulated here, please consider establishing a wholly separate working group and set of policies to promote vital research and development of preventive and therapeutic vaccines based on their unique characteristics.

Analysis:

A list of considerations may show why HIV vaccines and chemical compound drugs are different species and need different responses:

1. Biologics and drugs are fundamentally different; follow on proteins cannot be fully characterized for vaccines. Drug products consist of small molecules made from known compounds in a well understood method. Biologics are made from living cells or cell lines. More so than with drugs, impurities or tiny differences in structure can result in complete differences in safety, purity and potency especially in the case of HIV which is known to evade highly conformed surface regions. A vaccine will be a unique medical product.
2. Innovation, public health and property rights evaluations for HIV/AIDS drug therapies take place in the context of a relatively mature global program for multiple products. The U.S. Food and Drug Administration (FDA) recently announced approval for its 51st antiretroviral HIV drug, many of which are also prequalified by WHO for use as essential drugs.³ WHO's innovation efforts have been directed towards balancing the need to invent and pay research costs for newer chemical drug therapies while at the same time promoting safe, fair and beneficial global access to existing drugs. Challenges driven by compulsory licensing, generics production, parallel imports and other policies affect those efforts significantly.
3. But those challenges are unlikely to affect HIV vaccine research, production or eventual access programs. As EMEA has already concluded, "it seems unlikely that ...[vaccines] may be thoroughly characterized," to a degree sufficient to permit approval of any biosimilar product that could be produced by others.⁴ There are no HIV vaccines currently, and the prospect for discovering the first safe and efficacious product is still out of reach. The scientific discovery challenge is certainly the most significant, perhaps the overriding, challenge to consider. As a consequence, provisions of international agreements such as TRIPS or related discussions describing exceptions to protection of intellectual property rights that have set the terms for evaluation of research and access to drugs, may play only a small role in discussions related to vaccines.
4. The set of intellectual property rights affecting research and development for vaccines is comparatively much more complex than it is for drugs. Whereas patents for drugs may be limited to one or two patents for chemical compounds and manufacturing, necessary patents for complex vaccines are subject to multiple thickets of overlapping rights. Those

³ <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01681.html> and <http://www.who.int/prequal/>

⁴ GUIDELINE ON SIMILAR BIOLOGICAL MEDICINAL PRODUCTS <http://www.emea.europa.eu/pdfs/human/biosimilar/043704en.pdf> ; a regulatory system to advance approvals of biosimilars in the United States has also been delayed http://biz.yahoo.com/ap/070920/generic_biotech_congress.html?v=1

thickets are made even more dense when research must consider combinations of two or more vaccine products in a potential prime boost arrangement, to test the use of an adjuvant with a specific strategy or to apply valuable research tools.⁵ Are clinical trials involving combinations designed to be based on best immunological considerations for this field or are sponsors proposing combinations based on their own access to convenient rights? The necessary and complex intellectual property rights are not limited to patents. Detailed manufacturing know how to produce products in a quality system are closely guarded secrets that resist transfer to others. Data, access to sufficient biological samples, use of comprehensive genetic information make the totality of rights affecting vaccine research different in kind or degree from that pertaining to drugs.

5. Even as to patents, recent legal considerations in important jurisdictions may chill the willingness of assignees to share or grant permission for others to practice inventions related to vaccines or to make data or materials available. Stricter views about the obviousness of a discovery, regulatory limits on the allowable number of claims when applying for a patent or concerns over the rights to products based on associations could make assignees hold their assets closely or in private in situations where team or shared efforts are preferable. Biological materials, cell line technology and samples necessary to conduct early research may be closely guarded.⁶ Even if freedom to operate exceptions for patents are allowed during clinical research phases, the protection of other rights effectively limits that freedom in the short and long term.
6. WHO's earlier proposals are useful to define research and development stimuli for vaccines but may not be sufficient. Clearly, additional research funds, public-private partnerships, infrastructure development, data libraries and support are welcome. It is unclear to what extent all stakeholders will agree to pursue each of these voluntary efforts or to what extent nimble but undercapitalized innovators will see incentives to embrace these opportunities. Proposals for patent pooling may run into practical obstacles when HIV vaccines are considered at a time when more preclinical research and vaccine design is so important. Pools may not be deft at valuing for participants the large number of rights required when early stage research is at issue or of defining future rewards that emerge from inventions created by a consortium.
7. For all of these reasons, please consider convening a separate workgroup on public health, innovation and intellectual property for HIV vaccines. The workgroup would identify best means to facilitate early stage R&D and clinical research for vaccines considering all intellectual property necessary for this enterprise. The workgroup may probably de-emphasize, relatively, the potential for pricing, "biosimilarity," purchase commitments and other access issues to affect innovation since the pressures and factors affecting vaccines are so different from those pertaining to drugs. In addition to funding stimuli, WHO could promote new means to encourage sharing – such as limited and targeted covenants not to sue that increase freedom to operate – while preserving ownership of property rights that assignees hold closely. The workgroup could craft

⁵ One analysis of the patent thickets applicable to HIV vaccines was presented at AIDS Vaccine Advocacy Coalition. Intellectual Property at the Crossroads (2005) http://www.avac.org/pdf/reports/2005_Chapter4.pdf WHO received preliminary comments from AVAC in the first (November, 2006) public hearing for the Intergovernmental Working Group.

⁶ A Mandavill (2007) Scientists, NIH in conflict over precious HIV samples. *Nature Medicine* **13**, 515 – 515 doi: 10.1038/nm0507-515

proposals to describe incentives and security so that owners of property would be willing to share materials, data and other rights.

Thank you for considering these remarks. I can be reached at tel: 01-1-415-268-7469 or email at rreinhard@mofa.com I look forward to learning more about the WHO's strategic initiatives or working with others to advance these suggestions.

Sincerely,

A handwritten signature in black ink that reads "Robert Reinhard". The signature is written in a cursive, slightly slanted style.

Robert Reinhard
Member, Community Advisory Group, San Francisco Department of Public Health Research
Section