Editorial

How can the public health community help to invigorate a 'health first' perspective in global drug development debates?

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An Indian Supreme Court decision against a pharmaceutical giant, Novartis, is good news for public health. In this issue, 't Hoen explains the importance of the Indian Court ruling.[1] The Indian Court rejected a patent application for a new form of a known compound; their decision will extend benefits of an immensely beneficial drug to many more people.[2] Patents, intended to encourage inventions, provide market exclusivity for a certain period of time and thus higher profits for the inventor. However, this also results in limited availability of drugs, diagnostics, and vaccines. With monopolies created by patent protection, newly invented products often remain too expensive for people living in low- or middle-resource countries, (in excess of 80 per cent of the world's population). More diversity in financing of pharmaceutical R&D could break through this cycle and provide a system where innovation is paid for and access to innovations secured.

Every nation, the United Nations, and even the World Trade Organization, has declared itself in favor of actions that would improve population health. Governments of countries that are home to the largest pharmaceutical companies assert that they are committed to improving health globally. However, in the world race for affluence and power, when faced with choices between the economic competitiveness of their industries, and health of neglected populations, the United States (US) and the European Union (EU) continue to side with industry.

We call your attention to several developments that might, with the support of the public health community, reshape research, development, regulatory approval, production, and distribution of biologics, diagnostics, and drugs. We conclude with ways all of us in public health can help.

Background

Our colleagues Moon, Bermudez, and 't Hoen explain how the 'system' has failed to invent, produce, or sell at affordable prices. They distinguish between *neglected diseases*, a relatively narrow concept that historically drew attention to HIV, tuberculosis, malaria, and less common diseases, such as leishmaniasis, endemic in tropical countries, and *neglected populations*, people who need treatment they cannot afford, often for common diseases. Neglected populations exist in most countries.[3]

Even in wealthy countries, clinicians and clinical researchers have protested the pricing of drugs such as Gleevec – the drug at issue in the Indian Supreme Court decision. In the words of oncologist Hagpop Kantarjian at MD Anderson Cancer Center:

> Before the year 2000, when we saw patients with chronic myeloid leukemia, we told them that they had a very bad disease, that their course was fatal, their prognosis was poor with a median survival of maybe three to six years, frontline therapy was allogeneic transplant … and there was no second-line treatment … Today when I see a patient with CML, I tell them that the disease is an indolent leukemia with an excellent prognosis, that they will usually live their functional life span provided they take an oral medicine, Gleevec, for the rest of their lives. (pp. 438–439)[4]

In developing countries, some cancer experts continue to urge potentially dangerous bone marrow transplants instead of Gleevec because a one-time procedure costs less than safe but continuous treatment with the drug.[5]

The pharmaceutical industry's ledgers continue to reveal the greatest return on investment of any industrial sector. 'Big pharma' in the US, Europe, and Japan resists changing 'the system'. It rejects transparency. It resists global health priorities.

Is this changing? The head of Glaxo-SmithKline has recently revealed that the average cost for developing a new drug is not 'one billion dollars' that companies used to assert whenever asked. He suggested that prices of future drugs are likely to be lower. Meanwhile, return on R&D investment has risen recently because fewer drugs have failed late in the process.[6]

Public sector institutions

Growth in the role of public sector research in vaccine and drug development is important. Public sector research institutions – universities, research hospitals, non-profit research institutes, and Federal laboratories in the US – have, since the start of the biotechnology revolution – contributed increasingly to 'downstream' or applied research, where products are discovered and patented. Not only has their contribution grown, they are more likely now than the private pharmaceutical companies to contribute new tools for improving health. A 2011 study of the contributions of public sector research institutions to products approved by the US Food and Drug Administration (FDA) over 40 years (1970–2009) showed that 143 of 1541 drugs, vaccines, or new indications for drugs emerged from public sector research institutions. Importantly, almost half of 'new drug' applications (46.2 per cent) that FDA treated as 'priority reviews' – meaning they were likely to make important contributions to health – came from these public institutions, contributing 'disproportionately important clinical effects'.[7]

Targeting specific diseases

Initiatives targeting specific diseases, usually 'neglected diseases' have attracted new funding, much of it philanthropic. Despite success, even participants criticize the disease-by-disease approach as piecemeal; yet, they are also the building blocks of a more comprehensive approach. The initiatives described by our colleagues in PLoS Medicine[1] target 'neglected diseases' or explore ways to spur development of needed products and to lower prices:

- *Expanded use of patented drugs*, especially of generic antiretroviral drugs for HIV. UNITAID supported a Medicines Patent Pool to facilitate competition among manufacturers of generic HIV medicines and to develop improved products for lower resource settings.[8]
- *Disease-specific initiatives*: Increases in financing for drug and vaccine development; prizes for successful product development; use of patent pools; and exploration of a new approach to sharing knowledge based on 'open source', low-cost software that has enabled mass online collaboration to expedite high-priority products.[9]

- '*Product development partnerships*': Public and foundation funds have focused on new drugs and drug combinations. The Drugs for Neglected Diseases Initiative (DNDi) has attracted many participants and produced combination treatments: for malaria, sleeping sickness, visceral leishmaniasis, and pediatric Chagas disease. The Medicines for Malaria Venture has spawned new collaborations, resulting in several new products.

A More Comprehensive 'Framework' Approach

The World Health Organization (WHO) in 2003 embarked on a process that in 2008 led to the adoption of the WHO *Global Strategy and Plan of Action on Public Health, Innovation, and Intellectual Property.* The Strategy described a 'system failure' and outlined actions to address needs of developing countries, both for access to medicines and innovation to tackle neglected diseases and the needs of neglected populations. The Consultative Expert Working Group (CEWG), created as part of the Strategy and tasked with identifying proposals to strengthen global financing and coordination in health research and development, recommended that negotiations commence on a new global framework for R&D – analogous to the WHO Framework Convention on Tobacco Control (under Section 19 of the WHO Constitution).

Advocates of the framework approach want a binding treaty on 'medical R&D'. (We hope for a term indicating a broader reach than medicine, 'public health R&D'). The treaty would create norms and incentives to speed development of high-priority public health tools, share knowledge widely, and require contributions that factor in ability of countries to share the costs of developing new products. A working group spelled out how to meet those objectives.[10,11]

In November 2012, WHO convened its member countries to consider the recommendations of the CEWG and begin negotiations on a treaty. The treaty project immediately provoked predictable pushback from the pharmaceutical industry. Key proposals include:

- Long-term national commitments to finance product development. Costs would be shared and a treaty could 'delink' development cost from the price of the product – thus offering relief from the undesirable effects of using monopoly pricing as a way to finance

innovation. It could finance product development by pooling national contributions to a new global system and allow many manufacturers to produce generics. UNITAID set a precedent by organizing 29 countries to contribute US$2.1 billion over 5 years, primarily through a tax on air travel, to make drugs and diagnostics for malaria, HIV, and tuberculosis more affordable or better adapted to low-resource settings.[12]

- Incorporating global norms about research priorities and transparency in investment decisions. To speed development of high-priority health products, parties would negotiate ways to share knowledge now impeded by intellectual property laws. Financial rewards might be structured according to a product's health benefit.
- Open source R&D initiatives built at publicly funded research labs.
- Pre-competitive platforms established among pharmaceutical firms to facilitate sharing of knowledge.
- Incentives to discourage 'me too' drugs – duplicative investments that reward mostly investors.
- Regional regulatory cooperation to speed product approval and enhance transparency in clinical trial results.

Colombia, Bolivia, and Thailand favor a binding treaty. Not surprisingly, industry cajoled the US and EU to demand delay, putting off consideration of a new treaty until 2016. Médecins Sans Frontières (MSF) shot back: 'Instead of pushing forward with a real plan to address the continued lack of suitable and affordable vaccines, drugs and diagnostics that our teams in the field face, all countries have really pledged to do is to continue observing the situation'.[13]

As of November 2012, WHO member states had agreed only to endorse a report. It contained a strategic work plan to shape proposals for coordination, financing, and monitoring of R&D expenditures by something called a Global Health R&D Observatory. Exploration of existing funding and coordinating mechanisms would be permitted, *but not an overarching framework*. Pressed by the US and EU, the WHO member states delayed further deliberations of a treaty proposal until 2016 and the final adoption of the next steps until May 2013.[12]

However, in May 2013, the US surprised observers by proposing that the WHO convene discussions on the core of the treaty proposal, namely, the principle of delinking of paying for R&D cost from the

product price.[14] Member states approved a decision with four areas for action:

- Address R&D gaps
- Use collaborative and open source approaches
- Promote delinkage of the cost of R&D from product price, and
- Pursue ways to raise and pool funds to sustain innovation of needed products[15,16]

There is always a danger that global policymakers may limit the scope of treaty deliberations to 'neglected diseases' and lose sight of the needs of 'neglected populations'. However, three developments encourage us:

- Health leaders, if not leaders from trade and finance, now recognize the *system failure* in health R&D;
- Advocates are thinking big, and realizing that money and political clout will be needed to steer the pharmaceutical and vaccine industries away from their profits that come at the expense of public health; and
- Researchers who manage experiments and initiatives are starting to call for global governance of medical R&D to reduce the influence of and dependence on philanthropic organizations and other private contributors.

What the Public Health Community Can Do

Many countries are inconsistent – one might say *schizophrenic* – apparent when one compares global health goals with their trade policies. Even as countries endorse health targets and projects (evidenced by commitments to the Millenium Development Goals, contributions to the Global Fund to Fight AIDS, tuberculosis, malaria, and the like) they end up putting the interests of their industries – in this case the pharmaceutical industry – ahead of neglected populations.

The principal advocacy role for public health is to push our governments to live up to their pledges to improve health, particularly for neglected populations. We can learn from and collaborate with eloquent advocates such as MSF, DNDi, Knowledge Ecology International (KEI), Universities Allied for Essential Medicines (UAEM), and UNITAID. These sophisticated advocates do not let anything slip by without describing who is doing what to whom. In addition, these

advocates have an important role in formulating proposals for change as in the consultation processes of the CEWG report now under discussion at the WHO.

Public health researchers, health department personnel, and clinicians can explain clearly the needs for health products that already benefit some – but remain unaffordable for others – if not most of those for whom they are well suited. The public health community can also contribute importantly to specifications of products yet to be developed. Both government health officials and non-government advocates can use evidence from the world of public health to challenge trade and intellectual property policies where governments have been too quick to support industry and forget the needs of people. As the recent battles over cancer drugs in the US illustrate, the unavailability and pricing of drugs is provoking a broad swath of public health into activism.[4] We need to claim priority for health over trade.

We can support our universities. In April 2013, 54 leading research universities in the US and Canada joined to create UAEM and released a 'Report Card' grading themselves in three domains:

- Are universities investing in innovative medical research that addresses the neglected health needs of low-income communities worldwide?
- When universities license their medical breakthroughs for commercial development, are they doing so in socially responsible ways that ensure that those treatments reach developing world patients at affordable prices? (alternative licensing models)
- Are universities educating the next generation of global health leaders about the crucial impact that academic institutions can have on global health through their research and licensing activities?[17]

UAEM's exercise depends on self-reporting by universities that agree to be compared with others. A fourth-year medical student leader at Boston University who helped to develop the Report Card tells us that the UAEM analysis revealed that alternative licensing models had no negative impact on schools' ability to fund and conduct research; some universities increased their licensing activity while increasing the global availability of health technologies that they share.[18]

Other public sector research institutions could undertake similar accounting. The US National Institutes of Health and other public

institutions around the world could aid transparency and collaboration among public institutions.

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We invited Ellen 't Hoen to join our Editorial Board because of her global leadership on access and development issues. We are committed to pursuing these issues in the journal and hope we can convince more within the public health community to join in this struggle. The lives of the populations whose health you work to protect and the patients whom you treat depend on it.

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