

# Expanding global research and development for neglected diseases

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In May 2003, the 56th World Health Assembly mandated the creation of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH), in large part because the traditional mechanisms of research and development (R&D) for new medicines are not performing well for diseases that affect the majority of the world's poor.<sup>1</sup> Consequently, inequities of access to medical innovations continue to grow. The CIPIH report takes us much further ahead in understanding the complex relationship of intellectual property to advances in medicine, but solutions will require difficult compromises. Genuine commitments will have to be made by senior health leaders and global institutions for system-wide changes and more equitable R&D investments, if the widening gap between technical discoveries and access to their life-saving benefits is to be halted.

## A polarized debate

The current debate on global reform of R&D structures is polarized mainly because the stakes are high for all concerned: industry, government and consumers. On one hand, the pharmaceutical industry is accustomed to unrealistic profit margins in the production of public goods (with significant tax dollars and credits), yet it does not want to be told what to develop or to be completely transparent about its costs. (See a comparative chart of profit margin trends between the pharmaceutical industry, mining, and Fortune 500 companies<sup>2</sup> and an analysis of R&D costs.<sup>3</sup>) Patents are critical to the current system as they limit competitors' abilities to reap benefits from innovations without paying the costs for unsuccessful developments. Understandably, industry sees any change as a threat to its interests. Patents protect investments, provide incentives for innovation, and stimulate the development of new medicines.<sup>4,5</sup> As profit-making industries, the pharmaceutical and biotechnology companies

are merely meeting their shareholders' expectations.

In contrast, in many developing countries people are dying for lack of appropriate R&D investments. Their needs are overlooked because their markets are simply not profitable compared with those in developed countries. Even paying lower "differential" prices for patented products still leaves many poor people without access to medicines. To governments and civil society groups with commitments to human rights, these challenges represent a violation and require redress.

Until a credible, neutral institution can arbitrate the conflicting interests between industry and consumers on medical R&D, the debate will remain entrenched and the global marketplace will continue to produce very expensive drugs for very limited, but profitable markets in the industrialized countries. The CIPIH has laid an important foundation to shape future discussions on R&D for neglected diseases; now WHO needs to provide on-going intellectual and policy leadership to interpret the CIPIH findings within a rights-based framework of equity and develop appropriate solutions to realize greater expansion of R&D for neglected diseases.

For example, with respect to financing, the cost quotations for bringing a product to market vary widely. One study claims that costs are as high as US\$ 402–793 million,<sup>6</sup> while another estimates US\$ 115–240 million.<sup>7</sup> How can global institutions formulate realistic rights-based policies accurately if there is no consensus on the real costs? WHO would be well suited to convene an independent budgetary working group to establish an accounting standard that assesses the costs of R&D investments. While it is perfectly understandable that industry needs to protect investment information, an independent commission could assess real costs and legitimate categories while respecting confidentiality.

## Change the locus of control

Presently, medical R&D capacity — and investment capital — is situated mostly in developed countries, and not surprisingly the focus of its investments is towards their own markets. Until this locus of power and resources shifts demonstrably towards their markets, most developing countries will remain passive recipients of industrialized countries' R&D agendas or, worse, produce R&D for the more profitable markets of the developed world.<sup>8</sup>

What kinds of regional collaboration could maximize economies of scale and lay the groundwork to correct this imbalance? In some instances, progress is already being made to develop legal and policy frameworks for market systems that could help supply current pharmaceutical needs (e.g. using trade-related aspects of intellectual property rights (TRIPS) flexibilities) and begin to build capacity for future R&D on neglected diseases. For example, Brazil is working with eight other countries to share its expertise and find ways of combining resources to produce more affordable antiretroviral treatment for HIV/AIDS.<sup>9</sup> The experience of such collaborations will be valuable in future scale-up efforts.

Regional enterprises would require significant new commitments from both developed and developing countries in terms of public and private resources. With genuine direct commitments to capacity development — and not the spurious assumption that stronger intellectual property regimes equal development — the health care concerns of developing countries will become independent upon development aid from bilateral, multilateral and philanthropic institutions. This dependency places peoples' health in jeopardy, especially when supply chains fail or political expediency affects prices or funding streams. In what ways could the Southern African Development Community (SADC), the

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Association of Southeast Asian Nations (ASEAN), the East African Economic Community (EAEC), Mercosur and others advance innovative regional regulatory policies and practices to capitalize on national economies of scale, protect the consumer, and lay the foundation for investments in R&D on neglected diseases?

Significant public and philanthropic investment in such regional market development for pharmaceuticals and other health-related products could provide opportunities for integrating traditional healing systems in new ways that assess their safety and efficacy while simultaneously developing a home-grown (regional) industry. The CIPIH report deserves congratulations for including traditional medicines in its study of new and evolving frameworks for stimulating R&D. In Africa, some figures claim that as many as 80% of patients choose traditional health care.<sup>10</sup> Long neglected and marginalized by allopathic medical systems, traditional medicine offers a wealth of potential remedies — beyond the mere exploitation of natural assets — that need empirical scrutiny and development in order to ensure their safety and efficacy. Unfortunately, however, traditional medicine submissions to the CIPIH were few and generally not instructive on how they could recommend systematic changes to advance R&D for their products and services and apply this knowledge within a sustainable development framework. Much more serious scholarship needs to be supported and systems developed for integrating traditional medicine into allopathic frameworks or, at the very least, the development of alternative evaluative frameworks for assessing its safety and efficacy in dealing with neglected diseases.

### Reward innovation instead of subsidizing risk

The CIPIH reviewed many studies about how to address the fact that financial incentives must reasonably outweigh the risk of investment, but only Love & Hubbard's Medical Research and Development Treaty (MRDT) considered the global *architecture* of pharmaceutical R&D in a comprehensive manner.<sup>11</sup> In a patent-based R&D system, consumers (mainly in wealthy countries) subsidize risk by paying “whatever the market can bear” for successful drugs.<sup>12</sup> Profits earned from these products are then,

theoretically, fed back into R&D, but it is at this point that definitions of R&D type and quality are important, and this is where R&D for neglected diseases gets short shrift. For example, from 1975 to 1999, of the 1393 new chemical entities (NCEs) approved, only 1% were for infectious diseases that account for approximately 12% of the global burden of disease (the vast majority in developing countries).<sup>13</sup> Approximately 70% of NCEs were “me too” drugs — improvements upon chemical entities already on the market (and overwhelmingly developed for industrialized country consumers).<sup>13</sup> A patent-based system will necessarily neglect R&D on many diseases when there is no profit potential relative to the cost of product development, or if there are higher returns with less risk by developing “me too” drugs. When profit margins determine investment strategies, neglected diseases receive, relatively, only charitable mention.

The MRDT model, promoted by 162 scientists and professional organizations, proposes several novel features to stimulate R&D on neglected diseases. First, it changes the current market paradigm by separating innovation from production and distribution, creating essentially two distinct markets. Second, instead of leaving R&D financing beholden to profits from patented successes, the MRDT rewards innovation directly with a substantial prize fund — continuously replenished by pre-determined GDP percentage point contributions and administered by a lean secretariat. The size of the prize is negotiable; however, it is proportionate to objectified clinical evidence of the innovation's ability to improve disability-adjusted life years (DALYs) or other evaluative criteria. Finally, in order to receive the prize, successful innovators would be required to pool their patents for generic production, thus removing patent barriers to access. Companies would be “pulled” into developing drugs for infectious diseases, as these would receive higher rewards than mere reformulations of existing products. Companies might also reduce costs by spending less on advertising and more on developing innovations in clinical trial testing.

Unlike public–private partnerships or discreet push–pull mechanisms, the MRDT takes into account the global phenomenon known as “free-riding” where lesser developed economies with limited or no capacity to produce pharmaceuticals, diagnostics, or other health

care related products forego the development of those products because the relative benefit of having others produce them outweighs the opportunity cost of their production.<sup>13</sup> Instead of investing scarce or limited resources in medical R&D, developing economies “ride for free” on other countries' productive capacities while investing (or not) their own R&D in other sectors (agriculture, information technology, etc.) where they may have competitive advantages in a global trading system. Under the MRDT, R&D financing becomes a globally shared responsibility where investments in neglected diseases, including in traditional medicines, find friendly market incentives. Like the Kyoto Protocol's market-based system for trading emissions' reduction credits, the MRDT creates a system of tradable credits for R&D financing to address neglected diseases.

### Conclusion

To ensure that everyone attains the highest standard of health possible, public health professionals and leaders must continuously question whether the systems and policies we design disproportionately preference profits at the expense of neglecting basic health care needs, especially for people who do not have the power or resources to create solutions for themselves. While reform of medical R&D systems in the developed world is important for many reasons — especially cost reductions — equal attention must be paid to investment in developing-world R&D.

It would be naïve to conclude that the answer to the world's R&D problems is simply a question of more discreet funding of neglected diseases, as many suggest. If rich governments and philanthropists would commit a few billion more dollars, could we not cure malaria or tuberculosis or visceral leishmaniasis? Perhaps, but each would be a one-off, short-term diversion from longer-term sustainable answers. Humankind will always face evolving health threats, and whether they are new or old we must continuously question whether our global, regional and national institutions meet these health challenges in a cost-effective and equitable manner. While money certainly matters, so too does the efficiency of the global systems we create that expend those resources. ■

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