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Editorial

Global health policy coordination to address neglected tropical diseases

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The GlaxoSmithKline paediatric malarial vaccine candidate RTS,S has sparked interest in innovation for infectious tropical diseases (White 2011). Yet, reliance upon *ad hoc* partnerships and lack of adequate incentives for research and development (R&D) addressing neglected tropic diseases (NTDs) has resulted in limited progress (Mrazek 2003). This creates significant barriers to achieving UN health-related Millennium Development Goals and global health equity (WHO 2010).

With about 1-billion people across 149 sovereignties affected, NTDs are the most common infections of the world's poorest (Hotez & Pecoul 2010; WHO 2010). NTDs flourish where lack of sanitation, substandard housing and rapid urbanisation have created impoverished and unhygienic environments (WHO 2010). Negative social impacts are exacerbated as NTDs result in adverse economic impact, because of disease-based disability, mortality and resulting productivity loss (WHO 2010; Hotez 2011).

Many existing NTD treatments originate from early 20th century discoveries (Trouiller *et al.* 2002; Croft 2005) – even RTS,S was initially developed for the US military 25 years ago (McNeil 2011). Current NTD treatments may require long-term protocols, have inconvenient administration, require refrigeration, lack available vaccines, have low efficacy/poor safety profiles and serious side effects and are susceptible to drug resistance (Mrazek 2003; Croft 2005; Nwaka & Hudson 2006; Anderson 2009; Hotez 2011).

Although NTDs have recently attracted attention, such as the recent partnership of pharmaceutical companies, governments, the Gates Foundation, World Bank, World Health Organization (WHO) and others (London Declaration on Neglected Diseases) and the UK's decision to a fivefold increase for NTD control programmes, work on many NTDs is insufficient (Hotez *et al.* 2007; WHO 2010; Allen & Parker n.d.). NTD innovation especially remains neglected as a private-sector priority, as affected populations are in poor settings which are considered small and uncertain markets, rendering costly drug R&D a risky undertaking (Hotez *et al.* 2007; Anderson 2009). Commercial drug pipelines are therefore mostly devoid of NTD products (Mrazek 2003; Nwaka & Hudson 2006; Hotez *et al.* 2007).

Current funding, initiatives and partnerships may also overemphasise drug development at expense of practical considerations of economic and trade barriers impeding clinical delivery. Hence, challenges of encouraging sustained incentives for innovation and lowering barriers to actual delivery need to be addressed in tandem.

Tax credits

NTD R&D tax credits have been explored in conjunction with other tax credit proposals, including for HIV/AIDS, tuberculosis and malaria (Anderson 2009; Rao 2011; Attaran *et al.* n.d.). Targeted credits provide advantages, such as subsidies for global health R&D to encourage investment and/or financial incentives for new market entrants (Rao 2011), whereas state-based tax codes allow pharmaceutical companies to write-off expenses or earn tax credits providing R&D funding sources (Mrazek 2003).

However, the overall impact of tax credits on NTD innovation is difficult to quantify, as the majority of existing tax credits cover general pharmaceutical R&D, are not specifically NTD-targeted and are often applied for other more profitable disease research (Mrazek 2003). Further, questions have been raised regarding appropriate rates, combined or separate treatment from existing tax credits, design aspects favouring large or profitable firms; and uncertainty of their effectiveness compared with direct

forms of financing (Mrazek 2003; Rao 2011). Thus, we propose global health policy mechanisms of targeted taxation incentives and reducing trade barriers to improve investment and delivery for NTD treatments.

Targeted tax reform

Tax credits provide incentives that can influence private-sector behaviour, particularly if coordinated across jurisdictions. In this setting, more focused promotion of NTD drug development combined with lowering/eliminating other tax incentives could be beneficial. This can be accomplished through targeted tax subsidies/credits for commercial entities and partnerships (e.g. public–private partnerships and product development partnerships) pre-qualified as engaged in NTD innovation.

This process could focus on creating state-based tax credits for NTDs identified as global health priorities by organisations such as WHO in consultation with local stakeholders. Such efforts could be modelled after US Food and Drug Administration's priority-review voucher programme, which provides expedited review of new drug applications for NTD development, and could be expanded to the identification of NTDs meriting preferential tax treatment (Anderson 2009).

Entities such as Product Development Partnerships (PDPs), which commit to NTD innovation, are of scientific merit, undergo rigorous peer-review and provide a feasible business plan to develop NTD-related commodities and services (drugs, vaccines, biologics, diagnostic devices, vector control technology, surveillance systems, NTD clinical trial expenses, logistic expenses and drug discovery software/tools) would be pre-qualified and given access to preferential tax incentives in addition to 'general' pharmaceutical R&D credits.

Tax incentives could be structured to provide increasing milestone benefits as entities move through different stages of drug/technology development. This avoids overinvestment in early stage research and encourages final product development. This process would allow for a holistic approach, directing and promoting biomedical innovation and development of health-related technologies addressing public health needs and social determinants of NTD control and prevention (Spiegel *et al.* 2010).

To offset NTD tax subsidy public spending and as a means to establish sustainable funding instruments, tax benefits could be expressly reduced or eliminated for R&D of low-priority drugs for lifestyle, non-threatening conditions, or for drug classes already available (i.e. 'me-too drugs'). Note that these drugs may still represent profitable business models and, hence, may not require tax incentives for commercialisation.

This progressive pharmaceutical R&D tax credit system could better assist underserved populations through targeted incentives for diseases of immediate need, instead of wholesale tax credits for broad-based pharmaceutical R&D. Policies should be targeted towards emerging markets with potential to engage in NTD innovation. This includes innovative developing countries (IDCs) such as India and Brazil, which enjoy relative low cost production and are major exporters to developing countries (Morel 2005; Gardner *et al.* 2007; Frew *et al.* 2009). However, only a small portion of IDC drug research is devoted to diseases affecting the poor or local needs, hence, necessitating better incentives (Morel 2005).

Promotion efforts should also target small and medium-sized enterprises often amenable to NTD R&D by providing funding support, academic collaboration and strategic partnerships (Croft 2005). For example, the USA Small Business Innovation and Research award programme and similar programmes in other countries provide grants to small businesses engaged in NTD R&D and could be expanded to provide NTD tax incentive pre-qualifications (GFHR 2011). These state-based policy approaches could refocus R&D to NTDs by prioritising tax incentives and delivering investments to vetted partnerships/enterprises.

Global trade and tariff adjustment

Economic barriers preventing access to NTD products should also be addressed. After development of an NTD product, trade policies may impede actual implementation and delivery. Fifty-four per cent of countries levy tariffs on imported medicines, just over half in sub-Saharan Africa apply drug tariffs (ranging from 2% to 15%), and 40 countries apply tariffs on imported vaccines (Stevens & Linfield 2010). Tariffs persist in countries with poor health indicators and limited local manufacturing, despite this representing a regressive tax disproportionately impacting the poor (Olcay & Laing 2005; Stevens & Linfield 2010). Although tariff revenues may support general public expenditures, they may not be earmarked for impacted public health systems.

The World Trade Organization's (WTO) current Doha trade rounds have been characterised as the 'development round,' offering an opportunity for policymakers to improve health equity for resource-poor countries. Hence, ensuring medication and effective interventions by eliminating trade-related barriers to NTD-associated products should be a Doha Agenda priority with equal importance to climate change and food/energy security. This would improve the health of millions, and also boost development efforts by lowering NTD-related social and economic burdens (WHO 2010).

Tariff reduction could be accomplished by establishing global harmonised system tariff codes for all NTD-related products and services mutually recognised across WTO members. Identified tariffs could then be lowered/eliminated for multiple classes of NTD-priority medicines, active pharmaceutical ingredients/excipients, NTD-related commodities and services and technical information/transfer accompanying NTD R&D. Reform should also include elimination of non-tariff trade barriers, such as export controls and national regulatory requirements already identified as impediments to tropical disease treatment development (Trouiller *et al.* 2001; Nwaka *et al.* 2009). This can build on efforts to reduce or eliminate tariffs/taxes on antimalarials and insecticide-treated bed nets for malaria interventions (Alilio *et al.* 2007). Special and differential treatment (S&D), providing special rights and favourable terms to developing countries in WTO negotiations, should be ensured to increase NTD treatment trade and access (WTO n.d.). S&D principles should also be expanded to other trade agreements, including negotiations on the Trans Pacific Partnership Agreement.

Once tariff-lowering and harmonisation policies are implemented by developing countries, developed countries with technology and manufacturing capacity should commit to improving availability and funding for NTD innovations. This should include S&D treatment to enable NTD technology transfer and capacity building to developing countries. Private-sector partnership with local stakeholders promoting local manufacturing, equitable voluntary licensing and potential use of differential pricing possibly as preconditions for pre-qualification for tax incentives programmes/grants should also be explored (Mrazek 2003; Morel 2005; Gardner *et al.* 2007). Local manufacturing can employ business models of high-volume, low-margin drugs unattractive to developed country drug manufacturers, which can increase access and grow the local economy (Morel 2005).

Failure to innovate NTD treatments is a global health crisis that remains, despite recent progress. Through targeted tax incentives and lowering of global trade barriers, effective incentives may be implemented to address diseases of the world's poorest and most vulnerable patients.

References

Alilio M, Mwenesi H, Barat LM *et al.* (2007) Broken promise? Taxes and tariffs on insecticide treated mosquito nets. *The American Journal of Tropical Medicine and Hygiene* **77**(6 Suppl.), 227–231.

Allen T & Parker M (2012) Will increased funding for neglected tropical diseases really make poverty history? *The Lancet* **379**, 1097–1098.

Anderson GF (2009) Spurring new research for neglected diseases. *Health Affairs* **28**, 1750–1759.

Attaran A, Kremer M, Sachs J, Sievers S (n.d.) A tax credit for sales of HIV, tuberculosis, and malaria vaccines. http://www.economics.harvard.edu/faculty/kremer/files/Tax_Credit.pdf (accessed 20 October 2011).

Croft SL (2005) Public-private partnership: from there to here. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **99**, 9–14.

Frew SE, Liu VY & Singer PA (2009) A business plan to help the "global south" in its fight against neglected diseases. *Health Affairs* **28**, 1760–1773.

Gardner CA, Acharya T & Yach D (2007) Technological and social innovation: a unifying new paradigm for global health. *Health Affairs* **26**, 1052–1061.

GFHR (2011) New investment strategy: innovative developing country research awards. WHO. http://www.who.int/phi/news/phi_5_new_investmt_strat_SBIR_model_en.pdf (accessed 5 March 2012).

Hotez P (2011) A handful of 'Antipoverty' vaccines exist for neglected diseases, but the world's poorest billion people need more. *Health Affairs* **30**, 1080–1087.

Hotez PJ & Pecoul B (2010) "Manifesto" for advancing the control and elimination of neglected tropical diseases. *PLoS Neglected Tropical Diseases* **4**, e718.

Hotez PJ, Molyneux DH, Fenwick A *et al.* (2007) Control of neglected tropical diseases. *The New England Journal of Medicine* **357**, 1018–1027.

McNeil DG (2011) Glaxo's RTS,S Malaria Vaccine Shows Promise, Scientists Say – NYTimes.com. http://www.nytimes.com/2011/10/19/health/19malaria.html (Accessed 20 October 2011).

Morel CM (2005) Health innovation networks to help developing countries address neglected diseases. *Science (New York, N.Y.)* **309**, 401–404.

Mrazek M (2003) Stimulating pharmaceutical research and development for neglected diseases 10.1016/S0168-8510(02)00138-0 : Health Policy | ScienceDirect.com. *Health Policy* **64**, 75–88. http://www.sciencedirect.com/science/article/pii/S0168851002001380.

Nwaka S & Hudson A (2006) Innovative lead discovery strategies for tropical diseases. *Nature Reviews Drug Discovery* **5**, 941–955.

Nwaka S, Ramirez B, Brun R, Maes L, Douglas F & Ridley R (2009) Advancing drug innovation for neglected diseases—criteria for lead progression. *PLoS Neglected Tropical Diseases* **3**, e440.

Olcay M & Laing R (2005) Pharmaceutical tariffs: what is their effect on prices, protection of local industry and revenue generation? WHO. http://www.who.int/intellectualproperty/studies/TariffsOnEssentialMedicines.pdf (accessed 16 December 2011).

Rao A (2011) *Can a R&D Tax Credit Expand Investment in Product Development for Global Health?* Results for Development Institute, Washington, DC.

Spiegel JM, Dharamsi S, Wasan KM *et al.* (2010) Which new approaches to tackling neglected tropical diseases show promise? *PLoS Medicine* **7**, e1000255.

Stevens P & Linfield H (2010) Death and taxes: government mark-ups on the price of drugs. International Policy Network. http://www.policynetwork.net/sites/default/files/Death&Taxesweb.pdf (accessed 16 December 2011).

Trouiller P, Torreele E, Olliaro P *et al.* (2001) Drugs for neglected diseases: a failure of the market and a public health failure? *Tropical Medicine and International Health* **6**, 945–951.

Trouiller P, Olliaro P, Torreele E, Orbinski J, Laing R & Ford N (2002) Drug development for neglected diseases: a deficient market and a public-health policy failure. *The Lancet* **359**, 2188–2194.

White NJ (2011) A vaccine for malaria. *The New England Journal of Medicine* **365**, 1927–1927.

WHO (2010) Working to overcome the global impact of neglected tropical diseases: first WHO report on neglected tropical diseases. http://whqlibdoc.who.int/publications/2010/9789241564090_eng.pdf (accessed 19 October 2011).

World Trade Organization (WTO) (n.d.) Work on the special and differential provisions. http://www.wto.org/english/tratop_e/devel_e/dev_special_differential_provisions_e.htm (accessed 16 December 2011).

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