To harness the potential of the private sector in a future emergency scenario, the relevant coordinating mechanisms must be put in place before, not during, the crisis. Those players who had an established point of communication with public entities, such as through preexisting UN Clusters or Global Ebola Response Coalition weekly calls, felt they were better equipped to engage effectively and support other responders [51]. Efforts to widen this network and create a well-defined coordinating structure could pay dividends in future emergencies.

Surveillance and information management offer an additional challenge. Private firms' caution regarding employee health hindered efforts to partner for the creation of an efficient real-time information system [59]. In this case, humanitarian NGOs such as Doctors Without Borders may provide a better option for partners in generating on-the-ground intelligence. Of course, effective use of this intelligence requires collaboration with other local partners and rapid action on the information generated, neither of which happened when Doctors Without Borders sounded the alarm in the early days of the Ebola outbreak [49].

4.3 Recovery efforts

Finally, strong disaster management partnerships should focus on "resilience": not just preparedness and response, but recovery in the aftermath [60]. Even with the Ebola outbreak in check, the damage wreaked on local health systems will have an ongoing negative impact on services targeted at other endemic health issues, such as malaria [49]. This is ripe territory for a variety of both vertical and HSS-focused partnerships, who must work quickly to rebuild these vital capacities as soon as possible to prevent the peripheral damage from the crisis from multiplying out of control.

Moreover, the negative effects of the Ebola outbreak extend well beyond pure health system concerns. The World Bank predicts that the three core countries affected by the crisis will forgo a combined US $1.6 billion GDP in 2015, with another US $550 million lost in the rest of sub-Saharan Africa, and significantly more if the disease spreads any further [62]. Additionally, World Food Programme models estimated that the spread of Ebola will have created food insecurity for between 750,000 and 1.4 million people as of March 2015 [63]. A strong recovery will require not only the rebuilding of health systems, but the rebuilding of lives and livelihoods through economic stimulation and provision of basic needs. Here, in-country operators in particular are in a prime position to aid in recovery efforts, by returning to local business and investment activity after the worst of the crisis [51]. Reopening trade flows and resuming stalled projects as soon as possible will encourage a more rapid return to a positive growth trajectory for the region.

5. Options for resilient global R&D framework during an emergency

One of the major lessons learned from the recent Ebola outbreak and its response is the importance of developing an effective and efficient global research and development (R&D) framework during an emergency.

In this paper, we performed an analysis based on the 7-S Framework, which evaluates how well the resilient global R&D framework can be developed to effectively counter infectious disease threats: (1) Structure; (2) Style and Skill; (3) Stakeholders and Staff; (4) Shared value; (5) Strategy; (6) System; and (7) Size. Based on the analysis, we propose four recommendations.

Firstly, the World Health Organization (WHO) should lead in establishing an independent Pandemic Product Development Committee (PPDC), supervised by the Technical Governing Board (TGB) [64]. The PPDC is mainly responsible for oversee global R&D progress, mobilize, prioritize, and allocate R&D resources relating to pandemic threats whereas the TGB is

supervising body to accelerate the PPDC's works by coordinating with and increasing coherence in global health community.

The global community realized during the recent Ebola outbreak that there are no supervising authority that oversees and lead global R&D efforts. Even within the WHO, the clusters are formed according to issues such as Family, Women's and Children's Health (FWC), HIV/AIDS, TB, Malaria and Neglected Tropical Disease (HTM), or Health Systems and Innovation (HIS) apart from administrative offices. Special Programme of Research, Development and Research Training in Human Reproduction (HPR) under the FWC cluster may be the only program that manages R&D issues, but limited to R&D related to FWC and not necessarily pandemic or epidemics [65]. In addition, most of the global R&D efforts are driven by market mechanisms. This resulted in R&D expertise mainly remains in private sector, and in only a few areas of the world, such as North America, Europe, Australia and Japan. In order to globally monitor potential pandemic threats, progress towards R&D according to the threats and effectively response, the WHO should lead the initiative to establish the independent PPDC given its constitutional mandate as well as the nature of pandemic that may affect every human being without distinction of race, religion, political belief, economic or social condition. However, the PPDC should not be established within the WHO, such as under the Outbreaks and Health Emergencies (OHE) cluster but remains independent primarily to promote private-sector involvement. The committee should include public health and R&D experts and representatives from each WHO regions, with a size of less than 15 members respectively. Internationally recognized R&D experts in discovery, development, manufacture, and approval should participate in the committee in a private capacity given its nature of conflict of interest. The committee should also include public specialist who have expertise in distribution of existing and newly available medical products. The TGB should be composed of representatives from the UN Family including WHO, regulatory agencies and industries in order to lead design-institutional arrangements on various regulations for R&D during an emergency, which will be illustrated as follows. To facilitate the linkage, the chair of the PPDC should be a member of the TGB.

Secondly, the PPDC should work to define priorities, map global R&D progress, raise and manage the budget including gap analyses, and draft a pandemic-preparedness plan that illustrates R&D's role, responsibility, and operations during an emergency. Over the last few decades, Product Development Partnerships (PDPs) have accelerated product development for diseases whose solutions lack commercial incentives and which disproportionately affect the poor in developing countries. The PDPs has successfully created 39 products up to now, but most of the targeted diseases are HIV/AIDS, tuberculosis, malaria, NTDs, diarrhea and respiratory diseases [66]. The PPDC should focus primarily on diseases of high pandemic or epidemic potentials including coronaviruses and influenza viruses, prioritize and map global R&D progress according to the list of high-priorities. Prioritization should not confine to potential pandemics among humans but should apply the One Health concept - working locally, nationally, and globally to attain optimal health for people, animals and the environment [67]. Defining priorities should also work along with efforts to strengthening disease surveillance. Although WHO should take a lead on strengthening disease surveillance mechanism in partnership with regional and national focal points, there is also a need to promote non-medical R&D such as implementation of mobile Health or mHealth. Though internet access and mobile phone coverage differs substantially across countries, the number of population who reaches such technologies are certainly increasing even in the rural areas in developing countries [68], and such innovations in information and communications technology (ICTs) will advance surveillance capacities. Raising fund and managing the budget allocation based on the gap analyses of relevant R&D should also led by the PPDC. In addition, the PPDC should draft a pandemic-preparedness plan that illustrates R&D's role, responsibility, and operations during an emergency at least over the next 5 years. This not only provides clear roadmap for various

global R&D stakeholders in government, multi-lateral organizations, academia, regulatory agencies, industry and civil-societies but also accelerates involvement of emerging contributors from education, communication, environment and defense sectors.

Thirdly and the most presumably important, the PPDC should focus to lead design-institutional arrangements on various regulations for R&D during an emergency. Given the fact that it is extremely important to swiftly counter pandemics, it is reasonable to redesign existing protocols and frameworks: especially during clinical trials, manufacture, and approval of medical products as these three phases often require the most time and investment. In practice, there are seven phases where R&D stakeholders can be coordinated and should align. First, during the initial phases of the product development, there's a need to mobilize resources on R&D not only from traditional funders but also from other sectors such as education, communication, environment and defense throughout the different R&D phases. For example, engagement of the locals in the community is indispensable to implement clinical trials during an emergency and long-term education in partnership with education sector is critical. Strengthening local R&D capacities also require long-term investments. Additionally, U.S. Department of Defense (DOD) spending US$70 billion on R&D [69] reflects pandemic threats as a matter of national security. Second, the R&D community should expand its efforts to upstream stage of product development led by the PDPs into high-priority pandemic diseases. Although donor governments supporting PDPs have increased to 21 for now [70], half of the funding comes from the Bill & Melinda Gates Foundation. There remains room to increase other donors involvement both from public and private sectors. Third, R&D community should commit to and agree on new approaches and protocols during clinical trial phase such as introducing adaptive design into clinical trials, ensuring involvement of local government, scientists and communities as well as benefit-share scheme, developing pre-approval for the clinical trial designs and master protocols. Generally, clinical trial is the stage that requires longest period of time and high level of funding, how to effectively and efficiently accelerate product development during this phase is the key to swiftly counter the pandemic threats. Fourth, the R&D community should work to agree on streamlined process for regulatory requirements across countries or regions for approval. Fifth, the R&D community should agree to ensure timely sharing of biomaterials and intellectual property management. The WHO's Pandemic Influenza Preparedness Framework (PIP Framework), which lays out a streamlined process for the sharing of pathogens with pandemic potential and creates fair benefit-share scheme [71], should be expanded to high-priority pandemic diseases. Sixth, the R&D community should identify manufacture facilities, develop and agree on protection against product liability claims during an emergency. Last, R&D community should plan for access and distribution of available medical products. Even when the products are available, it is highly likely they are often unaffordable or inaccessible for the people most in need. To avoid such cases, pre-agreement on stockpiling and pricing schemes at international level as well as developing effective distribution and administration system at national level are needed.

Lastly, the PPDC should work to secure and deploy a minimum of US $1 billion per year, which is relevant to half of the annual budget for global PDPs, to implement operations described above. The funding source should include donor contribution to the WHO, given there is an equal risk of pandemic threats to the nations worldwide, voluntary contribution from government, outside health sectors, private foundations and business, as well as utilization of innovative financing mechanisms. While prioritization, R&D mapping and gap analysis may not require a large amount of funding, design-institutional arrangements on various regulations for R&D during an emergency may require large amount of funding as well as enormous negotiations, consensus buildings amongst various stakeholders. Therefore, we have to keep in mind that potential pandemics are threats to every human being without distinction of race, religion, political belief, economic or social condition, and we have to have a united effort to fight against them.

6. Strengthening global health governance

Fidler defines global health governance as "the use of formal and informal institutions, rules, and processes by states, intergovernmental organizations, and nonstate actors to deal with challenges to health that require cross-border collective action to address effectively" [72]. The WHO identifies its role in global health governance as "the directing and coordinating authority on international health work" [73]. The expansion and diversity of the global health landscape, then, suggests that a variety of explicit coordinating initiatives may be worthy priorities for the WHO in strengthening governance.

For example, the WHO should take a leading role in setting the global HSS agenda, through a platform to coordinate funding and activities from a variety of global health actors. With respect to the case of HSS, the WHO has outlined a framework for health systems, but there is a weak evidence base for HSS activities and limited agreement on the optimal cost-effective interventions [74-75] . Thus, the framework is interpreted in numerous different ways by a wide variety of global health actors, resulting in diffuse HSS spending and few clear international policy goals. As a leading partner on an umbrella platform, the WHO could put itself in a position to concretely define a health policy research agenda and, in turn, set actionable global HSS priorities. One such platform, the Health Systems Funding Platform, was proposed just a few years ago as a partnership between the World Bank, GAVI, and the Global Fund. However, the proposal ultimately stalled due to the complexities of coordinating the partners' distinctive funding channels, schedules, business models, and governance structures [76], and perhaps also due to the failure of the World Bank to collaborate effectively with its partners and to actively respect national ownership [77]. The challenges of establishing such a platform are more than evident, but the goal remains admirable, and if past mistakes are heeded a new HSFP-like initiative could turn HSS from an amorphous buzzword to an actionable cornerstone of global health policy.

Innovation in global health represents another area with which the WHO and other governance structures should engage at a high level. The biopharmaceutical research industry clearly has enormous resources at its disposal, but PDPs have only succeeded in leveraging a small fraction of these resources in service of neglected diseases or other global health problems. A broader reform of incentives could help drive R&D for global health on a larger scale. Other initiatives like the GHIT Fund and the proposed HIF already show promise on this front, and they should absolutely earn the backing and investment of the WHO and other major global health agencies. Of course, generating the funds and political will sufficient to create a worldwide impact remains a challenge. Some innovative financing mechanisms indicate investor interest in social good, such as IFFIm vaccine bonds, but such programs have yet to be scaled up or replicated beyond their current, narrow domains [78].

One potential, under-utilized source of public funding might come not from health or development agencies, but from defense agencies. Proposed US federal spending on health security in fiscal year 2016 totals US $13.7 billion, including over $2.5 billion specifically for biodefense and pandemic threats, in addition to funds for multipurpose preparedness [79]. While the actual potential for weaponization of Ebola is probably low [80-81], the threat has been sufficient to drive biodefense spending and research, an important catalyst for the first waves of vaccine development [81]. Indeed, there are past precedents for increases in defense spending following the 2003 SARS outbreak and the 2009 influenza outbreak [82], and for using this funding to engage the private sector [83]. Working to identify diseases that pose potential biosecurity threats, well before they pose an actual biosecurity threat, could contribute to increased funding for vital global health R&D from the defense sector. However, this strategy is limited primarily to pathogens with clear security implications, which may not apply to many neglected diseases (such as the helminthic NTDs).

While outside the scope of this report's discussion, other economic incentives should also be considered to encourage greater participation in global health R&D. For example, perhaps lessons can be taken from tax or trade incentives for environmental protection and applied to create similar incentives for the global health arena.

With respect to global health emergencies, the decentralized bureaucracy of the WHO makes mounting a strong, rapid response very difficult. Their recent report examining the Ebola response recommends the creation of a centralized, command-and-control Center for Emergency Preparedness and Response, but it remains unclear whether this can be achieved while leaving the basic decentralized structure intact [84]. Moreover, the WHO's capacity to respond has been restricted by recent budget cuts, which slashed crisis and outbreak funding in half [85]. In response to criticisms, officials have asserted that the role of the WHO is merely to advise states how to handle crises, rather than direct the response themselves [85]. But while a preference for national ownership is admirable in many aid situations, it is very obviously incompatible with the poor capacity of health systems in nations like Guinea, Liberia, and Sierra Leone. Investing in a stronger network of disaster management partnerships could serve to alleviate both of these issues. Pre-agreement mechanisms with an expanded network of outside responders would connect more private resources to response efforts more quickly, potentially bypassing much of the internal bureaucracy of the WHO. Moreover, these mechanisms should be built first and foremost around local action rather than outside intervention, with external actors primarily supporting in-country operators or even community-based disaster preparedness teams. Making the focus local not only represents a commitment to effective aid, but also permits flexible action attuned to a country's individual needs, and may help bridge the trust gap between communities and the larger health establishments that serve them. With social media increasingly entering the global health toolbox [86-87], more avenues to community engagement are open than ever before for such endeavors.

In its current state, global health governance might be best described as a regime complex, a "'collective of partially overlapping and nonhierarchical regimes'" or regime clusters [72]. The WHO is central to this regime complex, and if it takes its self-proclaimed position as the coordinating authority on international health work seriously, it should invest in developing networks and platforms that helps these varied regime clusters cohere towards coordinated policy objectives. While there are clear problems with the WHO's bureaucracy, political inertia makes radical reform unlikely; instead, as Fidler suggests, efforts should focus on iterative improvements to generate resilience [72]. Strong partnerships and networks can build this resilience by shoring up the weaknesses of the WHO and offering timely access to a greatly expanded pool of resources and expertise, while bringing a wide variety of global health actors under a more unified policy umbrella.

Importantly, Japan has the specific expertise to offer unique contributions in these areas. First, Japan has over 50 years of experience with UHC, and moreover, has achieved this goal at modest levels of health expenditure compared to other developed countries [88-90]. Thus, when considering HSS from the perspective of moving towards UHC, the Japan case may offer some lessons, or at least a starting point from which to develop ideas about how to build strong systems at low cost and target spending effectively. Second, Japan is home to the GHIT Fund, a promising model for encouraging more private sector involvement in innovative global health R&D. The Japanese government's sustained engagement with major pharmaceutical companies in this partnership might serve as a model for sparking broader private engagement worldwide, particularly with increased support from other major global health actors. Third, Japan has already taken a leading role in several major global health issues, including smallpox eradication, DOTS therapy for TB, and the creation of the Global Fund [91], as well as more

recent polio eradication efforts. With this history of leadership under its belt, Japan is positioned once again to bring the pressing issues discussed in this paper to the attention of the world, and set a global health agenda that will garner the international support needed to generate real collective action.

7. Recommendations

Below are the six recommendations to effectively respond to future global health threats based on the public-private partnerships.

- Health systems strengthening will be critical to achieving the SDGs and promoting UHC worldwide. The WHO should develop initiatives, beyond merely proposing a framework, that position it as a leader in this developing field. This will require:
  - Setting a research agenda. HSS needs to be better understood before more effective initiatives can be enacted. The WHO should convene experts and health policy researchers to identify and answer the key questions pertinent to future policy.
  - Coordinating actors. With an increased evidence base, the WHO should develop a platform to synchronize HSS spending in pursuit of optimal policy interventions. Despite the challenges of implementing HSFP, it was an excellent idea, and building a similar platform could be an important step towards smarter HSS spending.
- Innovative global health R&D represents only a small fraction of total biotech research spending, and PDPs are a successful but limited solution. High-level structures to promote better incentives for global health R&D, such as the GHIT Fund or the HIF, should be supported by the WHO and other major global health actors.
  - Gathering significant funding for these initiatives may be challenging, but one possibility beyond traditional sources is defense. Biosecurity is deeply tied to global health, and in some cases, global health R&D could have important security implications. Bringing the two together could open up new sources of funding from worldwide defense departments.
  - Existing innovative financing mechanisms may offer a useful model, if replicated and scaled up. Other tax and trade incentives should also be considered, with lessons taken from areas such as environmental policy.
- The decentralized, bureaucratic structure of the WHO, coupled with recent cuts to disaster response budgets, leaves it in a poor position to respond in a crisis situation. But by creating a network of partners, especially private partners, and establishing pre-agreement mechanisms, it can leverage the resources and flexibility of the private sector to create a faster, stronger response in the future.
  - Actively invest in these connections now! The WHO should snowball its networks through its current points of contact, and organize meetings for interested partners in order to establish communication.
  - Build from the local level. Center national pre-agreement mechanisms on local operators in that country, and get citizens and community groups involved as well. Build locals' capacity to be their own first line of defense, with international resources in a supporting role. Consider community engagement through social media.
- Japan is in a position to contribute specialized expertise to the pursuit of many of these goals. Specifically, this includes:
  - Experience with low-cost UHC, which may guide future explorations of HSS.
  - The GHIT Fund, offering lessons on sustained engagement of the private sector for innovative global health R&D.
  - Global health leadership that can help bring these issues to the attention of the world and hopefully lead to effective action.

- It bears repeating that all policy measures must adhere to principles of aid effectiveness, particularly *national ownership*. Make coordination with local needs a top priority.
- The global community should invest to develop an effective and efficient global research and development (R&D) framework during an emergency.
    - WHO should lead in establishing an independent Pandemic Product Development Committee (PPDC), supervised by the Technical Governing Board (TGB).
    - PPDC should work to define priorities, map global R&D progress, raise and manage the budget including gap analyses, and draft a pandemic-preparedness plan that illustrates R&D`s role, responsibility, and operations during an emergency.
    - PPDC should focus to lead design-institutional arrangements on various regulations for R&D during an emergency. Given the fact that it is extremely important to swiftly counter pandemics, it is reasonable to redesign existing protocols and frameworks: especially during clinical trials, manufacture, and approval of medical products as these three phases often require the most time and investment.
    - PPDC should work to secure and deploy a minimum of US $1 billion per year, which is relevant to half of the annual budget for global PDPs, to implement operations described above.

References:

1. Organization for Economic Cooperation and Development. "International Development Statistics (IDS) online databases." Updated June 24, 2015. http://www.oecd.org/dac/stats/idsonline.htm
2. Institute for Health Metrics and Evaluation. "Financing Global Health 2013: Transition in an age of austerity." Seattle, WA: IHME, 2014. http://www.healthdata.org/policy-report/financing-global-health-2013-transition-age-austerity
3. Buse, K. and Walt, G. "Global public-private partnerships: part I – a new development in health?" *Bulletin of the World Health Organization* Jan. 2000, 78(4). doi:10.1590/S0042-96862000000400019.
4. Reich, M. "Public-private partnerships for public health." *Nature Medicine* June 2000, 6(6): 617-20. doi:10.1038/76176.
5. World Health Organization. "Public-private partnerships for health." Accessed Aug. 13, 2015. http://www.who.int/trade/glossary/story077/en/
6. Hafner, T. and Shiffman, J. "The emergence of global attention to health systems strengthening." *Health Policy and Planning* 2013, 28(1): 41-50. doi:10.1093/heapol/czs023.
7. Storeng, K. "The GAVI Alliance and the 'Gates approach' to health system strengthening." *Global Public Health* Sep. 2014, 9(8): 865-79. doi:10.1080/17441692.2014.940362.
8. Gavi, the Vaccine Alliance. "Mission indicators." Accessed Aug. 11, 2015. http://www.gavi.org/results/goal-level-indicators/mission-indicators/
9. The Global Fund. "Results." Accessed Aug. 11, 2015. http://www.theglobalfund.org/en/about/results/
10. UK Department for International Development. "Multilateral aid review: ensuring maximum value for money for UK aid through multilateral organizations." Mar. 2011. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/67583/multilateral_aid_review.pdf
11. Buse, K. and Waxman, A. "Public-private health partnerships: a strategy for WHO." *Bulletin of the World Health Organization* Oct. 2001, 79(8): 748-54. doi:10.1590/S0042-96862001000800011.
12. Ooms, G., et al. "The 'diagonal' approach to Global Fund financing: a cure for the broader malaise of health systems?" *Globalization and Health* Mar. 2008, 4(6). doi:10.1186/1744-8603-4-6.
13. Marchal, B., Cavalli, A., and Kegels, G. "Global health actors claim to support health system strengthening – is this reality or rhetoric?" *PLoS Medicine* Apr. 2009, 6(4): e1000059. doi:10.1371/journal.pmed.1000059.
14. Biesma, R., et al. "The effects of global health initiatives on country health systems: a review of the evidence from HIV/AIDS control." *Health Policy and Planning* July 2009, 24(4): 239-52. doi:10.1093/heapol/czp025.
15. World Health Organization Maximizing Positive Synergies Collaborative Group. "An assessment of interactions between global health initiatives and country health systems." *Lancet* June 2009, 373: 2137-69. Updated Apr. 17, 2015. doi:10.1016/S0140-6736(09)60919-3.
16. World Health Organization. "Everybody's business – strengthening health systems to improve health outcomes: WHO's framework for action." 2007. http://www.who.int/healthsystems/strategy/everybodys_business.pdf
17. GAVI. "Health systems strengthening support." Accessed Aug. 13, 2015. http://www.gavi.org/support/hss/
18. Global Fund. "Health systems strengthening." Accessed Aug. 13, 2015. http://www.theglobalfund.org/en/about/diseases/hss/
19. Hill, P., et al. "The Health Systems Funding Platform: Is this where we thought we were going?" *Globalization and Health* May 2011, 7(16). doi:10.1186/1744-8603-7-16.
20. Galichet, B., et al. "Linking programmes and systems: lessons from the GAVI Health Systems Strengthening window." *Tropical Medicine and International Health* Feb. 2010, 15(2): 208-15. doi:10.1111/j.1365-3156.2009.02441.x.
21. Moran, M., et al. "The role of product development partnerships in research and development for neglected diseases." *International Health* June 2010, 2(2): 114-22. doi:10.1016/j.inhe.2010.04.002.
22. Policy Cures. "G-FINDER Public Search Tool." Accessed Aug. 11, 2015. https://gfinder.policycures.org/PublicSearchTool/search
23. Pharmaceutical Research and Manufacturers of America. "2015 biopharmaceutical research industry profile." Apr. 2015. http://www.phrma.org/sites/default/files/pdf/2015_phrma_profile.pdf

24. Trouiller, P., et al. "Drug development for neglected diseases: a deficient market and a public-health policy failure." *Lancet* June 2002, 359: 2188-94. doi:10.1016/S0140-6736(02)09096-7.
25. Drugs for Neglected Diseases Initiative. "DNDi Treatments: treatments delivered." Accessed Aug. 13, 2015. http://www.dndi.org/treatments/overview-treatments.html
26. Boulton, I., et al. "Evaluation of the product development partnership (PDP) funding activities of the UK Department for International Development and the German Ministry for Education and Research." 2015. http://www.bmbf.de/pubRD/Evaluation_of_the_Product_Development_Partnerships_(PDP)_funding_activities.pdf
27. Banerjee, A., Hollis, A., and Pogge, T. "The Health Impact Fund: incentives for improving access to medicines." *Lancet* Jan. 2010, 375: 166-69. doi:10.1016/S0140-6736(09)61296-4
28. GHIT Fund. "The GHIT Fund business model." Accessed Aug. 20, 2015. https://www.ghitfund.org/hww/businessmodel
29. Incentives for Global Health. "The Health Impact Fund: a summary overview." Accessed Aug. 13, 2015. http://healthimpactfund.org/the-health-impact-fund-a-summary-overview/
30. Incentives for Global Health. Email correspondence. July 18, 2015.
31. Elias, C., Gerrans, Y., and LaForce, M. "Public-private partnerships drive innovation to improve the health of poor populations." *Global Forum for Health Research* 2008, 5: 157-60. http://www.isn.ethz.ch/Digital-Library/Publications/Detail/?ots591=eb06339b-2726-928e-0216-1b3f15392dd8&lng=en&id=93579
32. Brooke, S., et al. "How public–private partnerships handle intellectual property: the PATH experience." *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices,* 2007. http://www.meningvax.org/files/ipHandbook-Ch-17-Brooke-et-al-PATH.pdf
33. Bishai, D., et al. "Product development partnerships hit their stride: lessons from developing a meningitis vaccine for Africa." *Health Affairs* June 2011, 30(6): 1058-64. doi:10.1377/hlthaff.2011.0295.
34. Mitchell, M. "An overview of public private partnerships in health." Harvard School of Public Health, 2008. https://www.hsph.harvard.edu/ihsg/publications/pdf/PPP-final-MDM.pdf
35. Buse, K. and Tanaka, S. "Global public-private health partnerships: lessons learned from ten years of experience and evaluation." *International Dental Journal* Aug. 2011, 61(s2): 2-10. doi:10.1111/j.1875-595X.2011.00034.x.
36. Buse, K. and Walt, G. "Global public-private partnerships: part II – what are the health issues for global governance?" *Bulletin of the World Health Organization* Jan. 2000, 78(5). doi:10.1590/S0042-96862000000500015.
37. Jamali, D. "Success and failure mechanisms of public-private partnerships (PPPs) in developing countries: insights from the Lebanese context." *International Journal of Public Sector Management* 2004, 17(5): 414-30. doi:10.1108/09513550410546598.
38. United Nations Economic and Social Council. "Presidential Statement – The role of partnerships in achieving the post-2015 development agenda: making it happen." May 2015. http://www.un.org/en/ecosoc/partnership2015/pdf/presidential_statement.pdf
39. Gilmore, A., Savell, E., and Collin, J. "Public health, corporations, and the New Responsibility Deal: promoting partnerships with vectors of disease?" *Journal of Public Health* 2011, 33(1): 2-4. doi:10.1093/pubmed/fdr008.
40. Lee, M. "A review of the theories of corporate social responsibility: its evolutionary path and the road ahead." *International Journal of Management Reviews* Mar. 2008, 10(1): 53-73. doi:10.1111/j.1468-2370.2007.00226.x.
41. Droppert, H. and Bennett, S. "Corporate social responsibility in global health: an exploratory study of multinational pharmaceutical firms." *Globalization and Health* Apr. 2015, 11(15). doi:10.1186/s12992-015-0100-5.
42. Vian, T., et al. "Corporate social responsibility in global health: the Pfizer Global Health Fellows international volunteering program." *Human Resource Planning Journal* Jan. 2007, 30(1): 30-35. http://www.bu.edu/actforhealth/reference/HRP%20Pfizer%20GHF%20Final.pdf
43. Dobers, P. and Halme, M. "Editorial: Corporate social responsibility and developing countries." *Corporate Social Responsibility and Environmental Management* 2009, 16: 237-49. doi:10.1002/csr.212.
44. Marmot, M. et al. "Closing the gap in a generation: health equity through action on the social determinants of health." *Lancet* Nov. 2008, 372: 1661-69. doi:10.1016/S0140-6736(08)61690-6.

45. Hall, T., Gundersen, E., and Jensen, T. "Global health 'actors' and their programs." Global Health Education Consortium. Apr. 14, 2011. http://cugh.org/sites/default/files/content/resources/modules/To%20Post%20Both%20Faculty%20and%20Trainees/22_Organizations_involved_in_Global_Health_programs_FINAL.pdf
46. Doyle, C. and Patel, P. "Civil society organizations and global health initiatives: problems of legitimacy." *Social Science and Medicine* May 2008, 66(9): 1928-38. doi:10.1016/j.socscimed.2007.12.029.
47. Chan, E., et al. "Global capacity for emerging infectious disease detection." *PNAS* Dec. 2010, 107(50). http://www.pnas.org/content/107/50/21701.long
48. Polonsky, J., et al. "Public health surveillance after the 2010 Haiti earthquake: the experience of Médecins Sans Frontières." *PLoS Currents: Disasters* Jan. 2013, 1. doi:10.1371/currents.dis.6aec18e84816c055b8c2a06456811c7a.
49. Doctors Without Borders. "Pushed to the limit and beyond: a year into the largest ever Ebola outbreak." Mar. 23, 2015. https://www.doctorswithoutborders.org/sites/usa/files/msf143061.pdf
50. World Health Organization. "WHO leadership statement on the Ebola response and WHO reforms." Apr. 16, 2015. http://www.who.int/csr/disease/Ebola/joint-statement-Ebola/en/
51. World Economic Forum and Boston Consulting Group. "Managing the risk and impact of future epidemics: options for public-private cooperation." June 2015. http://www3.weforum.org/docs/WEF_Managing_Risk_Epidemics_report_2015.pdf
52. Buseh, A., et al. "The Ebola epidemic in West Africa: challenges, opportunities, and policy priority areas." *Nursing Outlook* 2015, 63(1): 30-40. doi:10.1016/j.outlook.2014.12.013.
53. Karan, A. and Pogge, T. "Ebola and the need for restructuring pharmaceutical incentives." *Journal of Global Health* June 2015, 5(1): 010303. doi:10.7189/jogh.05.010303.
54. Research America. "Federal health agencies ramp up efforts to fight Ebola." Aug. 15, 2014. http://www.researchamerica.org/blog/federal-health-agencies-ramp-efforts-fight-Ebola
55. National Institutes of Health. "Liberia-US clinical research partnership opens trial to test Ebola treatments." Feb. 27, 2015. http://www.nih.gov/news/health/feb2015/niaid-27.htm
56. PR Newswire. "Johnson & Johnson announces formation of Ebola vaccine development consortia, gains funding from Innovative Medicines Initiative." Jan. 16, 2015. http://www.prnewswire.com/news-releases/johnson--johnson-announces-formation-of-Ebola-vaccine-development-consortia-gains-funding-from-innovative-medicines-initiative-300021712.html
57. Mercy Corps. "Making connections: linking local government with communities and schools. A case study on community-based disaster risk reduction and local government capacity building in West Sumatra." 2011. http://d2zyf8ayvg1369.cloudfront.net/sites/default/files/prepare_sumbar_case_study_2.pdf
58. Lassa, J. "Public private partnership in disaster reduction in a developing country: findings from West Sumatra, Indonesia." Institute of Resource Governance and Social Change, Kupang: April 2013. http://www.preventionweb.net/english/professional/publications/v.php?id=32825
59. World Bank. Interview. July 2, 2015.
60. Busch, N. and Givens, A. "Achieving resilience in disaster management: the role of public-private partnerships." *Journal of Strategic Security* 2013, 6(2): 1-19. doi:10.5038/1944-0472.6.2.1.
61. Auzzir, Z., Haigh, R., and Amaratunga, D. "Public-private partnerships (PPP) in disaster management in developing countries: a conceptual framework." *Procedia Economics and Finance* 2014, 18: 807-14. doi:10.1016/S2212-5671(14)01006-5.
62. World Bank. "Ebola: most African countries avoid major economic loss but impact on Guinea, Liberia, Sierra Leone remains crippling." Jan. 20, 2015. https://www.worldbank.org/en/news/press-release/2015/01/20/Ebola-most-african-countries-avoid-major-economic-loss-but-impact-on-guinea-liberia-sierra-leone-remains-crippling
63. World Food Programme. "Special Focus Ebola: how can we estimate the impact of Ebola on food security in Guinea, Liberia and Sierra Leone?" Nov. 2014. http://documents.wfp.org/stellent/groups/public/documents/ena/wfp268882.pdf
64. Commission on a Global Health Risk Framework for the Future. "The Neglected Dimension of Global Security - A Framework to Counter Infectious Disease Crisis" January 2016. http://nam.edu/wp-content/uploads/2016/01/Neglected-Dimension-of-Global-Security.pdf
65. World Health Organization. "World Health Organization Organigram" December 2015. http://www.who.int/about/structure/who-organigram-2015.pdf?ua=1
66. Global Health Innovative Technology Fund. "Chapter 3. An Epoch-Making New R&D Mechanism". Accessed April. 17, 2016. https://www.ghitfund.org/motivation/motivation3

67. The American Veterinary Medical Association. One Health Initiative Task Force. "One Health: A New Professional Imperative". July 15, 2008. Accessed April. 17, 2016.https://www.avma.org/KB/Resources/Reports/Documents/onehealth_final.pdf
68. International Telecommunication Union. "ICT Facts & Figures." Accessed April. 17, 2016. https://www.itu.int/en/ITU-D/Statistics/Documents/facts/ICTFactsFigures2015.pdf
69. American Association for the Advancement of Science. " Historical Trends in Federal R&D". Accessed April. 17, 2016. http://www.aaas.org/page/historical-trends-federal-rd
70. Global Health Technologies Coalition. Accessed April. 17, 2016. http://www.ghtcoalition.org/home
71. World Health Organization. 2011. " Pandemic influenza preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits". http://apps.who.int/iris/bitstream/10665/44796/1/9789241503082_eng.pdf
72. Fidler, D. "The challenges of global health governance." Council on Foreign Relations, International Institutions and Global Governance Program, May 2010. http://www.cfr.org/global-governance/challenges-global-health-governance/p22202
73. World Health Organization. "WHO's role in global health governance: report by the Director-General." Jan. 18, 2013. http://apps.who.int/gb/ebwha/pdf_files/EB132/B132_5Add5-en.pdf
74. Warren, A., et al. "Global health initiative investments and health systems strengthening: a content analysis of Global Fund investments." *Globalization and Health* July 2013, 9(30). doi:10.1186/1744-8603-9-30.
75. Adam, T., et al. "Evaluating health systems strengthening interventions in low-income and middle-income countries: are we asking the right questions?" *Health Policy and Planning* 2012, 27(s4): iv9-iv19. doi:10.1093/heapol/czs086.
76. Evidence to Policy Initiative. "The Health Systems Funding Platform – a primer." 2011. http://seekdevelopment.org/e2pi_health_systems_funding_platform_-_a_primer.pdf
77. Brown, S., Sen, K., and Decoster, K. "The Health Systems Funding Platform and World Bank legacy: the gap between rhetoric and reality." *Globalization and Health* Mar. 2013, 9(9). doi:10.1186/1744-8603-9-9.
78. Tadros, E. "Vaccine bonds for a healthy return on saving lives." *Australian Financial Review*, May 31, 2015. http://www.afr.com/news/world/vaccine-bonds-for-a-healthy-return-on-saving-lives-20150524-gh8p8w
79. Boddie, C., Sell, T., and Watson, M. "Federal funding for health security in FY2016." *Health Security* June 2015, 13(3): 186-206. doi:10.1089/hs.2015.0017.
80. Stewart, S. "Evaluating Ebola as a biological weapon." *Security Weekly,* Oct. 23, 2014. https://mysu.susqu.edu/personal/rusek/news/Saved%20Articles/Ebola%20as%20a%20Biological%20Weapon.pdf
81. Strauss, S. "Ebola research fueled by bioterrorism threat." *Canadian Medical Association Journal* Nov. 2014, 186(16): 1206. doi:10.1503/cmaj.109-4910.
82. Franco, C. and Sell, T. "Federal agency biodefense funding, FY2010-FY2011." *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* June 2010, 8(2): 129-49. doi:10.1089/bsp.2010.0013.
83. Harjivan, C. "The $6 billion bio-defense opportunity." *Forbes*, Oct. 22, 2010. http://www.forbes.com/2010/10/21/bioterror-vaccines-manufacturing-technology-breakthroughs-biodefense.html
84. Clift, C. "WHO Ebola report is a missed opportunity." Chatham House, the Royal Institute of International Affairs. July 14, 2015. http://www.chathamhouse.org/expert/comment/who-Ebola-report-missed-opportunity#
85. Flynn, D. and Nebehay, S. "Aid workers ask where was WHO in Ebola outbreak?" *Reuters*, Oct. 5, 2014. http://uk.reuters.com/article/2014/10/05/us-health-Ebola-who-idUKKCN0HU03Q20141005
86. Olson, D. "WHO finds social media indispensable in managing global health crises." *Huffington Post*, May 21, 2012. http://www.huffingtonpost.com/david-j-olson/who-social-media_b_1530016.html
87. Perkins, N. "The pros and cons of social media in global health." *SciDev.Net*, Oct. 21, 2013. http://www.scidev.net/global/icts/scidev-net-at-large/the-pros-and-cons-of-social-media-in-global-health.html
88. Ikegami, N., et al. "Japanese universal health coverage: evolution, achievements, and challenges." *Lancet* Sept. 2011, 378: 1106-15. doi:10.1016/S0140-6736(11)60828-3.

89. Murray, C. "Why is Japanese life expectancy so high?" *Lancet* Sept. 2011, 378: 1124-25. doi:10.1016/S0140-6736(11)61221-X.
90. Jamison, D., et al. "Global health 2035: a world converging within a generation." *Lancet* Dec. 2013, 382: 1898-1955. doi:10.1016/S0140-6736(13)62105-4.
91. Llano, R., and Shibuya, K. "Japan's evolving role in global health." The National Bureau of Asian Research, Center for Health and Aging. 2011. http://www.nbr.org/research/activity.aspx?id=148

Global Health Working Group
White Paper on Fostering Global Health Innovation

GROUP 7

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Introduction: An Opportunity to Foster Global Health Innovation

The recent outbreak of Ebola hemorrhagic fever in West Africa was tragic for thousands of people and terrifying for millions. The outbreak of this highly infectious diseases also reminded policy makers, global health professionals and scientists[1] about the challenges facing health systems across the world, and the global risks created when these systems are weak or nonexistent.

The recent outbreak of Ebola hemorrhagic fever in West Africa was tragic for thousands of people and terrifying for millions. The outbreak of this highly infectious disease also reminded policy makers, global health professionals and scientists about the challenges facing health systems across the world, and the global risks created when these systems are weak or nonexistent.[2]

While many problems arose in the global response to Ebola, key stakeholders collaborated in successful ways to rapidly develop a new vaccine.[3] This exceptional instance – the innovation of a critically needed new product for global health – highlights an endless global health challenge. How can global health research and development (R&D), the scientific discovery and development of new products to fight neglected diseases, be promoted in the absence of news-making crises?

At Ise-Shima G7 Summit in Japan in May 2016, the G7 governments can review prior successes in global health innovation and put in place new mechanisms to sustain and leverage the impact of recent investments in global health. The Ise-Shima Summit provides an excellent opportunity to build on lessons learned in recent years about successful approaches to fostering global health innovation by making bold commitments of new financial, technical and human resources.[4]

This policy brief argues that increasing the G7's investments in global health innovation is a sound – and necessary – investment that will yield dividends in terms of economic, diplomatic and humanitarian progress. Based on interviews with key leaders in global health, this policy brief concludes that the most significant impediments to global health innovation are:

- *Insufficient funding* invested in research and development of new vaccines, diagnostics and medicines needed for those diseases that disproportionately affect developing countries;
- The *regulatory complexities and systemic redundancies* in licensing new global health products, especially in countries that lack a strong national regulatory framework; and,
- Profound *inefficiencies in global information sharing* and collaboration on innovation processes for global health products.

In response to these challenges, we propose that the G7 countries take three actions to foster global health innovation:

- *Increase government and philanthropic funding* to support global health innovation processes;

- Advance efforts to *streamline and harmonize national regulatory practices* for new global health products; and,

- Follow through with *support for more effective information/knowledge-sharing systems* in order to promote collaboration in global health innovation.

Despite the medical advances of the past century, the world is still struggling with how to assure that scientific discovery and technological progress benefit all people. In short, how do we assure the fair distribution of investment in the development of new health products, both among and within countries? The three proposals presented in this policy brief will lead to improvements in global health innovation, and thus to progress in global health. Ultimately, the investments in global health innovation proposed here will benefit people, and will strengthen health systems and economies, around the world.

The Need for Technological Innovation in Global Health

Global health is the "study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide."[5] Global health practice emphasizes interdisciplinary and transnational approaches to understanding the determinants of health, prominent health issues and the implementation of proposed solutions at all levels. Many global health programs focus on infectious diseases, which disproportionately affect people living in developing countries. Increasingly, however, global health programs are addressing heart disease, diabetes, cancers, and other non-communicable and lifestyle diseases that affect all countries.

This policy brief focuses primarily on policies to foster innovation of products to address infectious diseases, because they continue to present major obstacles to economic growth, health security and human development in poor countries. By extension, infectious diseases also have a major impact on global development. However, infectious diseases are increasingly rare in industrialized countries. The infectious diseases that cause a majority of associated death and disability are endemic only in poor countries. (In this paper, the term "endemic diseases" is used to refer to HIV/AIDS, tuberculosis, malaria and the 17 neglected tropical diseases (NTDs) that disproportionately affect people in poor countries.)

The health burden of endemic infectious diseases is immense. Over 25 million people are living with HIV, more than 2 billion people are infected with tuberculosis, and over 500 million people die each year of malaria.[6] Infectious diseases are the leading cause of death in children worldwide.[7] And non-fatal endemic diseases cause considerable disability. The effects of these diseases extend across generations, limiting the ability of individuals, their communities and their nations to thrive.

Despite the global toll of infectious diseases, many of the "tools" (vaccines, diagnostics and medicines) needed to prevent, treat and control them have not been discovered. A few examples of the need for technological innovation for endemic diseases: there is neither a vaccine for HIV nor a cure for AIDS; there is no medicine to treat Dengue fever, chikungunya disease or dracunculiasis; and there are no clinical diagnostic tests available for Buruli Ulcer and Chagas disease, while the diagnostic methods use for tuberculosis are notoriously unreliable. Table 1 shows which of the top 20 endemic diseases have a vaccine, diagnostic, and treatment, and which diseases do not have these technologies or have only suboptimal options. (Additional information is available in Appendix A.)

In addition to the 20 endemic diseases listed, the world regularly experiences sudden emergent infectious diseases such as Ebola, SARS, avian influenza, and MERS. These outbreaks generate fear

around the world, as they threaten not only individuals but also national and economic security, and because existing tools often do not work to fight these new diseases.

Another critical global problem related to infectious diseases is that the effectiveness of existing tools, particularly medicines, is increasingly threatened by the evolution of resistance among the infectious agents. Anti-microbial resistance (AMR) exacerbates the spread of both endemic and emerging infectious diseases by undercutting existing prevention and treatment options.

Widespread resistance to antibiotics among disease-causing organisms is rolling back previously achieved health gains, while no major new antibiotics have been developed in the last 30 years.[8] Resistance problems are occurring with various endemic diseases. For example, after a decade of decreases, malaria deaths increased among African children under age five beginning in the 1970s due to spreading chloroquine resistance in the malaria parasite.[9] Similarly, new strains of multi-drug resistant tuberculosis, streptococci and other diseases are increasingly ubiquitous.

All of these problems – missing tools, tools for emerging new diseases, and new tools to replace those becoming obsolete – urgently require global health innovation. Strengthening global investments in R&D for global health innovation is vitally important.

Table 1: The Need for Innovations for Endemic Diseases: Current Portfolio and Gaps in Key Global Health Tools (Vaccines, Diagnostics, and Medicines)

Disease	Vaccine	Diagnostic	Therapeutic
HIV/AIDS	NO	Yes	Yes
Tuberculosis	NO	SUBOPTIMAL	Yes
Malaria	SUBOPTIMAL	Yes	SUBOPTIMAL
Buruli Ulcer	NO	NO	SUBOPTIMAL
Chagas Disease	NO	NO	SUBOPTIMAL
Dengue and Chikungunya	SUBOPTIMAL	Yes	NO
Dracunculiasis	NO	SUBOPTIMAL	Worm extraction
Echinococcosis	NO	NO	Surgery
Endemic treponematoses	NO	NO	Yes
Foodborne trematodiases	NO	NO	Yes
Human African trypanosomiasis	NO	SUBOPTIMAL	SUBOPTIMAL
Leishmaniasis	NO	Yes	SUBOPTIMAL
Leprosy (Hansen's disease)	NO	NO	Yes
Lymphatic filariasis	NO	SUBOPTIMAL	SUBOPTIMAL
Onchocerciasis	NO	SUBOPTIMAL	Yes
Rabies	Yes	NO	NO
Schistosomiasis	NO	SUBOPTIMAL	Yes
Soil-transmitted helminthiases	NO	SUBOPTIMAL	Yes
Taeniasis/Cysticercosis	NO	NO	SUBOPTIMAL
Trachoma	NO	NO	Yes

Barriers to Global Health Innovation

Significant hurdles exist in improving global health, particularly around the development of new vaccines, drugs, and diagnostics. Yet there is little consensus about how to accelerate investment in global health innovation, especially for products that will primarily benefit people in poorer countries.

Major stakeholders in global health innovation include governments, donors, multilaterals, industry, and non-government organizations. In 2013, more than three quarters of all funding for R&D for global health was provided by seven institutions, including five governments and two philanthropies. In preparing this policy brief, we interviewed representatives in the seven funding

institutions. (Details on the methodology and results are in Appendix B.) Key stakeholders from these institutions were asked to identify the major bottlenecks that impede global health R&D for vaccines, diagnostics, and medicines needed to control and eradicate endemic infectious diseases.

The respondents noted that considerable progress has been made in the fight against infectious diseases, thanks in part to economic development, improved health systems and targeted control programs, along with increased access to effective vaccines, diagnostics, and medicines. All of these factors have contributed to reducing the global burden of infectious diseases. But in many areas the rate of decline of infectious diseases has plateaued or fallen short—especially in countries with weak health systems. The respondents were then asked to identify the key obstacles, as well as the most promising strategies, to fostering global health innovation that could address the persistent challenges of endemic infectious diseases. Their responses pinpointed three areas: funding, regulation, and knowledge management.

Strategies for Accelerating Innovation for Global Health

I. Substantially Increase Funding for Global Health Innovation

The Problem

Major, and systemic, funding gaps exist for financing the processes that lead to the introduction of a novel, licensed product for an endemic disease. Further, the sources of funding for global health innovation are different from other areas.

Funding for global health R&D has already increased significantly over the past decade, and the investments are beginning to pay off, leading to new innovations and subsequent formulations. Over the past half century, governments and philanthropic foundations have been the primary funders of research and development of new products targeting infectious diseases of the developing world. Their investment totaled US$3.2 billion in 2013.[10] The pipeline of new products is steadily increasing. For example, by 2011 the Drugs for Neglected Diseases initiative (DND*i*), which was founded in 2003, enabled the development of two antimalarials, a new treatment for visceral leishmaniasis, and pediatric formulations for Chagas disease treatment, among others.

The pharmaceutical industry, on the other hand, spent an aggregate US$400 million on global health research and development in 2013. For-profit companies in the biomedical industry are the primary developers of new vaccines, diagnostics and medicines for developed markets, and they have the infrastructure, professional expertise and other resources needed to bring new products from discovery to market. Yet for-profit companies typically invest only in areas where they see potential for profitable financial return. Market incentives are minimal to encourage for-profit companies to invest in developing new products for endemic infectious diseases that primarily affect poor people in poor countries. The potential returns on investment are viewed as low because of the limited market power of the people who need the products.

These arguments, however, are now being challenged. Recent studies at the national and global levels demonstrate that investment in global health innovation has both economic and social benefits. According to a 2013 report in *The Lancet,* funds invested in global health R&D generate a benefit between 9 and 20 times the cost in the global economy.[11] Likewise, GHPD investments have a significant benefit at the national level. In the U.S.A., for example, approximately 64 cents of every government dollar on global health R&D is invested domestically.[12] In the European Union, 66 cents of every Euro invested in global health R&D is spent within the E.U.[13] Research!America, an advocacy and education alliance made up of over 350 institutions, has examined the issue in depth, and prepared a top-ten list of reasons to invest in global health R&D (see panel).[14]

Public and private donors have often stepped in to fill gaps left by pharmaceutical companies in funding for global health innovation. However, government and other non-industry funding is often directed to basic science, discovery and early product development phases; funding later stage clinical trials, for example, is far less common. Increasingly, donors are partnering with the biomedical industry to shepherd important scientific research into usable products efficiently. Product-development and public-private partnerships (PDPs and PPPs) are mechanisms frequently used to incentivize these collaborations.

Public and private philanthropic funding is subject to politics, local particularities, and changing priorities. Fear and mounting panic often drive a surge of funding for emerging infectious diseases. With the 2014-2015 outbreak of Ebola in West Africa, governments and charities pledged nearly US$8 billion for control programs and R&D. But once an outbreak recedes, funding invariably does as well. Meanwhile, endemic infectious diseases like malaria and tuberculosis do not generate a similar response. They infect large numbers of people, but they have little money to pay for life-saving products, and because they are not perceived as an imminent threat to wealthier nations, they attract less funding. Finally, although governments may have significant resources, priority-setting and decision-making processes can be spread across several different agencies, with independent mandates and funding processes.

10 Reasons to Invest in Global Health R&D

Global Health R&D:
1. Saves lives
2. Creates jobs and opportunity for [donor country citizens]
3. Helps countries maintain competitive edge in the global economy
4. Benefits citizens and soldiers when they are abroad
5. Supports research universities and fulfills students' interest
6. Intersects with domestic R&D to drive cutting-edge medical discovery
7. Contributes to economic development and export markets
8. Investments save money in the long term
9. Is supported by a majority of Americans – and likely the citizens in other G7 countries
10. And finally, global diseases do not recognize national borders

Adapted from: *Research!America's Top 10 Reasons to Invest in Global Health R&D*[13]

Proposed Solution

More funding is needed for all stages of innovative global health R&D in order to secure critically needed vaccines, diagnostics, medicines and other tools. We propose that the G7 should double their investments in global health innovation over the next five years to ensure a robust pipeline of new products that will radically improve the health of the people who need them. This applies to ongoing

initiatives as well as the need for explore the establishment of a funding mechanism to support the development of vaccines for emerging infections and epidemics for which there is no market incentive such as Ebola, Marburg and Lassa infections.

We propose, in particular, that Japan initiate this doubling with a pledge to double its investment in innovative global health R&D, beginning with a replenishment of the Global Health Innovative Technology (GHIT) Fund. This Japanese model is demonstrating that pairing front-loaded investments with incentives for partnerships among research institutions and the pharmaceutical industry is highly effective in accelerating global health innovation. Within three years since its conception, GHIT has invested in more than 40 potential products, facilitating the use of Japanese technology in the process. Further, the government funding invested through GHIT is leveraged one-to-one with contributions from philanthropic and corporate partners.[15] With this strong foundation, GHIT's partners are poised to generate major contributions to global health innovation, particularly as industry partners are engaged early in the process. Doubling Japan's financial commitment would also push Japan into the top ten public funders of global health research and product development (for more detail see Figure 2 in Appendix A).

II. Streamline Regulatory Review Processes Globally

The Problem

Regulatory policies are critically important – they exist to ensure the safety of consumer products. However, in most instances, each country requires the data for each new vaccine, diagnostic or medicine to be reviewed and approved by its national regulatory agency (NRA). In some instances, the NRA may require additional clinical trials to be conducted locally. The many requirements, some of which are redundant, and the pervasive lack of adequate resources at the NRAs in developing countries, contribute to notoriously slow review and approval process timelines.

Should individual countries actually have to act independently in these processes, especially if they lack the capacity to do so efficiently? This brief argues that supranational policies or practices could be used to expedite approvals for new vaccines, diagnostics and medicines for priority endemic diseases.[16] Already, international law allows regulatory review processes to be expedited in cases of "public health emergency of international concern". For Ebola, WHO served as a convening body which negotiated expedited regulatory processes for new tools. A vaccine and other products were moved into clinical trials in a matter of months rather than years.[17] When, inevitably, there is another outbreak in the future, critical tools will be available which did not exist this time around.

Yet as these approvals jumped ahead in the queue, other products for endemic diseases continue to languish for years.[18] WHO's "pre-qualification program" for essential medicines aims to obviate some of the obstacles. The program, which generates "unified standards of quality, safety and efficacy/performance" for use in product assessment, offers one proven model for avoiding redundancies in regulation.[19] Other models include the *Pan American Network for Drug Regulatory Harmonization* and the unified registration procedures of the European Union. These examples indicate that it is possible to engage nations in harmonizing and streamlining regulatory mechanisms in order to expedite reviews and approvals of new vaccines, diagnostics and medicines for priority diseases. Policy options to consider would include the use of surrogate endpoints (e.g., biomarkers) for licensure, priority and/or expedited licensing mechanisms for diseases with low market potential and the facilitation of mutual recognition of licensure among countries, based on common technical guidelines.

Regulatory processes can be difficult to change. Achieving reform through legislation necessitates

the engagement, and ultimately the agreement, of high-level decision makers. And if the intent is to create supranational policies and structures, lawmakers may have concerns about national autonomy, maintaining standards and protecting citizens.

Proposed Solution

In the short-term, G7 countries should empower WHO or other convening bodies to establish an expedited path of review for new products for infectious diseases or to combat antimicrobial resistance. Over the longer term, the G7 should convene stakeholders to design a process to streamline national regulatory processes, as well as to invest in building capacity within the NRAs.

III. Create Efficient Mechanisms for Collaboration and Knowledge-Sharing

The Problem

When a highly infectious disease outbreak like Ebola occurs, leaders and policy makers frequently commit resources to creating new tools. Time and again, however, as the various actors rush to implement a flurry of activities, some efforts are needlessly duplicated while large gaps exist. Developing mechanisms for working collectively emerge more gradually.[20] Intense global collaboration is required to minimize the damage and control further spread.[21] As was evident during the Ebola outbreak, however, sharing information and knowledge can be an endeavor fraught with difficulties.

Further, the urgency and the resulting political commitment is often lacking when addressing endemic diseases and AMR. And in many instances, the collaborations that do emerge are bilateral, not global. The lack of an efficient global "ecosystem" for sharing and coordinating activities significantly hampers the ability of funders to pursue innovations in global health product development. Prior initiatives aimed at coordinating work across multiple funders and organizations have been perceived as adding work without bringing the desired benefits of efficiency and effectiveness. Even the creation of coordination mechanisms faces duplication, as new funding mechanisms, frameworks and collaboration platforms are developed. While the major global health innovation funders also agree that better collaboration and knowledge sharing could speed support for innovations, many stakeholders are skeptical of ceding authority, proprietary information or priority-setting to a third party.

The challenges of incentivizing and facilitating information-sharing among global health innovators was acknowledged by the G7 during its 2015 meeting in Schloss Elmau, Germany. However, concrete steps to improve the situation have not been forthcoming.

Proposed solution

Japan can lead the G7 to build on the foundation laid in Germany. The Ise-Shima Summit offers an opportunity to follow up by clarifying a process and concrete milestones for the rapid development and deployment of functional global platforms to allow information-sharing, knowledge dissemination and creation of collaborative efforts across national and regional lines and among public, philanthropic and for-profit sectors. A G7 commitment to develop and announce a plan to realize this solution by the 2017 G7 Summit is achievable.

The Way Forward: Implementation Considerations

The world's arsenal of tools – vaccines, diagnostics and medicines, among others – against infectious

diseases remains insufficient, particularly when considering endemic diseases in poor countries. Effective vaccines and medicines are not yet available for prevalent killers. Powerful existing diagnostic technologies are often unsuitable for widespread use in the developing world. And for many existing medicines, the formulations and costs present insurmountable problems in patient access and adherence. Further, the development of AMR threatens the many gains that have already been made.

Global health innovation is therefore necessary to sustaining and expanding efforts to control and eradicate infectious diseases with heavy global burdens. Yet while developing countries experience a disproportionate burden of infectious disease, the majority of funding remains in high-income countries, and among for-profit companies. This results in a lack of urgency, poorly aligned incentives, and ineffective market structures.

The 2016 Ise-Shima G7 Summit offers nations a critical opportunity to develop and promote new mechanisms to incentivize global health innovation and to increase global public accountability. The Summit is a chance to create blueprints for increasing innovation in the discovery, development, and regulatory approval of essential new vaccines, diagnostics, and medicines.

The following steps are therefore recommended for consideration by Japan and its colleagues at the G7 Summit:

1. **Double the current global funding for global health innovation.** We recommend setting a global goal of reaching US$6.4 billion per year for global health R&D within ten years. This level of funding would enable a sea change in GHPD, in particular by making later stage clinical trials possible. Japan, for instance, could lead by doubling its support to initiatives such as the GHIT Fund.

2. **Convene a process to harmonize and streamline regulatory pathways. Allowing** endemic and emerging infectious diseases, as well as instances of emerging anti-microbial resistance, to be eligible for accelerated and/or coordinated review will reduce duplication and time to market for new products. Further, additional resource capacity for regulatory review must be developed in endemic country governments. Japan can support high-level meetings to champion harmonization of policies.

3. **Initiate a process to follow through on establishment of knowledge-sharing platforms for global health innovation.** The G7 countries have already made commitments in this area; now, with Japan as the organizer, next steps need to be elaborated to support platforms to share information on global health R&D strategies in order to identify duplication, encourage collaboration and limit gaps. A commitment to announce a plan to realize this solution by the 2017 G7 Summit is achievable.

A significant increase in funding, a more streamlined process for product approval, and a global platform for collaboration would, together, lead to more innovation. Establishing and advancing a robust pipeline for, and portfolio of, new products we need to control, eliminate, and eradicate infectious diseases. These diseases continue to pose significant risks to human security and health; they also menace the global economy.

At this Summit, the G7 countries have an unprecedented opportunity to radically transform the environment for global health innovation; Japan, which is known for its support of health innovations and global health policy, can offer critical leadership by championing these recommendations.

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