Response to the UN High Commission on Access to Medicines
February 28, 2016

"Incentives, Agreements and Stockpiling to Accelerate the Response to Infectious Disease Outbreaks"

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Executive Summary

The critical need for an accelerated global response to existing and future disease outbreaks is widely accepted. A new response will require new structures, processes and policies engaging both the public and private sectors. The new system must be designed to address chronically under-funded diseases (e.g. leishmaniasis, Chagas), high profile current outbreaks (Ebola, Zika virus) and establish a surveillance and response capability for future outbreaks. Moe & Barnes-Weise support a "reform from within" approach including the creation of a Center for Health Emergency Preparedness and Response (CHEPR) which includes capabilities for "surveillance for outbreaks and events, risk assessment, planning and execution of response, assessment of IHR functions and compliance, coordination with partners, risk communication, quality assurance, and monitoring"[3] as described in "The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises". While endorsing the Framework they argue it is silent or vague on critical additional capabilities which include: new incentives, new national policies, public/private partnerships, model language for agreements to share data and intellectual property, and stockpiling of existing medicines based upon mechanisms such as those used by BARDA (the Biomedical Advanced Research and Development Authority within the Office of the Assistant Secretary for Preparedness and Response in the U.S. Department of Health and Human Services.) Formation of these capabilities and structures has the added benefit of creating a blueprint for global cooperation on the development and distribution of medicines outside the infectious disease space (e.g. non-communicable diseases).

Moe & Barnes-Weise argue that two US based programs form a conceptual basis for a global accelerated response capability housed in part within and externally to the proposed "Center": BARDA and the Critical Path Initiative. They recommend that a proposed new WHO Center:

- convene selected regulatory agencies (e.g. EU countries, EMA, China, Japan), International Council for Harmonization, and the International Coalition of Medicines Regulatory Authority, to review and advocate for the appropriate use of "push" and

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[3] The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises." P. 49

"pull" incentives to reward research investment and new therapies for neglected and outbreak diseases;

- coordinate the surveillance necessary to predict future outbreaks and to consult with constituents' agencies responsible for domestic medical protection,

- WHO, GAVI and other purchasers and providers of global health needs accelerate access to these medicines and vaccines through the scaling of US Defense Department Biomedical Advanced Research and Development Authority (BARDA) programs,

- develop public/private collaborations to 1) accelerate the translation of scientific insights to new product development, 2) accelerate regulatory review, 3) accelerate the dissemination of information on appropriate and emerging uses of existing medicines and emergent new therapies for neglected and outbreak diseases.

Response to the UN High Commission on Access to Medicines

The need for global innovation and rapid disease response: important amendments to the Framework proposal

Recent high profile outbreaks of Ebola and Zika demonstrate 1) there is insufficient investment in pharmaceutical research for 1) high burden neglected diseases (e.g. TB, malaria, leishmaniasis, Chagas) and 2) for outbreak diseases (e.g. Ebola, Zika virus) that have relatively low disease burden but high threat due to global contagion. High global burden and outbreak diseases occur initially where health systems have weak or inconsistent capabilities in services, clinical delivery structures, human resources and infrastructure such as roads and power supply. These health system inadequacies are exacerbated by a lack of access to medicines. Innovation to discover and develop new therapies and new steps to increase the availability of existing medicines must be coupled with health system strengthening if the global response to outbreak diseases and high global burden diseases is to improve. Innovative drug research and drug development steps to improve drug access without health systems strengthening are shortsighted and will ultimately under-perform.

The recent disease outbreaks have also created a crisis of confidence in the global capability to respond effectively with appropriate speed. Criticisms have focused on the WHO, its governance structures and the lack of coordination among member states.[4] It is beyond the scope of our response and expertise to describe and defend alternatives to the WHO as a global coordinator. We agree with the general observation that switching costs for creating and operationalizing an alternative global coordinator, replacing many primary functions of the WHO to respond to disease outbreaks, would be high. Significantly, during the lengthy period of transition, responses would be even more fragmented as organizations compete for the global coordinator role. Therefore, a more prudent approach would be to re-vitalize and reform the WHO's capabilities from within while creating external structures which are independent and nimble. New and existing organizations such as the International Council for Harmonization and the International Coalition of Medicines Regulatory Authorities are working to improve the speed to market of new therapies and can be linked as resources with the efforts of the new Center.

The recently published report of the Commission on Creating a Global Health Risk Framework for the Future, highlights infectious diseases as one of the biggest risks facing humankind. It estimates that pandemics cost the world more than £40bn ($60bn) each year, and match wars and natural disasters in their capacity to endanger human life and health and disrupt societies.

[4] WHO, Final Report of the Ebola Interim Assessment Panel (Geneva, July 2015); S. Moon et al., The Lancet, online http://dx.doi.org/10.1016/S0140-6736(15) 00946-0 (Nov. 22, 2015)

Acknowledging our pre-disposition to revitalize and reform the responsiveness of WHO, we support the Commission's recommendations to:

- reinforce national public health capabilities and infrastructure as the first line of defense against potential pandemics, especially in low-income countries.
- establish a permanent WHO Center for Health Emergency Preparedness and Response, with sustainable funding and operational independence, which would lead and co-ordinate defences and action against pandemic threats.
- accelerate research and development in the infectious disease arena, through annual global investment of at least £686m ($1bn) a year in prevention and treatment of threats, and a coordinating body to prioritize and oversee these activities.

However, we find the Framework's articulation of steps to "accelerate research and development" vague or silent on critical additional capabilities: new incentives, new national policies, public/private partnerships, model language for agreements to share data and intellectual property, stockpiling of existing medicines based upon mechanisms used by BARDA and public/private collaborations that have been successfully initiated by the U.S. FDA. We describe below additional structures, processes, policies and capabilities to be housed in the "Center" itself as a global coordinator, and activities that must lie outside the center yet look to the Center to expedite, such as broad agreements and coordinated action plans.

<u>High Risk in Pharmaceutical Innovation</u>

The FDA (2002) estimates that "[n]o more than 5 in 5,000 tested compounds pass… preclinical trials and are proposed for clinical studies." While the success rates for drugs in clinical testing are greater than in the preclinical setting, the failure risk is still substantial. More than 80% of all drugs that enter clinical testing ultimately fail to receive marketing approval in the United States.

Drug development costs can involve up-front investments of several hundred million dollars. They are high for a number of reasons.[5] The size and complexity of clinical trials have been growing significantly over time and there remains a high level of uncertainty to the R&D process. The revenues generated by drugs that do make it to market vary greatly. [6] Given these industry risks, the pharmaceutical industry has little or no incentive to invest in research and development for infectious diseases of the global poor nations since those medicines cannot be

[5] DiMasi, JA, Hansen, RW, and Grabowski, HG. "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 2003 22(151): 161-163.

[6] Grabowski, HG, Vernon, J, and DiMasi, JA. 2002. "Returns on R&D for 1990s New Drug Introductions." *PharmacoEconomics* 20(15, Supplement 3): 11-29.

sold at a market clearing price that recovers the R&D investments. [7] An additional disincentive is the infrastructure problems in countries where high burden and outbreak diseases occur: safe and effective drugs are often inaccessible due to procurement and distributional gaps.

Intellectual Property Rights and the Biopharmaceutical Industry's Obligation to Access and Research

Inaccessibility of drugs has led some to argue that patents, which give the innovator limited market exclusivity, should be replaced (e.g. prizes) or subverted (e.g. compulsory licensing). We argue that patents serve an important and useful societal purpose to reward innovation and beget more innovation by publically disclosing important information to other innovators in exchange for exclusivity. DeGeorge[8] has made a convincing argument that intellectual property regimes can be defended on ethical grounds: "justice", fair returns to those who have invested in the discovery; "consequences" – limited exclusivity to gain a commensurate return on the investment. He also suggests that the biopharmaceutical industry has over-used the patents/innovation defense too broadly to deflect other criticisms and resist other obligations. We agree with both DeGeorge's defense of patents and the force of his argument that the biopharmaceutical industry has an obligation to work to expand access to its medicines and to invest in research on high burden diseases. In fact, we extend DeGeorge's argument, which we believe is in concert with the intent of the Framework proposal (although we acknowledge that Framework authors may not share our support of intellectual property protections as argued herein), to recommend that outbreak diseases are included in our understanding of the dual obligations to "access" and "research".

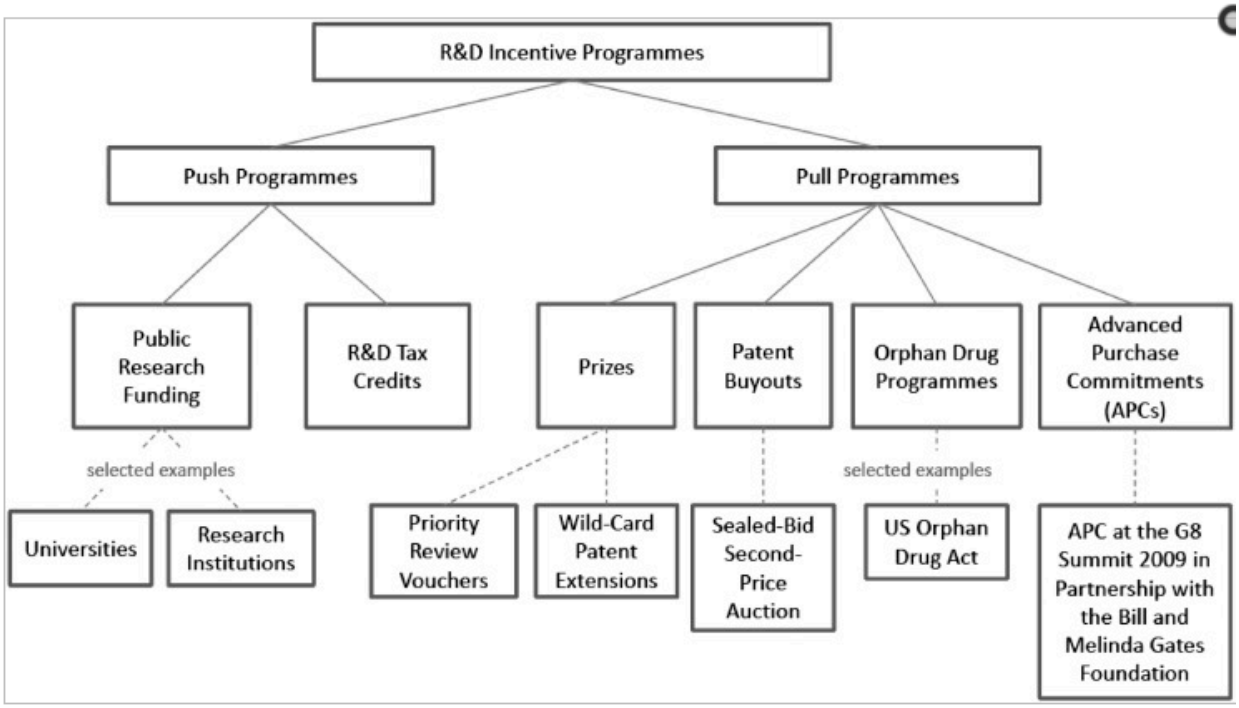
As a practical matter, we see expanding access to existing medicines as a company by company, jurisdiction by jurisdiction issue requiring concomitant structures, policies and practices to support company/country interactions. Increasing research investment is an industry-wide and multi-country challenge and therefore requires differing structures, processes and policies described in this response. Our response speaks to both circumstances: expanded access and expanded research.

[7] Buckup S. (2008), 'Global public–private partnerships against neglected diseases: building governance structures for effective outcomes', Health Economics, Policy and Law, 3: 31–50

[8] DeGeorge, R. "Intellectual Property and Pharmaceutical Drugs: An Ethical Analysis" 2005. *Business Ethics Quarterly* 15, no. 4

New Incentives contextualized to the disease target; expand "pull" incentives such as priority review voucher

Accepting there is a market failure (and inadequate policies) regarding R&D investment, incentives can mitigate the problem. Mueller-Langer[9] has depicted the types of R&D incentives below.



"Push" incentives, such as tax credits for R&D investments, encourage investment with no guarantee of an outcome; "pull" incentives, such as an advance market commitment, reward only outcomes. We argue that both are needed to accelerate a response to disease outbreaks, neglected diseases and emerging new diseases. The Commission estimates $1 Billion in financing primarily for "push" incentives for R&D and suggests the funds will be effective in "catalyzing private-sector R&D". [10] While we agree that "push" incentives to support new research and development, are needed, we note that 1) incentives, in general, are, as an order of magnitude, primarily provided by governments in the form of tax credits or prizes, 2) non-governmental foundations can provide other forms of "push" and "pull" incentives, but at a lesser magnitude, 3) that private actors such as universities, generic manufacturers and biomedical research firms are responsive to incentives where they are appropriately sized and efficiently administered and 4) incentives for vaccines and medicines for potential infectious

[9] Mueller-Langer, F. "Neglected infectious diseases: Are push and pull incentive mechanisms suitable for promoting drug development research?" Health Econ Policy Law. 2013 Apr; 8(2): 185–208

[10] The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises." P. 87

disease outbreaks will need to be targeted (types of incentives, magnitudes of incentives) and fitted to the unique characteristics of the disease target.

A pull incentive that is fulfilling its promise as an incentive to mitigate the market failure problem is the priority review voucher (PRV). A drug sponsor that receives FDA approval for a novel medicine (novel defined as heretofore not reviewed by FDA) to treat an eligible tropical disease (16 were on the voucher-eligible list in 2007) is rewarded by US FDA with a "voucher" (priority review voucher or PRV) which can be applied to a second drug for "priority review." Priority review is one of four designations offered by FDA for a drug to receive speedier review by the agency. Note that priority review is different from the other expedited designations such that it does not reduce safety and efficacy study requirements.

Ridley, Grabowski and Moe [11] estimated the value of the priority review, as compared with standard review, at $322 million. They also estimated tax savings because drugs that qualify for PRV would also qualify for Orphan Drug Act tax push incentives. Congress passed Section 524, the "priority review voucher", as part of the 2007 FDA Amendments Act. Since its passage, 10 PRV's have been awarded, pediatric cancers has been added as a voucher-eligible category, Ebola and Chagas disease have been added to the list of voucher-eligible tropical diseases, and procedural issues have been clarified through subsequent amendments made as recently as December 2014.

While $300 million is a relatively small incentive compared with the fully loaded costs of biomedical research, it is significant and the estimated value to a manufacturer who seeks to be first-to-market when racing with a competitor could be much greater. The purchases of vouchers in 2014-15 have demonstrated that the market value is ~$300 million, equaling the estimates made by the researchers in 2006. While there are detractors who complain the PRV is too little (research and development costs are typically > $300 million), too broad (covers too many disease states with the inclusion of pediatric cancers) or too narrow (doesn't cover combination drugs; incentivizes innovation that would have occurred without the incentive) it has quickly become an established incentive in the neglected disease landscape. PRV is therefore a realistic and proven incentive to overcome a market failure. We advocate that the PRV prize-worthy disease list should be amended to include existing breakout diseases or potential breakout diseases.

<u>Expand PRV and other incentives</u>

National governments approve medicines for use in their jurisdictions. High income countries (e.g. US, Europe, China) have medicines regulatory agencies to review, approve and register medicines for their populations. These agencies have a variety of specialized mechanisms to encourage new treatments for rare domestic diseases and neglected global diseases.[12] We advocate that public and private sectors in high income countries make global diseases that are

[11] Ridley D, Grabowski H, Moe J "Developing Drugs for Developing Countries" Mar/Apr Health Affairs, 2006
[12] e.g. "Critical Path Priority list"

not endemic to their domestic populations a greater priority for their public (e.g. NIH, public universities) research programs, private sector (e.g. biopharma industry) and government regulatory processes.

> **Recommendation 1: The proposed Center shall convene selected regulatory agencies (e.g. EU countries, EMA, China, Japan) to consider prizes or other incentives (e.g. PRV) to reward manufacturers which register new treatments for targeted neglected and outbreak diseases.**
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> **Recommendation 2: The proposed Center shall work with International Council for Harmonization and/or the International Coalition of Medicines Regulatory Authorities to review and advocate for the appropriate use of "push" and "pull" incentives to create new incentives for research investment and new therapies for neglected and outbreak diseases.**

<u>Incentives supplemented by increasing public/private collaborations</u>

The current Zika and the recent Ebola outbreaks have illustrated the need for partnering between public and private players to meet the needs of existing patients and to predict and develop these vaccines and medicines needed to address future outbreaks.

One of the less well-known factors in the accelerated development of vaccines against the recent Ebola outbreak has been the unprecedented alliances which were formed, and continue to be formed, between commercial companies, large and small, governments and regions, university laboratories and hospitals, and funding agencies in order to accelerate the development, manufacture and distribution of vaccines for the outbreak. Continued discussion and development of actionable tools and protocols to replicate the successes of these alliances and to proactively deal with the difficulties which these alliances have faced are crucial.

The industry response to the 2014 Ebola outbreak was unusual. Mobilization of key players occurred quickly and once they engaged, players -- and the groundbreaking web of partnerships that emerged -- accelerated the development of Ebola vaccines in unprecedented ways.

Pre-existing formal and informal relationships between many of the parties set the groundwork for the rapid formation of consortia that enabled this extraordinarily fast and broad response. From the beginning, it became clear that these alliances were much wider across functions and borders than responses to any previous global epidemics.

The diversity of the members of these consortia and alliances had the potential to mire the negotiations and efforts in thickets of bureaucracy. Under normal circumstances, the number of formal agreements required to designate rights and obligations between biopharma companies and other participants in global health partnerships would have taken years to

complete. Formation of the informal GSK consortia alone required approximately 50 agreements. [13]

In the Ebola case, at least two major factors contributed to the unusual fast response: first, the parties began acting before the agreements were finalized in some cases and simultaneously in others, given the urgency of the situations; and second, they agreed on the sharing of rights and obligations at an unheard of speed. This shows how therapies for medical emergencies can be accelerated by broad partnerships when the will and urgent need is present. These broader ways of partnering have the potential to accelerate the race to address global health crises.

However, aside from the moral imperative that many of the major vaccine companies felt to mobilize their resources to accelerate the Ebola vaccine candidates as quickly as possible, they were also relying on other factors which they felt enabled them to engage:

- Appreciation of a public health imperative and opportunity for each to contribute in a valuable, and in some ways unique, manner to accelerate the development of a promising vaccine candidate

- Recognition and ready acceptance of the fact that engagement in Ebola vaccine development was for public health and not commercial reasons

- Expectation that vaccine development efforts would be advanced in collaboration with public sector partners to pool expertise, to share costs and risks, and to manage uncertainties

- Commitment of donor/funding organizations such as GAVI and UNICEF to procure and deliver an Ebola vaccine should it prove efficacious and safe[14]

The last two engagement conditions of sharing risk and commitment of funding organizations proved less straightforward than the industry had relied upon. Although there was supportive public funding, there was very little risk sharing, and a commitment of a funding organization did not occur until January 20th of this year when GAVI signed an agreement with Merck (known as MSD outside the U.S. and Canada) to "support the provision of a vaccine to protect against future deadly Ebola outbreaks" almost 2 years after the initial outbreak and over a year after Merck took a license to and began development of NewLink's vaccine candidate. [15]

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[13] author's private communication *with Julian Bouchard, Director of Licensing, GSK Vaccines*

[14] *authors* interpretation from private discussions with Mark Feinberg and based upon Feinberg IOM presentation March, 2015

[15] *GAVI press release dated January 20, 2016 and NewLink press release dated November 24th, 2014*

The agreement, announced at the World Economic Forum in Davos, is intended as an incentive for Merck to take the vaccine through licensure and WHO prequalification.

Under the Advance Purchase Commitment, GAVI provided US$ 5 million towards the development of Merck's rVSVΔG-ZEBOV-GP live attenuated Ebola Zaire vaccine, on the understanding that it will be submitted for licensure by the end of 2017. If approved, it would become the world's first licensed Ebola vaccines and GAVI would be able to begin purchasing the vaccine to create a stockpile for future outbreaks.

Additionally, Merck will ensure that 300,000 doses of the vaccine are available from May 2016 for use in expanded use clinical trials and/or for emergency use as needed while vaccine development continues. Merck has already submitted an application through the WHO's Emergency Use Assessment and Listing (EUAL) procedure. If the EUAL is approved, this will provide an opportunity for the investigational vaccine to be used if another public health emergency with Ebola occurs before the vaccine is approved.

This incentive, while necessary, is arguably too late in the process to encourage larger biopharmaceutical companies to engage again in such an intense, risky development program. Developed countries such as the U.S. are constructing and applying incentives to encourage companies with the abilities to develop and manufacture medicines and vaccines to protect against and treat infectious diseases. It would be even less attractive as an incentive for a smaller company to lead such an effort.

Developed countries such as the U.S., and regions such as the EU, through its IMI initiative, are constructing and beginning to apply a broader array of incentives to encourage the existing vaccine companies to continue to contribute to these global efforts as well as to engage more companies with the abilities to develop and manufacture medicines and vaccines to protect against and treat infectious diseases.

> **Recommendation 3: WHO, in collaboration with others, shall coordinate the surveillance necessary to predict future outbreaks and to consult with constituents' agencies responsible for their own internal medical protection, so that global needs can be coordinated with these efforts in developed countries and regions. The WHO can then fulfill its role in addressing current outbreaks and preparing for future ones. The resulting vaccines and medicines, as well as secure supplies of existing medicines and vaccines, can be scaled to fulfill orders placed by the WHO in consultation with its member organizations.**

<u>Biomedical Advanced Research and Development Authority (BARDA) as one model of a bundled incentives/procurement/supply capability</u>

At least one model exists for how the WHO may design and operate its new Center for Health Emergency Preparedness and Response. The Biomedical Advanced Research and Development Authority (BARDA), within the Office of the Assistant Secretary for Preparedness and Response

in the U.S. Department of Health and Human Services, is intended to provide an integrated, systematic approach to the development and purchase of the necessary vaccines, drugs, therapies, and diagnostic tools for public health medical emergencies. [16]

Recommendation 4: We recommendation that WHO, GAVI and other purchasers and providers of global health needs accelerate access to these medicines and vaccines through the scaling of BARDA's programs and results, as well as with those of other governmental and regional departments charged with similar responsibilities.

The US Pandemic All-Hazards Preparedness Act (PAHPA) of 2006 established BARDA as the lead agency in HHS for medical countermeasure development and has grown over the years into a surveillance, financial supporter, buyer and provider of vaccines and medicines to treat and prepare for the treatment of infectious diseases on a worldwide basis. Although its mission is to protect US citizens and military from these potential diseases, in fact this protection is needed for most of the world. BARDA's programs have resulted in 24 FDA approved drugs and vaccines. Fourteen of them are currently stockpiled by the United States.

A current example of a BARDA incentive program focuses on development of new antibiotics. In May 2013, BARDA entered into a strategic alliance with GlaxoSmithKline to launch a Portfolio Partnership. This partnership is a five-year, $200 million agreement formed under the Other Transactional Authority (OTA) granted to the US Health and Human Services department by the Pandemic and All Hazards Preparedness Act of 2006. Partnerships formed using OTA are not traditional government contracts and so allow for more flexible partnering arrangements.

In this case, instead of focusing the partnership on a single antibiotic candidate, this partnership supports an entire portfolio of candidate antibiotic therapies. The benefit of basing the partnership on a portfolio of candidates is that the partnership does not end if a particular product fails in clinical trials. [17] This type of flexible, long-term partnership could be duplicated on a global basis.

The parties receive reimbursement for drug development activities in real time. This approach is an alternative to and contrasts with that of models such as advanced market commitments, where reimbursement is provided only after the purchase of product, and milestone or prize payments, where awards are provided upon advancing a candidate antibiotic to predefined endpoints.

The near real-time direct reimbursement for drug development activities is a preferred structure for products in advanced development prior to approval. The "non-dilutive" funding provided by BARDA to support development activities does not need to be repaid and does not dilute shareholder's equity. Further, the funding can favorably impact the net present value calculation of the company partners when considering whether to undertake antibiotic

[16] *About/BARDA/Pages/default.aspx (US Public Health Emergency Home Page)*
[17] /Blog/ArticlePage.aspx?PostID=98

development projects by reducing their upfront costs. Three of the current six partnerships within this Broad Spectrum Antimicrobial program are now in Phase III clinical development.

BARDA is exploring and implementing a number of other incentive programs in order to fill not only the current projected needs for medicines and vaccines for medical countermeasures but to prepare for future infectious disease outbreaks. One goal is to bring vaccine candidates up through Phase 2a to prepare for the rapid acceleration through approval and manufacture which will be necessary upon the imminent onset of an emergency outbreak beyond local/regional manufacturing and stockpiling for priority infectious diseases, as exemplified by the Ebola outbreak.

In addition to such development incentives, BARDA also is responsible for developing and establishing stockpiles of lifesaving vaccines, drugs, and diagnostics. The Project BioShield Act of 2004 established the Special Reserve Fund (SRF), a one-time appropriation of $5.6 billion (2004 – 2013) to accelerate the research, development and acquisition of MCMs through eight Project BioShield programs which have led to the acquisition of MCMs for the Strategic National Stockpile (SNS). These include an anthrax vaccine for post-exposure prophylaxis, anthrax therapeutics, a novel smallpox vaccine, a smallpox antiviral drug, a botulinum antitoxin, and radiation countermeasures.

By scaling the manufacture of these and future medical countermeasures BARDA could quickly provide them to the WHO and other "purchasers" upon their request. Reimbursement could be through the partial satisfaction of the United States, or other supplier country's, level of contribution to the UN budget.

BARDA has stated[18] that developing MCMs for identified threats before they emerge needs risk acceptance and significant investment, but that the rapid development of MCMs in response to a disease after it emerges will be even more expensive. From BARDA's perspective, models in general need to have clear requirements, goals, and objectives, and a clearly defined marketplace. [19] Flexibility in the approach of incentive programs is essential, and should include the promotion of partnering mechanisms, such as are included in the EU's IMI program. Because of this Larsen said, traditional "BARDA's incentive programs to date have focused largely on push incentives for advanced research and development (e.g., subsidizing development costs) and pull incentives in the form of procurements (stockpiling or vendor-managed inventory of pharmaceuticals and supplies). Larsen acknowledged that, in order to respond to an emerging infectious disease, alternative business models will likely be required to incentivize industry, and a mix of push and pull mechanisms need to be considered and implemented, especially when considering how to appeal to both small, nimble companies and

[18] Author's private communication with Joe Larsen, Chief Broad Spectrum Antimicrobials Program at BARDA

[19] Author's private communication with Joe Larsen, BARDA

larger companies with more resources and capabilities. For products targeting emerging infectious disease threats, partial or full de-linkage pull models will likely be necessary to reward innovation in the face of market uncertainty, he said." [20]

The commission advocates for "stockpiling" in or near an affected country when feasable. We assert that beyond local/regional manufacturing and stockpiling, an additional consideration can be adjunctive: selected disease response should include scaling existing stockpiles managed by BARDA and similar institutions in other countries for therapies that are both pandemic diseases and pose security risks.[21] We describe these diseases as a unique category we call *priority diseases.*

Public/Private Collaborations

Governments and the proposed Framework Center should initiate public/private collaborations. U.S. federal agencies such as NIH, AHRQ, and the FDA have employed the public private partnership (PPP) structure in promising and novel organizational structures. PPPs provide an economically compelling way for federal agencies and stakeholders to leverage resources and know-how via aligned missions for the benefit of patients and consumers. There are numerous business models that may be developed to facilitate implementation of different public/private collaborations depending on the scientific goals, the resources available, the partners involved and the different leveraging mechanisms used. Regardless of their scope, and objectives, PPPs (as one structure for public/private collaboration) can achieve synergies in which the whole is greater than the sum of the parts/partners, and significant strides can be made in product development and regulatory review. Because PPPs represent a mechanism for FDA (other U.S. agencies; other countries) to accomplish their mission, by sharing risks and benefits, the FDA has been willing and eager to engage with stakeholders in appropriate, pre-competitive ways, to facilitate bringing safe and effective medicines to patients and consumers. These models can be adapted by the proposed Center and inform new public/private collaborations to accelerate research and development for neglected, outbreak and emergent new diseases.

Representative health-related PPP's with US federal government involvement are listed below. They are for illustrative purposes only. The purpose, structure and administration of PPP's or other public/private collaborations appropriate to accelerated global disease responses will differ in their purpose, structure, processes and policies; are not exclusively US-initiated.

• **Critical Path Institute: The Critical Path Institute (CPI)**, founded in 2005 in Tucson, Arizona, is an independent, non-profit organization dedicated to bringing scientists from the FDA, industry

[20] Footnote to *Rapid Medical Countermeasure Response to Infectious Diseases: Enabling Sustainable Capabilities Through Ongoing Public and Private Partnerships: Workshop Summary*

[21] Author's private communication with Joe Larsen, BARDA

and academia all together to collaborate and improve the drug development and regulatory process for medical products.
http://c-path.org/

Predictive Safety Testing Consortium (PSTC): PSTC brings together pharmaceutical companies to share and validate innovative safety testing methods under advisement of the FDA, its European counterpart, the EMA (European Medicines Agency), and PMDA (Japanese Pharmaceutical and Medical Devices Agency). Developed collaboration model, business plan and governance, co-authored and was lead FDA negotiator on all formal agreements among FDA and industry members. http://c-path.org/programs/pstc/

Clinical Trials Transformation Initiative (CTTI): CTTI engages all stakeholders as equal partners to analyze existing research impediments and recommend consensus-driven, actionable solutions that will lead to a more sustainable and effective clinical trial system
http://www.ctti-clinicaltrials.org/

Center for Education and Research on Therapeutics (CERT): The mission of CERTs is to conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products; increase awareness of the benefits and risks of therapeutics; and improve quality while cutting the costs of care.
CERTs consists of 6 research centers and a central scientific coordinating center, the CERTs Scientific Forum. The Centers receive funds from both public and private sources, with core financial support from the Agency for Healthcare Research and Quality (AHRQ).
http://certs.hhs.gov/index.html
Consortium):
http://c-path.org/programs/pro/

> **Recommendation 5: The proposed Center itself and/or in collaboration with individual country regulatory agencies or representative "aggregate" regulatory groups (International Council for Harmonization, International Coalition of Medicines Regulatory Authorities) shall participate in or initiate public/private collaborations to 1) accelerate the translation of scientific insights to new product development, 2) accelerate regulatory review, 3) accelerate the dissemination of information on appropriate and emerging uses of existing medicines and emergent new therapies for neglected and outbreak diseases.**

Summary: Accelerating the Response to Infectious Disease Outbreaks

An accelerated response to existing neglected diseases and disease outbreaks will require new structures, processes and policies, engaging both the public and private sectors. We endorse the creation of a Center for Health Emergency Preparedness and Response (CHEPR) which includes capabilities for "surveillance for outbreaks and events, risk assessment, planning and execution of response, assessment of IHR functions and compliance, coordination with partners, risk communication, quality assurance, and monitoring. The Framework, however,

does not attend to critical components that have demonstrated their effectiveness: new incentives, new national policies, public/private partnerships, model language for agreements to share data and intellectual property, and stockpiling of existing medicines based upon mechanisms used by the US Department of Health and Human Services through BARDA. We believe these additions, which emphasize collaboration with the private sector, will ensure rapidity of response and increasing the access of existing medicines and additional research on diseases where new treatments or vaccines are needed.