Broad-spectrum antiviral drugs: A survey of neglect

Policy, funding and R&D landscape

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ABSTRACT

Events that could cause human extinction or permanently alter the trajectory of humanity are known as **existential risks**¹. **Global catastrophic biological risks** (GCBRs) are a recognized subset of these risks, and include both natural and engineered pathogens². Viral pathogens are of particular concern due to their high virulence and transmissibility³.

Various actors including national governments, scientific agencies and philanthropic institutes have attempted to address the risk posed by viral pathogens by supporting **broad-spectrum antiviral** (BSAV) development. This report aims to describe the global landscape of this effort to date, including:

- 1: The **policy and practice** landscape for BSAV funding and research, internationally
- 2: The United States **policy and practice** landscape
- 3: Past and present United States **R&D efforts** towards BSAVs

This report will be most useful for those who are interested in biorisk/biosecurity, are somewhat aware of why antivirals are important, and would like to read in-depth regarding the current state of BSAV development.

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¹ (n.d.). Global Catastrophic Risks. Retrieved August 7, 2019, from <http://www.global-catastrophic-risks.com/>

² (n.d.). Global Catastrophic Biological Risks – Mary Ann Liebert, Inc.. Retrieved August 7, 2019, from <https://www.liebertpub.com/doi/full/10.1089/hs.2017.0038>

³ (n.d.). Research and Development to Decrease Biosecurity Risks from Viral Retrieved August 7, 2019, from <https://www.openphilanthropy.org/research/cause-reports/research-and-development-decrease-biosecurity-risks-viral-pathogens>

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INTRODUCTION

What are global catastrophic biological risks?

The Johns Hopkins Center for Health Security has created a working definition of global catastrophic biological risks (GCBRs)⁴.

“Those events in which biological agents—whether naturally emerging or reemerging, deliberately created and released, or laboratory engineered and escaped—could lead to sudden, extraordinary, widespread disaster beyond the collective capability of national and international governments and the private sector to control.

If unchecked, GCBRs would lead to great suffering, loss of life, and sustained damage to national governments, international relationships, economies, societal stability or global security.”

It is important to note that GCBRs are a wide class of risks. In this report, we focus on one slice of this risk, and one possible intervention to mitigate it, namely: viral pathogens and broad-spectrum antivirals.

Why are viral pathogens so concerning?

While many types of biological agents could satisfy this definition, viral pathogens are of most concern due to their ability to harm hosts (known as virulence/pathogenicity) as well as their capacity for airborne or contact transmission between hosts⁵. Examples of natural viral pandemics include the 1918 influenza pandemic, and more recently, the Ebola and Zika outbreaks.

We have yet to witness an engineered viral pathogen cause a pandemic. However, advancing biotechnology makes this a growing concern. Please also refer to Open Philanthropy Project’s [report](#) for a systematic analysis of why viral pathogens pose substantial existential risks⁶.

Why do we need broad-spectrum antivirals?

There is no standard definition of broad-spectrum in the scientific literature. **In this report, broad-spectrum antivirals are defined as antivirals efficacious against multiple viral species, that are not within the same genus or family.**

⁴ (n.d.). Global Catastrophic Biological Risks – Mary Ann Liebert, Inc.. Retrieved August 7, 2019, from <https://www.liebertpub.com/doi/full/10.1089/hs.2017.0038>

⁵ "Center for Health Security: Characteristics of Pandemic" 10 May. 2018, http://www.centerforhealthsecurity.org/newsroom/center-news/2018/2018-05-10_characteristics-of-pandemic-pathogens.html. Accessed 2 Oct. 2019.

⁶ (n.d.). Research and Development to Decrease Biosecurity Risks from Viral Retrieved August 7, 2019, from <https://www.openphilanthropy.org/research/cause-reports/research-and-development-decrease-biosecurity-risks-viral-pathogens>

Research indicates antivirals are an important measure that can help delay viral pandemics while additional strategies are implemented^{7,8}. They also represent a more cost-effective strategy than quarantine, which has significant economic impact⁷. Antivirals can be used to both treat infected patients, as well as reduce the susceptibility of uninfected individuals⁷.

However, existing antivirals are not suitable for the treatment of emerging viral pathogens. As noted by Adalja and Inglesby (2019)⁹:

“Nearly every novel viral epidemic of regional or global importance has been characterized by the common refrain that supportive care is the mainstay of therapy with drug trials coming, for the most part, post-outbreak.”

Small molecule antiviral drugs are available for the treatment of highly researched pathogens, such as herpesviruses, HIV, HBV, HCV and (with less efficacy) influenza¹⁰. Antiviral drugs, whether narrow or broad spectrum, are largely not available for emerging, neglected or entirely novel viral pathogens¹¹.

Scientific and technical challenges

Viral medical countermeasures face particular challenges. Viruses have small genomes and proteomes, often consisting of just a few genes and proteins, respectively. As a result, viruses are extremely divergent: they do not often share genes, proteins or mechanisms. It is therefore difficult to find compounds that can directly target and inhibit multiple different viruses.

One approach to creating broad-spectrum antiviral drugs is to inhibit host cell proteins. Viruses are obligate intracellular parasites, in that they rely on their hosts to survive and replicate. This host-targeting approach has the added advantage of reducing antiviral resistance. Resistance to drugs develops when viruses develop mutations that allow them to escape a drug's action (more pronounced in RNA viruses¹²). When the drug target is under host genetic control, viruses are less easily able to develop resistance. However, inhibiting host cell functions raises toxicity concerns. Kinase inhibitors, previously developed as cancer chemotherapies, may be repurposed as broad-spectrum antivirals but have many side-effects¹³. Another approach has been to boost existing immune system function. While these drugs can have broad-spectrum effects, they have also had high toxicity, such as in the case of interferons¹⁴.

⁷ "Pandemics: Risks, Impacts, and Mitigation – Disease Control ... – NCBI." <https://www.ncbi.nlm.nih.gov/books/NBK525302/>. Accessed 15 Aug. 2019.

⁸ "Effectiveness and Cost-Effectiveness of Expanded Antiviral" 15 Dec. 2009, <https://annals.org/aim/fullarticle/745380/effectiveness-cost-effectiveness-expanded-antiviral-pro-phylaxis-adjuvanted-vaccination-strategies-influenza>. Accessed 15 Aug. 2019.

⁹ "Broad-Spectrum Antiviral Agents: A Crucial Pandemic Tool. – NCBI." 24 Jun. 2019, <https://www.ncbi.nlm.nih.gov/pubmed/31216912>. Accessed 22 Aug. 2019.

¹⁰ (2013, April 4). Intervention strategies for emerging viruses: use of antivirals. – NCBI. Retrieved August 7, 2019, from <https://www.ncbi.nlm.nih.gov/pubmed/23562753>

¹¹ (2013, April 4). Intervention strategies for emerging viruses: use of antivirals. – NCBI. Retrieved August 7, 2019, from <https://www.ncbi.nlm.nih.gov/pubmed/23562753>

¹² "Center for Health Security: Characteristics of Pandemic" 10 May. 2018, http://www.centerforhealthsecurity.org/newsroom/center-news/2018/2018-05-10_characteristics-of-pandemic-pathogens.html. Accessed 8 Oct. 2019.

¹³ "Repurposing of Kinase Inhibitors as Broad-Spectrum Antiviral" 1 Feb. 2018, <https://www.liebertpub.com/doi/10.1089/dna.2017.4033>. Accessed 10 Feb. 2020.

¹⁴ "Antiviral Actions of Interferons | Clinical Microbiology Reviews." <https://cmr.asm.org/content/14/4/778.short>. Accessed 10 Feb. 2020.

Regulatory and commercial challenges

Drug development is highly regulated in most countries, requiring clinical trials to assess safety and efficacy. Most regulatory processes require drugs be approved for a specific, single indication. Broad-spectrum drugs, therefore, must undergo multiple approval processes for each disease indication, or be prescribed by physicians “off-label”. This makes the development of a broad-spectrum agent financially riskier than the development of specific, single-virus agents. It is also expensive to develop the facilities required to handle viruses, as they must be equipped with the highest security and safety standards¹⁵.

All medical countermeasures (MCMs) for rare, catastrophic events face challenges in securing interest and investment from the private sector. Pharmaceutical companies are often unwilling to develop medicines for rare events that risk destroying global economies and thus the very mechanism for return on investment¹⁶. Socioeconomic disparities contribute to this disincentive as well; emerging pathogens spread more quickly in structurally and economically weak regions¹⁰.

Researchers such as Adalja and Inglesby have recently espoused the development of potent, broad-spectrum antiviral drugs^{17,18,19,20,21}. These could be used in cases where the exact identity of a virus is as yet unknown, or when no specific treatments exist. Creation of such broad-acting agents necessarily requires an approach counter to the traditional “one bug-one drug” strategy of drug development.

¹⁵ "Defense Against Biological Attacks – Volume II | Sunit K. Singh | Springer."

<https://www.springer.com/gp/book/9783030030704>. Accessed 22 Aug. 2019.

¹⁶ (2017, November 28). Overview of the Department of Defense's (DoD) Advanced Retrieved August 7, 2019, from

https://www.cbdstconference.com/docs/default-source/2017/tues_1715_adm-overview.pdf

¹⁷ (2013, April 4). Intervention strategies for emerging viruses: use of antivirals. – NCBI. Retrieved August 7, 2019, from <https://www.ncbi.nlm.nih.gov/pubmed/23562753>

¹⁸ (n.d.). Antiviral drug discovery: broad-spectrum drugs from nature. – NCBI. Retrieved August 7, 2019, from <https://www.ncbi.nlm.nih.gov/pubmed/25315648>

¹⁹ (n.d.). The future of antivirals: broad-spectrum inhibitors. – NCBI. Retrieved August 7, 2019, from <https://www.ncbi.nlm.nih.gov/pubmed/26524332>

²⁰ (2015, June 15). Broad-spectrum antivirals against viral fusion | Nature Reviews Retrieved August 7, 2019, from <https://www.nature.com/articles/nrmicro3475>

²¹ (n.d.). Broad-spectrum antiviral agents | Microbiology – Frontiers. Retrieved August 7, 2019, from <https://www.frontiersin.org/articles/144511>

CHAPTER ONE:

International Policy and Practice

This chapter focuses on the relevant international, intergovernmental organizations under whose ambit viral medical countermeasures fall. Organizations that play a role more broadly in biosecurity and pandemics (such as the World Bank) are included in the [Appendix](#).

In short, some of these organizations are currently working on viral medical countermeasures. However, there are essentially no coordinated international efforts towards **broad-spectrum antivirals** in particular.

Year Est.	Actor	Broad-spectrum antiviral efforts	Notes
1948	World Health Organization	Yes	Antivirals a lower priority than vaccines. Influenza antivirals prioritized (categorized as narrow-spectrum by this report). Policies published in 2002 pertaining to both intentional and unintentional release.
2001	Global Health Security Initiative	No	Informal international partnership formed after global influenza outbreaks. Focused on mitigating pandemic influenza.
2011	The Global Virus Network	No	International academic research network. Annual summaries of activity for 2016–2018 show a focus on narrow-spectrum therapeutics. No broad-spectrum efforts as defined by this report.
2014	Global Health Security Agenda	No	International agenda that addresses both intentional and unintentional release, and the first to use global catastrophic terminology. Focuses on best practices for safety and diagnostics. Unclear efforts towards antivirals.
2016	Coalition for Epidemic Preparedness Innovations	No	Public & private partnership that includes many governments and the Gates Foundation. Works on vaccines only.

Table 1: International intergovernmental organizations and their efforts pertaining to broad-spectrum antivirals. Year the organization was established is included for chronological context, and has no relationship with specific antiviral efforts.

The World Health Organization and World Health Assembly

The WHA is the decision-making body of the WHO, composed of its member states. The WHO is a specialized agency of the United Nations focused on international public health. Control of the international spread of infectious disease has been a core function of the WHO since 1948²², and it remains one of its 6 leadership priorities²³:

- Advancing universal health coverage
- Achieving health-related development goals
- Noncommunicable diseases and mental health
- **Acute public health threats (disease outbreaks & humanitarian crises)**
- Access to safe, efficacious and affordable medical products
- Social, economic and environmental determinants of health

The WHO's Health Emergencies Programme uses the International Health Regulations (IHR 2005), a set of international laws last updated in 2005, to promote international collaboration with regards to outbreak control. It is each member state's obligation to incorporate IHR 2005 mandates into their national laws. The IHR 2005 establishes 24/7 communication between countries and the WHO, via National IHR Focal Points²⁴ which form a network of international communication.

Figure 1: Major epidemic threats since 2000 and resultant WHO international collaboration efforts.

²² "The Global Outbreak Alert and Response Network - NCBI - NIH." 4 Sep. 2014, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4205922/>. Accessed 15 Aug. 2019.

²³ "The Global Guardian of Public Health - World Health Organization." <https://www.who.int/about/what-we-do/global-guardian-of-public-health.pdf?ua=1>. Accessed 15 Aug. 2019.

²⁴ "WHO | World Health Organization." <https://www.who.int/ihr/nfp/en/>. Accessed 2 Oct. 2019.

The World Health Assembly has previously published agendas explicitly regarding global health security and medical countermeasures:

WHA 55.14: Ensuring accessibility of essential medicines²⁵

- The WHO maintains a list of essential medicines, and this list is continually updated based on evidence (“science-based, independent of external pressures, and subject to regular reviews”)
- Advocates “the necessary action worldwide to promote market-based differential pricing for essential medicines between high-, middle-, and low-income countries”

WHA 54.14 & 55.16: Global public health response to natural occurrence, accidental release or deliberate use of biological and chemical agents or radionuclear material that affect health²⁶

- Stresses the need for Member States to work together for epidemic alert & response, and global health security
- States “one of the most effective methods of preparing for deliberately caused disease is to strengthen public health surveillance and response”
- Urges Member States:
 - To have national disease surveillance plans
 - To collaborate
 - To treat deliberate use of biological agents as a global public health threat
- Requests
 - To strengthen global surveillance of infectious disease
 - To provide support for emergency preparedness plans
 - To issue international guidance for how to deal with deliberate use
 - To examine the development of new tools, such as modelling of natural epidemics

Year Est.	WHO Effort	Description	Antiviral provisions
1997	Outbreak Verification System	Verification of outbreaks and distribution of Outbreak Verification List to public health officials and scientists.	None intended.
1997	International Coordinating Group on Vaccine Provision (ICG)	Manages provision of emergency vaccine supplies and medicines to supply to countries during major outbreaks. It also works on forecasting vaccine stocks, negotiating prices, and evaluating treatment protocols. National distribution planning is a requirement for member states.	Some. Consists of stockpiling of existing antivirals. ICG stockpiles MCMs for cholera, meningitis & yellow fever only ²⁷ .
2000	Global Alliance for Vaccines and Immunisation	Financing body for ICG’s stockpiles, for GAVI member countries. Donors and international agencies support funding for non-GAVI countries.	As above for ICG.

²⁵ "Ensuring accessibility of essential medicines – World Health" 18 May. 2002, http://apps.who.int/gb/archive/pdf_files/WHA55/ewha5514.pdf. Accessed 2 Oct. 2019.

²⁶ "Global public health response to natural occurrence" 18 May. 2002, http://apps.who.int/gb/archive/pdf_files/WHA55/ewha5516.pdf. Accessed 2 Oct. 2019.

²⁷ "International Coordinating Group (ICG) on Vaccine Provision – WHO." 17 Jun. 2016, <https://www.who.int/csr/disease/icg/qa/en/>. Accessed 15 Aug. 2019.

2000	Global Outbreak Alert and Response Network (GOARN)	Network of institutions, NGOs etc. for the rapid identification, confirmation and response to outbreaks. Coordinated by WHO. The WHO uses 6 main criteria to determine whether a reported disease event is of international concern.	None intended.
2005	International Health Regulations	First established in 1969, with updates in 2005. Set of international laws that gave unprecedented authority to WHO to provide global public health security. Establishes 24/7 communication between countries and the WHO, procedures for notification of outbreaks.	None intended.
2009	Emerging and Dangerous Pathogens Lab Network (EDPLN)	Made up of highly secure diagnostic labs. Contributes to the rapid development of diagnostic assays. The WHO enforces standards in these labs and helps transfer technology to the point of care.	None intended.
2011	Pandemic Influenza Preparedness Framework	Established for the sharing of H5N1 & other emerging influenza viruses with pandemic potential, and access to vaccines & medicines. Under PIP, the WHO has real-time access to 10% of global vaccine production. <i>Of note, the WHO Antiviral Working Group (AVWG) focuses on influenza (full name of group is WHO expert working group on surveillance of influenza antiviral susceptibility)^{28, 29}.</i>	Yes, influenza only.
2011	Global Influenza Surveillance and Response System	This monitoring and response system originally dates back to 1952 when it was known as the Global Influenza Surveillance Network (GISN). GISRS is the network by which the PIP framework is implemented. Manufacturers get access to flu viruses via GISRS, in exchange for paying an annual fee totalling US \$28M . 70% of these funds are used for preparedness and 30% are allocated for response ³⁰ .	Yes, influenza only.
2013	Battle against Respiratory Viruses	A research agenda developed by the WHO in collaboration with clinicians and scientists.	Yes, advocates for broad-spectrum. See details below.
2016	Emerging Disease Clinical Assessment and Response Network (EDCARN)	Created in response to the Ebola epidemic. Intended to streamline agency's response to crises. Focuses on providing guidance for clinicians, for the diagnosis and treatment of infections.	Unclear.
2019	Global Influenza Strategy	Latest WHO strategy overview for influenza.	Yes, advocates for influenza antivirals .

Table 2: Overview of specific efforts by the WHO to counter epidemics and pandemics. The majority are focused on early detection of outbreaks. Of the various medical countermeasures, vaccines are the most prominent.

²⁸ "Influenza viruses – antiviral therapy and resistance – NCBI." 25 Apr. 2017, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6301739/>. Accessed 15 Aug. 2019.

²⁹ "Global update on the susceptibility of human ... – ScienceDirect.com." <https://www.sciencedirect.com/science/article/pii/S0166354218302250>. Accessed 15 Aug. 2019.

³⁰ "Pandemic Influenza Preparedness Framework – WHO." <https://www.who.int/features/qa/pandemic-influenza-preparedness/en/>. Accessed 15 Aug. 2019.

Antivirals are of some focus within the WHO. GISRS (summary in Table 2) hosts expert groups on antiviral drugs for influenza treatment. The WHO's most recent [Global Influenza Strategy](#) (2019–2030) addresses the need for broader-spectrum, more efficacious antivirals:

Action 1A:

ii. *Promote the development of more effective influenza treatments, including antiviral drugs, broadly reactive monoclonal antibodies and host-response immune modulators.*

Antiviral drugs and other treatments:

The current global use of antiviral drugs for seasonal influenza is low, thus limiting the current supplies and surge capacity.... Antiviral drugs will have a prominent role during a pandemic, especially during the early months, because vaccines will be unavailable initially.

Figure 2: Components of the WHO's global influenza surveillance and response system.

Figure 9: Antivirals Prescribed Compared to ICU and Ventilation Admissions (by Admit Date), April to December 2009

Figure 3: WHO data indicating a reduction in ICU admissions and ventilation admissions when antiviral prescription increases³¹.

Branching out from influenza to respiratory viruses in general, the WHO's Battle against Respiratory Viruses (BRaVe)³² research agenda states that "innovative approaches targeting broad-spectrum pathogens" are needed for patients with multiple infections, and for global health security.

WHO [BRaVe Priority Research Questions](#) (2013):

- 3.1 Develop and test new antivirals and combinations of antivirals for major respiratory viral pathogens according to their burden:
 - ...prioritize development of inhibitors for [respiratory syncytial virus] and rhinovirus
 - ...prioritize the development of influenza inhibitors
 - Test... combination antiviral therapy in... influenza
- 3.2 Develop novel antiviral modalities and test their effectiveness:
 - Existing **broad-spectrum antivirals** (favipiravir and nitazoxanide)
 - **Broad-spectrum antivirals against emerging viral threats (e.g. interferons for novel coronavirus)**
 - **Host pathway-directed therapies**, particularly those potentially inhibiting replication of multiple viral pathogens

No publicly available follow-up documents have been published since 2013 regarding the BRaVe Priority Research questions.

³¹ "World Health Organization - ppt video online download - SlidePlayer."

<https://slideplayer.com/slide/9131036/>. Accessed 15 Aug. 2019.

³² "Research needs for the Battle against Respiratory Viruses (BRaVe)."

https://www.who.int/influenza/patient_care/clinical/BRaVe_Research_Agenda_2013.pdf. Accessed 8 Aug. 2019.

Global Health Security Initiative

The GHSI is an “informal, international partnership among like-minded countries to strengthen health preparedness and response globally to threats of biological, chemical, radio-nuclear terrorism and pandemic influenza”³³. It was launched in 2001 by Canada and includes the EU, France, Germany, Italy, Japan, Mexico, the UK and the US. The WHO serves as expert advisor to the GHSI. The most recent Ministerial Statements from GHSI were published in March 2018 and focus on the threat of pandemic influenza³⁴.

The Global Virus Network

The GVN was established in 2011 to “strengthen research and responses to emerging viral causes of human disease and to prepare against new viral pandemics”³⁵. There are 45 GVN Centers of Excellence and 7 affiliate laboratories in 29 countries.

The GVN is not a public institution. However, they do work with governments to ensure that funding for virology is kept high. Each GVN Center of Excellence is directed by a medical virologist.

In the past, GVN has formed task forces in response to epidemics. They have not explicitly expressed an interest in developing broad-spectrum antivirals as a research priority.

“In response to the spread of chikungunya, the GVN formed a task force to identify research gaps and opportunities, including models of infection and disease, candidate vaccines and antivirals, epidemiology...”³⁶

Each year the network publishes an article in *Antiviral Research* summarizing the annual international meeting of the GVN. Reports from 2016–2018 describe efforts focused on narrow-spectrum therapeutics, with only 1 mention of a truly broad-spectrum agent as defined by this report^{37,38,39}. This was a citation of a previous paper published by the journal on favipiravir by Furuta et al. in 2013⁴⁰.

³³ "Global Health Security Initiative (GHSI)." <http://www.ghsi.ca/>. Accessed 8 Aug. 2019.

³⁴ "(GHSI), London, United Kingdom — March 9 – Global Health Security" 9 Mar. 2018, <http://www.ghsi.ca/english/statementLondon2018.asp>. Accessed 8 Aug. 2019.

³⁵ "2018 international meeting of the Global Virus Network – ResearchGate." 1 Feb. 2019, https://www.researchgate.net/publication/330658512_2018_international_meeting_of_the_Global_Virus_Network. Accessed 8 Aug. 2019.

³⁶ "The Global Virus Network: Challenging chikungunya – NCBI." 10 Jun. 2015, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4843800/>. Accessed 8 Aug. 2019.

³⁷ "2016 International meeting of the Global Virus Network. – NCBI." 16 Mar. 2017, <https://www.ncbi.nlm.nih.gov/pubmed/28315708>. Accessed 16 Aug. 2019.

³⁸ "2017 international meeting of the Global Virus Network. – NCBI." 5 Feb. 2018, <https://www.ncbi.nlm.nih.gov/pubmed/29421321>. Accessed 16 Aug. 2019.

³⁹ "2018 international meeting of the Global Virus Network. – NCBI." 25 Jan. 2019, <https://www.ncbi.nlm.nih.gov/pubmed/30690044>. Accessed 16 Aug. 2019.

⁴⁰ "Favipiravir (T-705), a novel viral RNA polymerase inhibitor.." <https://www.ncbi.nlm.nih.gov/pubmed/24084488>. Accessed 2 Oct. 2019.

Global Health Security Agenda

Not to be confused with the GHSI, the GHSA is a “five-year multilateral initiative aimed at enhancing public health capacities in order to better prevent, detect and respond to both human and animal infectious disease threats”⁴¹. Lead by the US, it was launched in February 2014 and the G7 endorsed GHSA in June 2014 (Canada, France, Germany, Italy, Japan, UK, US). It currently consists of 64 nations, international organizations and non-governmental stakeholders⁴² which differentiates it from the smaller, more informal GHSI group. It was renewed until 2024.

Actor	Date	Funding (\$USD)	Notes
United States	July 2015	\$1B	Committed
US - CDC	Dec 2017	\$453.8M	Towards US commitment above
US - USAID	Dec 2017	\$245.5M	Towards US commitment above
Canada	2016	\$20M	
Australia	2017	\$240M	Earmarked to establish Health Security Initiative for Indo-Pacific region.
South Korea	Unknown	\$100M	Focusing on immunization, labs, workforce development
World Bank IDA	Unknown	\$110M	Regional disease surveillance systems enhancement project
<i>Total</i>		~1.47B+	<i>Other contributors have provided unspecified amounts, including other governments & the Gates Foundation.</i>

Table 3: Funding to date towards the Global Health Security Agenda⁴³.

GHSA 2024 Framework [Action Packages](#): Biosafety and Biosecurity

- Issue
 - “Need to ensure proper biosafety (unintentional release) and biosecurity (intentional release)”
 - “The risk of a catastrophic biological event continues to be magnified by global travel, urbanization, terrorist interest in weapons of mass destruction, and rapid advances in technology”
- Desired national impact
 - “Comprehensive... national oversight programs”
 - “A cadre of biological risk management experts”
 - “Biological risk management best practices”
 - “Rapid and culture-free diagnostics”

⁴¹ "Mapping the Global Health Security Agenda | Global Biodefense." 29 Mar. 2016, <https://globalbiodefense.com/2016/03/29/mapping-global-health-security-agenda/>. Accessed 8 Aug. 2019.

⁴² "Global Health Security Agenda." <https://www.ghsagenda.org/>. Accessed 8 Aug. 2019.

⁴³ "Implementing the Global Health Security Agenda: Progress and" <https://www.ghsagenda.org/docs/default-source/default-document-library/global-health-security-agenda-2017-progress-and-impact-from-u-s-investments.pdf>. Accessed 15 Aug. 2019.

GHSA 2024 Framework [Action Packages](#): Immunization

- *This action package proposal was under development at the time of this report*

GHSA 2024 Framework [Action Packages](#): Emergency Operations Centers

- *This action package proposal was under development at the time of this report*

The **development of antivirals is not mentioned** as an action that GHSA will be taking as part of their 2024 framework.

Figure 4: GHSA member countries.

Coalition for Epidemic Preparedness Innovations

CEPI is a global partnership between public, private, philanthropic and civil society organizations. Their goal is to accelerate the development of vaccines against infectious diseases and ensure equitable access to these vaccines. CEPI was founded at Davos in 2016 by the governments of Norway and India, as well as the Bill & Melinda Gates Foundation, the Wellcome Trust and the World Economic Forum. They have offices in Oslo, London and Washington, D.C. As researchers in the field have noted, CEPI has not supported, and **does not plan to support other innovations such as antiviral drug discovery**⁴⁴.

⁴⁴ "Allen Ross: Vaccination alone will not halt the next global ... - BMJ Blogs." 9 Jun. 2017, <https://blogs.bmj.com/bmj/2017/06/09/allen-ross-vaccination-alone-will-not-halt-the-next-global-pandemic/>. Accessed 8 Aug. 2019.

CHAPTER TWO:

United States Policy and Practice

This chapter focuses on policies and practices regarding viral medical countermeasures by all relevant branches of the United States government. The United States government is a focus of this report as it is likely the single largest spender on health security issues. Much of their work is also public, and thus researchable, as compared to other nation states. It is also the leader of the recent Global Health Security Agenda (see Chapter 1).

The United States has funded and continues to fund broad-spectrum antiviral research. Despite the large budgets of their biosecurity initiatives, it is in fact their academic research institutes that are providing the majority of funding for this work. This may be due to a variety of factors, including the scientific difficulty of developing broad-spectrum antivirals. [Chapter 3](#) provides details on specific R&D efforts that are being funded within the US. Philanthropic actors within the United States are not covered in this report.

This chapter is a preliminary survey of funding for broad-spectrum antivirals in particular. For a more in-depth review of federal funding for health security overall, see [Federal Funding for Health Security in FY2019](#).

Actor	Broad-spectrum antiviral efforts	% of eligible funding going towards BSAVs	Notes
Centers for Disease Control (CDC)	No	None directly eligible.	In 2018, the CDC was separated from other biosecurity efforts. Focuses on disease prevention & monitoring, health promotion.
Food and Drug Administration (FDA)	No	None directly eligible.	The FDA partners with other offices to fast-track countermeasures during epidemics. To date, no fast-tracking has been authorized for a BSAV.
National Institutes of Health (NIH)	Yes	~7% of explicit countermeasures funding grants. Additional via standard grants.	Most funding announcements pertain to chemical/radiological threats, not biological ones. Biological threat funding is via NIAID – see below.
National Institute of Allergy and Infectious Disease (NIAID, within NIH)	Yes, ~\$245M+	Roughly 1% annually	% of funding available for <i>emerging infectious disease</i> and <i>biodefense</i> .
Office of the Assistant Secretary for Health (OASH)	No	None	OASH disease areas of focus include HIV/AIDS, viral hepatitis, antibiotic resistant bacteria, tick-borne disease. They formulate the National Vaccine Plan.
Office of the Assistant Secretary for Preparedness and Response (ASPR)	Yes	See below	The ASPR office contains several biosecurity initiatives, which are detailed in the rows below.

BARDA, the Biomedical Advanced Research and Development Authority (within ASPR)	Yes	1.5% of all initiatives to date (1/67)	Helps the public & private sectors in the development of medical countermeasures, through support resources and capital investment/grants. Prioritizes broad-spectrum MCMs, although mainly antibiotics vs. antivirals. To-date, has supported 42 FDA approved products to address chemical, radiological, biological, influenza and emerging infectious disease threats.
Strategic National Stockpile (within ASPR)	No	None	The Stockpile does not appear to contain broad-spectrum antivirals.
Office of Global Affairs (within ASPR)	No	None	The diplomatic arm of HHS. Broad-spectrum antivirals are not currently a priority.
Office of Science and Technology Policy	No	No published guidance on BSAVs.	Provides scientific guidance to the President. Previously advised a temporary ban on gain-of-function research.
DoD and DARPA	Yes	Not publicly available.	Military arm of US government. Has made biosecurity and medical countermeasure related grants.
National Biodefense Analysis and Countermeasures Center	Possibly	Unknown	Collaborates with DoD and NIH to plan and conduct biodefense research. Has BSL-4 capability.

Table 4: Branches of the US government and their current efforts towards broad-spectrum antivirals.

Department of Health and Human Services (HHS)

A cabinet-level department within the US federal government, HHS is responsible for providing all essential health services to Americans. It achieves this via multiple offices and operating divisions, including:

- Agency for Toxic Substances and Disease Registry
 - Includes chemical and environmental health emergencies
- Centers for Disease Control and Prevention
 - Includes the National Center for Emerging and Zoonotic Infectious Diseases
- Food and Drug Administration
- National Institutes of Health
- Office of the Assistant Secretary for Health
 - Office of Infectious Disease
 - National vaccine advisory committee (NVAC)
- Office of the Assistant Secretary for Preparedness and Response
 - Includes BARDA and the Strategic National Stockpile
- Office of Global Affairs
- Full list [here](#)

For the purposes of this report, relevant offices/divisions within HHS are listed separately below.

Centers for Disease Control and Prevention

Division within HHS. “Serves as the national focus for developing and applying disease prevention and control, environmental health, and health promotion & education activities designed to improve the health of the people of the United States”⁴⁵. Biosecurity and medical treatment generally does not fall under their jurisdiction.

FY	Budget section	Budget amount (USD)	%Δ from previous FY	Notes
2018	Centers for Disease Control	8.25B	N/A	Estimate of actual spend ⁴⁶
	CDC – Public Health and Preparedness	1.45B	N/A	Estimate of actual spend
	CDC – Emerging & Zoonotic Infectious Disease	615M	N/A	Estimate of actual spend
2019	Centers for Disease Control	5.6B	-32%	Budget requests ⁴⁷ Detailed budget outline
	CDC – Public Health and Preparedness	800+468M =1.286B	-11%	Budget request
	CDC – Emerging & Zoonotic Infectious Disease	508M	-17%	Budget request
2020	Centers for Disease Control	6.594B	+18%	Budget requests ⁴⁸
	CDC – Public Health and Preparedness	825+468M =1.293B	+0.5%	Budget request
	CDC – Emerging & Zoonotic Infectious Disease	509M	+0.2%	Budget request

Table 5: US government funding for the CDC in 2018, and budget requests for 2019 and 2020.

Notable changes between 2018 and 2019:

- The CDC (Public Health and Preparedness Response) stopped funding the Strategic National Stockpile, which previously received a ~\$604M budget allocation⁴⁹. Effective October 2018, the stockpile is managed by the Office for Preparedness and Response, which also manages BARDA.

⁴⁵ "CENTERS FOR DISEASE CONTROL AND PREVENTION (HC ... - CDC." 25 Sep. 2018, <https://www.cdc.gov/maso/pdf/cdcmiss.pdf>. Accessed 16 Aug. 2019.

⁴⁶ "CDC's Funding | CDC 24/7 Health Security Report | CDC." 11 Oct. 2018, <https://www.cdc.gov/about/report/cdc-funding.html>. Accessed 16 Aug. 2019.

⁴⁷ "CDC—BUDGET REQUEST OVERVIEW." <https://www.cdc.gov/budget/documents/fy2019/cdc-overview-factsheet.pdf>. Accessed 16 Aug. 2019.

⁴⁸ "CDC FY 20 Budget Overview Factsheet." <https://www.cdc.gov/budget/documents/fy2020/cdc-overview-factsheet.pdf>. Accessed 16 Aug. 2019.

⁴⁹ "FY 2019 Operating Plan - CDC." <https://www.cdc.gov/budget/documents/fy2019/fy-2019-cdc-operating-plan.pdf>. Accessed 16 Aug. 2019.

CDC's **Funding** in Fiscal Year 2018: \$8.25 Billion*

Figure 5: CDC funding in fiscal year 2018.

The CDC has not historically (since 2010) provided funding for projects specifically related to antiviral medications, broad-spectrum or otherwise. It does provide considerable discretionary funding to organizations studying emerging infectious diseases, which may then be put towards antiviral research.

See [Chapter 3](#) for CDC funded R&D efforts towards broad-spectrum antivirals.

Food and Drug Administration

Division within HHS. In 2018, the FDA released testimony before the US House of Representatives regarding the FDA's efforts to respond to biological threats⁵⁰.

"FDA plays a critical role in facilitating preparedness for, and response to, biological threats. FDA's role focuses largely on facilitating the development and availability of medical countermeasures—such as vaccines, therapeutics, and diagnostic tests—to protect against, and respond to, these threats."

⁵⁰ "The State Of US Public Health Biopreparedness: Responding ... - FDA." 15 Jun. 2018, <https://www.fda.gov/news-events/congressional-testimony/state-us-public-health-biopreparedness-responding-biological-attacks-pandemics-and-emerging>. Accessed 22 Aug. 2019.

“Since 2012, FDA has approved, licensed or cleared more than 120 medical countermeasures for a diverse array of threats including anthrax, botulinum toxin, plague, smallpox and pandemic influenza. 13 have been approved under the Animal Rule (see below).”

The FDA is split into offices and centers, several of which work on counterterrorism and countermeasures:

- Office of Counterterrorism and Emerging Threats (OCET)
 - FDA’s point of entry on global health security, counterterrorism, and emerging threats
 - Liaises with HHS’s and DOD’s medical countermeasures programs
 - Coordinates the FDA MCMi, Medical Countermeasure Initiative
 - Guides emergency products through the Emergency Use Authorization process
- Center for Biologics Evaluation and Research
 - Managed the Countering Bioterrorism and Emerging Infectious Diseases program, which allows the expeditious development and licensing of products used to treat bioterrorist agents⁵¹.
- Center for Drug Evaluation and Research
- Medical Countermeasures Initiative (MCMi)
 - An FDA-wide initiative that coordinates MCM development, preparedness, and response⁵²

Emergency Use Authorization⁵³: Under section 564 of the FD&C Act, the FDA Commissioner may allow “fast-tracking” of otherwise unapproved products to be used under chemical, biological radiological and nuclear (CBRN) threats. This largely applies to medical *diagnostics*, and has not been used for an antiviral.

- In 2004, this was amended by the Project Bioshield Act
- In 2013, it was amended by the Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA)
 - PAHPRA permits federal, state and local government entities to pre-position (stockpile) MCMs regardless of a product’s regulatory status⁵⁴
- 2016, 21st Century Cures Act
- 2017, Public Law 115-92

Current EUAs in effect include:

- Bacterial: Anthrax
- Viral: Ebola, Enterovirus, H7N9, MERS-CoV, Zika
- Freeze dried plasma
- Nerve agent

⁵¹ "Countering Bioterrorism and Emerging Infectious Diseases | FDA." 23 Mar. 2018, <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/countering-bioterrorism-and-emerging-infectious-diseases>. Accessed 22 Aug. 2019.

⁵² "Medical Countermeasures Initiative (MCMi) | FDA." 4 Sep. 2019, <https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/medical-countermeasures-initiative-mcmi>. Accessed 3 Oct. 2019.

⁵³ "Emergency Use Authorization | FDA." <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>. Accessed 22 Aug. 2019.

⁵⁴ "Pandemic and All-Hazards Preparedness Reauthorization Act ... - FDA." <https://www.fda.gov/media/87718/download>. Accessed 22 Aug. 2019.

Past EUAs can be found here: [EUA archive page](#)

To date, the FDA has licensed vaccines for anthrax and smallpox, and a treatment for complications from smallpox vaccination⁵⁰. FDA-licensed antiviral drugs “generally target one virus or a small group of closely-related viruses”⁵⁵.

In 2002, the FDA published the Animal Rule, which allows animal studies to be used in cases where human trials are neither ethically nor logistically possible⁵⁰. Two products have been approved under the rule to date (pyridostigmine bromide and Cyanokit), and several are in process.

National Institutes of Health

Division within HHS. The US’s National Institutes of Health is the primary federal agency responsible for biomedical and public health research. They provide annual estimates of their funding for research topics, conditions and disease categories.

[NIH Estimates of Funding \(2019 estimates, dollars in millions\):](#)

- Top funded research areas
 - Clinical Research – \$15,023
 - Genetics – \$9,551
 - Prevention – \$9,322
 - Neuroscience – \$8,945
 - Biotechnology – \$7,380
- Relevant to pandemic preparedness
 - Infectious Diseases – \$6,317
 - **Emerging Infectious Diseases – \$2,915**
 - **Biodefense – \$2,352**
 - Immunization – \$2,330
 - Vaccine related – \$2,220
 - Anthrax – \$45
 - Smallpox – \$14

The NIH and its composite agencies (NIAID, NINDS, NIDA etc.) also post funding opportunities for researchers. These opportunities indicate the NIH’s interest in funding a particular research agenda. The funding announcements are publicly available [here](#).

To date, the NIH continues to fund research related to health security. However, the majority of funding announcements pertain to chemical and radiological threats, not biological threats (see Table 6 below).

Please note that these funding announcements are in addition to (and thus do not include) traditional funding paths for researchers such as U01 grants.

⁵⁵ "Broad Spectrum Antiviral Activity of Favipiravir (T-705 ... – NCBI – NIH." 10 Apr. 2014, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3983105/>. Accessed 22 Aug. 2019.

Type	Total funding opportunity announcements pertaining to medical countermeasures for health security	# related to biological threats (%)	# related to broad spectrum antivirals (%)
Active	5	0 (0%)	0 (0%)
All	60	9* (15%) *The vast majority are for chemical and radiation threats, not biological threats.	4 (7%), all by NIAID ^{56,57,58,59}

Table 6: NIH Funding opportunity announcements and notices related to search term “countermeasure[s]” not including notices of change or clarification.

National Institute of Allergy and Infectious Disease

One of the 27 institutes that makes up the NIH, NIAID is the primary funder of basic and applied research to better understand, treat and prevent infectious, immunology and allergic diseases in the US.

The NIAID fiscal year 2019 budget is available [here](#). Highlights from this include:

- “NIAID is focused particularly on developing a **broad-spectrum antiviral drug** that could be used to treat a variety of flavivirus infections, including Zika”
- “[NIAID] scientists also identified a mechanism to enhance the normal antiviral response to HSV and other viruses. This approach could lead to the development of **broad-spectrum antiviral** therapies”
- “NIAID supports the development of medical countermeasures and new platform technologies against biodefense and emerging infectious disease pathogens and will continue to coordinate with the biomedical advanced research and development authority (BARDA) in the advanced development of therapeutics and vaccines”

These priorities appear consistent with previous budgets in FY2017 and FY2018.

Annual NIAID funding (at time of search, August 2019) for broad-spectrum antivirals is estimated to be **~\$25M**, based on grant funding viewable on NIH [RePORTER](#). These grantees, who are still currently pursuing active research in the broad-spectrum antivirals space, have received a total **~\$245M** since 2011. This represents a small fraction of NIH spending on *emerging infectious disease* and *biodefense* (**~0.86% and ~1.06% per annum, respectively**).

Please see [Chapter 3](#) for technical details regarding the broad-spectrum antiviral work NIAID is currently funding.

⁵⁶ "NOT-AI-12-009: Request for Information (RFI ... - NIH OER." 14 Sep. 2011, <https://grants.nih.gov/grants/guide/notice-files/NOT-AI-12-009.html>. Accessed 16 Aug. 2019.

⁵⁷ "NOT-AI-15-048: Broad Agency Announcement (BAA): Development of" 17 Jul. 2015, <https://grants.nih.gov/grants/guide/notice-files/NOT-AI-15-048.html>. Accessed 16 Aug. 2019.

⁵⁸ "NOT-AI-14-043: Request for Information (RFI): Optimizing Lead" 8 Apr. 2014, <https://grants.nih.gov/grants/guide/notice-files/NOT-AI-14-043.html>. Accessed 16 Aug. 2019.

⁵⁹ "NOT-AI-17-019: NIAID Omnibus Broad Agency Announcement No" 17 Mar. 2017, <https://grants.nih.gov/grants/guide/notice-files/NOT-AI-17-019.html>. Accessed 16 Aug. 2019.

Office of the Assistant Secretary for Health

Office within HHS. Oversees key public health offices and programs. Those relevant to GCBRs include the Office of Infectious Disease and the National Vaccine Program, as well as the Surgeon General.

OASH National Action Plans

- National adult immunization plan
- National HIV/AIDS strategy
- National vaccine plan
- National viral hepatitis action plan

OASH Advisory Committees

- AC on blood and tissue safety and availability
- President's AC on HIV/AIDS
- Presidential AC on combating antibiotic-resistant bacteria
- National vaccine advisory committee
- Tick-borne disease working group

Office of the Assistant Secretary for Preparedness and Response

Office within HHS, acronym ASPR. ASPR "leads the nation's medical and public health preparedness for, response to, and recovery from disasters and public health emergencies."⁶⁰ They are the primary office responsible for medical countermeasures to biological threats.

Programs within ASPR⁶¹

- Biomedical Advanced Research and Development Authority (BARDA)
- National Biodefense Strategy
- Regional Disaster Health Response System
- Hospital Preparedness Program
- Strategic National Stockpile
- National Health Security Strategy
- Critical Infrastructure Protection
- Public Health Emergency Medical Countermeasures Enterprise
- Centers for Innovation in Advanced Development and Manufacturing
- Medical Reserve Corps
- National Disaster Medical System

Relevant ASPR programs are detailed individually in separate sections below.

Biomedical Advanced Research and Development Authority (BARDA)

BARDA was "established to aid in securing [the] nation from chemical, biological, radiological and nuclear (CBRN) threats, as well as from pandemic influenza (PI) and emerging infectious diseases

⁶⁰ "Office of the Assistant Secretary for Preparedness and ... - PHE.gov."

<https://www.phe.gov/about/aspr/Pages/default.aspx>. Accessed 23 Aug. 2019.

⁶¹ "ASPR Highlights - PHE.gov." <https://www.phe.gov/about/Pages/highlights.aspx>. Accessed 9 Sep. 2019.

(EID)”⁶². BARDA funds the development of MCMs (including vaccines, drugs, diagnostics etc.) through the R&D stage, towards approval by the FDA and ultimate inclusion into the United States’ Strategic National Stockpile. They also provide support such as a clinical research network and a fill-finish manufacturing network. BARDA’s Strategic Plan 2011–2016 emphasizes five goals:

1. An advanced development pipeline replete with medical countermeasures and platforms to address unmet public health needs, emphasizing innovation, flexibility, multi-purpose and broad spectrum application, and long-term sustainability.
2. A capability base to provide enabling core services to MCM innovators.
3. Agile, robust and sustainability US manufacturing infrastructure capable of rapidly producing vaccines and other biologics against pandemic influenza and other emerging threats.
4. Responsive and nimble programs and capabilities to address novel and emerging threats
5. A ready capability to develop, manufacture and facilitate distribution of medical countermeasures during public health emergencies.

BARDA prioritizes the development of **broad-spectrum medical countermeasures**, and acknowledges pandemic influenza and novel/emerging threats. “BARDA’s Broad Spectrum Antimicrobial Program was established in January 2010 and is focused on developing novel antibacterial and antiviral drugs for the treatment or prevention of disease caused by currently defined and future biological threats.” To-date, BARDA has supported 42 FDA approvals for products addressing CBRN, PI and EID threats⁶³.

US Government Funding of BARDA

BARDA is a well-funded federal agency, with an annual budget of approximately \$1.5 billion dollars. However, there are difficulties with the mechanisms by which they are funded (see below).

Type	Description	FY 2017
Project BioShield	A \$2.8B fund (divided over 5 years). Engages in late-stage clinical development as well as procurement and stockpiling of MCMs.	531.1 M
Advanced research and development	Used for earlier stage development. De-risking of project before projects move on to Project BioShield.	452.0 M
Pandemic influenza	Largely dedicated to building out vaccine manufacturing capacity. BARDA now claims to have built capacity to manufacture 50M doses of vaccine for a novel influenza strain within 6 months of detection.	268.1 M
Zika <i>Temporary funding</i>	This was provided by Congress as “supplemental funding” during the Zika outbreak.	262.9 M
Ebola <i>Temporary funding</i>	This was provided by Congress as “supplemental funding” during the Ebola outbreak.	42.8 M
Total		1,556.9 B

Table 7: BARDA funding allocated by United States Congress. FY2017 data provided by [Dr. Joe Larsen](#). FY 2018 budget requests available in appendix.

A note regarding temporary supplemental funding from Congress:

⁶² "BARDA – PHE.gov." <https://www.phe.gov/about/bar-da/Pages/default.aspx>. Accessed 9 Sep. 2019.

⁶³ "BARDA – PHE.gov." <https://www.phe.gov/about/bar-da/Pages/default.aspx>. Accessed 9 Sep. 2019.

- Per [Dr. Joe Larsen](#), former Acting Director, Division of CBRN Medical Countermeasures, BARDA
- The mechanism by which Ebola and Zika supplemental funding was provided is the following:
 - The outbreak occurred and progressed
 - A supplemental funding proposal was drafted and presented to Congress
 - Congress voted to provide supplemental funding
 - This funding is meant to specifically fund efforts targeting that particular pathogen/outbreak
- The problems with this funding mechanism noted by Dr. Larsen
 - The funding cannot be used preventatively or in early stages of an outbreak
 - There is a delay between the timing of the outbreak and when funding is provided
 - This type of funding is short-term. It allows BARDA to fund MCMs in the early stages, but makes it difficult for them to follow-up on that funding in future stages (say, when the outbreak has subsided).
 - Their Zika vaccine program was unable to guarantee vaccine developers that they would be able to support them in future years.
 - **The agency would prefer an allocation on a consistent basis for all emerging infectious diseases in order to be able to provide consistent funding to their partners, vs. post-hoc supplemental funding tied to specific pathogens.**

BARDA MCM Procurements and Grants

Press-releases regarding BARDA successful procurements and grants are publicly available. At the time of this report, 66 announcements had been made since 2011 describing over 65 drugs, vaccines, diagnostic tests, etc.

Type	Bacterial threats	Viral threats	Chemical threats	Radiological threats	Total
Drug	11	10	1	4	25 (37%)
Vaccine	4	5	0	0	9 (13%)
Diagnostic test	8	5	2	6	21 (31%)
Other	0	2	2	8	12 (18%)
Total	23 (34%)	21 (31%)	5 (7.5%)	18 (27%)	67

Table 8: Projects funded by BARDA, as publicly listed in press releases⁶⁴. Please note the source webpage contains duplicates, but duplicates were not double counted for this table.

Pathogen	# of antivirals
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⁶⁴ "MCM Procurements and Grants – PHE.gov."

<https://www.phe.gov/newsroom/Pages/mcm-procurements.aspx>. Accessed 3 Oct. 2019.

Ebola	5
Influenza	3
Smallpox	1
Broad-spectrum	1

Table 9: Antiviral medications funded by BARDA, by pathogen targeted. For technical details on the 1 broad-spectrum antiviral medicine BARDA has funded to date, please refer to Chapter 3: United States.

Strategic National Stockpile

The Strategic National Stockpile is the US's supply of “potentially life-saving pharmaceuticals and medical supplies for use in a public health emergency severe enough to cause local supplies to run out”⁶⁵.

The Stockpile does not appear to house any broad-spectrum antiviral medicines to date (see below).

Figure 6: Slide from presentation by [Dr. Joe Larsen](#), Former Acting Director of the Division of CBRN Countermeasures, BARDA.

Office of Global Affairs (OGA)

⁶⁵ "Strategic National Stockpile – PHE.gov." <https://www.phe.gov/about/sns/Pages/default.aspx>. Accessed 3 Oct. 2019.

The Office of Global Affairs is the diplomatic arm of HHS⁶⁶. Within the OGA, the Office of Pandemics and Emerging Threats engages with other US agencies, foreign governments and multilateral organizations to “prevent, detect, and response to health threats whether natural, accidental or deliberate in origin”⁶⁷.

Their main initiatives include:

- Pandemic Influenza
- Antimicrobial Resistance
- The Global Health Security Agenda (detailed in Chapter 1: International)

They also serve as “the primary liaison for the U.S. government engagement with the WHO”⁶⁸.

OGA posts and supports health attaches in the following countries:

- Brazil
- China
- India
- Mexico
- South Africa
- United States Mission in Geneva

Office of Science and Technology Policy

An office in the Executive Office of the President, not HHS. Provides advice on the “scientific, engineering, and technological aspects of the economy, national security, homeland security, health, foreign relations, the environment, and the technological recovery and use of resources, among other topics”⁶⁹.

The Office has previously advised temporary bans on viral gain-of-function research⁷⁰ in response to concerns regarding accidental release.

Department of Defense

The United States Department of Defense (DoD) “provides the military forces needed to deter war and ensure our nation’s security”⁷¹.

The Department of Defense provides resources to mitigate emerging infectious diseases in a number of ways:

⁶⁶ "Office of Global Affairs (OGA) | HHS.gov." <https://www.hhs.gov/about/agencies/oga/index.html>. Accessed 3 Oct. 2019.

⁶⁷ "Global Health Security | HHS.gov." <https://www.hhs.gov/about/agencies/oga/global-health-security/index.html>. Accessed 3 Oct. 2019.

⁶⁸ "Global Health Diplomacy | HHS.gov." <https://www.hhs.gov/about/agencies/oga/global-health-diplomacy/index.html>. Accessed 3 Oct. 2019.

⁶⁹ "Office of Science and Technology Policy" <https://www.whitehouse.gov/ostp/>. Accessed 3 Oct. 2019.

⁷⁰ "US suspends risky disease research : Nature News & Comment." 22 Oct. 2014, <https://www.nature.com/news/us-suspends-risky-disease-research-1.16192>. Accessed 3 Oct. 2019.

⁷¹ "Our Story - Defense.gov." <https://www.defense.gov/our-story/>. Accessed 15 Oct. 2019.

- Logistical support
 - The Department of Defense collaborates with other agencies towards biosecurity initiatives, such as Ebola control. The DoD's contribution consists of "logistical support and training for health care workers, to test medical samples and to construct Ebola treatment units"⁷².
- Stockpiling medical countermeasures
 - The DoD was also previously involved in stockpiling medical countermeasures⁷³ however this responsibility appears to have been taken over by the Strategic National Stockpile⁷⁴.
- Grant-making
 - The DoD has previously made grants towards biosecurity and pandemic preparedness work. Current and previous grant postings are viewable on [Grants.gov](https://www.dod.mil/Grants). Please refer to [Chapter 3](#) for details on individual grants by the DoD and its subagencies, such as DARPA and DTRA.

Within the DoD, certain subagencies are involved in biosecurity:

- **DARPA:** The Defense Advanced Research Projects Agency (DARPA) is an agency within the DoD responsible for the development of emerging technologies for use by the military⁷⁵.
- **DTRA:** The Defense Threat Reduction Agency is the official agency for countering weapons of mass destruction⁷⁶.
 - The DTRA produces the Cooperative Biological Engagement Program (CBEP)⁷⁷. MCM development is "generally not supported by CBEP" due to its overlap with other US or international agencies. However "research projects may inform medical countermeasure development and support validation and verification testing" (see grant stating this [here](#)).

National Biodefense Analysis and Countermeasures Center

NBACC is a government research laboratory in Frederick, MD, USA. It was founded in 2002 after the anthrax attacks in 2001⁷⁸. The facility operates at biosafety levels 2, 3 and 4. Its BBSL-4 accreditation makes it one of seven such facilities in the US.

⁷² "DoD Releases Breakdown of Ebola Response Effort > U.S." 8 Jan. 2015, <https://www.defense.gov/Newsroom/News/Article/Article/603892/dod-releases-breakdown-of-ebola-response-effort/>. Accessed 15 Oct. 2019.

⁷³ "Policy for Release and Use of DoD Antiviral ... - Health.mil." 10 Aug. 2007, <https://www.health.mil/Reference-Center/Policies/2007/08/10/Policy-for-Release-and-Use-of-DoD-Antiviral-Stockpile-During-an-Influenza-Pandemic>. Accessed 15 Oct. 2019.

⁷⁴ "Strategic National Stockpile Program: Implications for Military" <https://academic.oup.com/milmed/article/171/8/698/4578196>. Accessed 15 Oct. 2019.

⁷⁵ "Darpa." <https://www.darpa.mil/>. Accessed 15 Oct. 2019.

⁷⁶ "DTRA." <https://www.dtra.mil/>. Accessed 15 Oct. 2019.

⁷⁷ "The Cooperative Biological Engagement Program Research Strategic." https://www.dtra.mil/Portals/61/Documents/Missions/CBEP%20Research%20Strategy_FINAL_July%202015.pdf. Accessed 15 Oct. 2019.

⁷⁸ "National Biodefense Analysis and Countermeasures Center" <https://www.dhs.gov/science-and-technology/national-biodefense-analysis-and-countermeasures-center>. Accessed 15 Oct. 2019.

CHAPTER THREE:

United States Past and Present R&D in BSAVs

Here we outline known research and development efforts within the US towards broad-spectrum antivirals. This chapter is not meant to be exhaustive and does not represent the full breadth of R&D efforts in the area. It provides a brief overview of efforts discovered during the process of writing Chapters 1 & 2.

In particular, this chapter **does not represent a systematic review** of the global scientific literature on broad-spectrum antivirals.

Nevertheless, the research described below should be of interest to various audiences, including:

- Early- and mid-career researchers interested in broad-spectrum antiviral research
- Public and private grantmakers interested in funding broad-spectrum antivirals
- Policy decision makers and others wanting to understand the tractability of BSAVs

Background

Using the definition of broad-spectrum in this report, there is at present a single FDA-approved broad-spectrum antiviral for respiratory RNA viruses (ribavirin)⁷⁹. Ribavirin is a traditional small-molecule drug, however monoclonal antibodies and immunomodulators are also being investigated as potential BSAVs. To date, “only one virally targeted monoclonal antibody is FDA-approved: palivizumab”⁷⁷.

The Open Philanthropy Project has previously expressed interest in host-targeting antivirals, and has provided the following grants in the area:

- [Raul Andino, UCSF](#) - HSP90i Broad Spectrum Host-directed Antiviral Drugs
- [Timothy Haystead, Duke](#) - HSP70i and Inhibitor HS-72
- [Alexander Tarakhovsky, Rockefeller](#) - Viral Histone Mimics

The following grant was not for antiviral development per se, but for a platform that could be used to develop antiviral peptide-based nanoparticles:

- David Baker, [U Wash Institute for Protein Design](#) - Universal Flu Vaccine

⁷⁹ "Center for Health Security: Characteristics of Pandemic" 10 May. 2018, http://www.centerforhealthsecurity.org/newsroom/center-news/2018-05-10_characteristics-of-pandemic-pathogens.html. Accessed 15 Oct. 2019.

Centres for Disease Control

Previous funding by CDC for broad-spectrum antivirals (via CDC [Funding Profiles](#))

Dates: Past projects only (2010–2018)

Search terms: broad, spectrum, anti, viral, antiviral, virus, microbial, antimicrobial, counter, measure, countermeasure, treatment (within project title)

Exclusion criteria: Narrow-spectrum antivirals, defined as active against a specific family, genus or species, as determined by review of grant abstract. General “emerging infectious diseases” grants were not included.

Laamscience, Inc. Raleigh, North Carolina – \$275K, 2010 (for total 3 grants)
[Durable visible light-activated antiviral coatings for fabrics used for personal respirator such as N95](#)

- In response to the Omnibus solicitation of NIH, CDC, FDA and ACF for small business innovation research grants (Parent SBIR [R43/R44])
- Grant #: R44OH009459-02A1

The following grant met our search criteria, however was not included as it is for a bleach-like compound that can only be used outside the body (e.g. on surfaces). It is not a therapeutic antiviral.

Laamscience, Inc. Raleigh, North Carolina – \$357K, 2011 (for total 2 grants)
[Durable visible light-activated antiviral coatings for fabrics used for personal respirator such as N95](#)
Efficiency of light-activated antimicrobial fabrics against human pathogens

- In response to the Omnibus solicitation of NIH, CDC, FDA and ACF for small business innovation research grants (Parent SBIR [R43/R44])
- Grant #: R43OH009692-01A1, R44OH009459-03

National Institute of Allergy and Infectious Disease

Active grants by NIAID for broad-spectrum antivirals (via NIH [RePORTER](#))

Dates: Active projects only (at time of search, August 2019). Project grant histories span 2011–2020. Please note that currently active projects may be part of multi-year grants, and it is the total amount of these grants that is listed below.

Search terms: broad, spectrum, anti, viral, antiviral

Exclusion criteria: Narrow-spectrum antivirals, defined as active against a specific family, genus or species, as determined by review of grant abstract.

Total funding: ~\$245.895M

These grants are also searchable via [Grantome](#).

Paul Malone Allen Washington University – \$32.7M, 2014–2018

[*Autophagy modulators as novel broad-spectrum anti-infective agents*](#)

- Autophagy and ATG genes are central to immune defense against many pathogens. This project aims to produce semi-optimized lead compounds with protective effects in animals against a range of pathogens.
- Team includes Drs. Skin Virgin, Beth Levin, Ramnik Xavier, Stuart Schreiber.
- Collaborating with Broad Institute, Mass General, Wash U, UT Southwestern.
- Paul Allen holds MERIT status with the National Institutes of Health.

Jeffrey Glen Stanford University – \$28.6M, 2014–2019

[*Advancing broad spectrum host-targeting antiviral strategies to the clinic*](#)

- Overall aim is to develop new classes of host-targeting antivirals that are capable of treating multiple NIAID emerging and re-emerging priority pathogen viruses. Spans the translational development spectrum: target generation, validation, lead optimization.
- Genetic screening to identify host genes required by multiple RNA viruses, then use viral vectors to validate.
- There is apparent widespread dependence of RNA viruses on phosphoinositides such as PI4P.
- Computational methods can be used to repurpose existing approved drugs.

Ulrich H Von Andrian Harvard Medical School – \$9.751 M, 2014–2018

[*Mechanisms and immunological consequences of host-virus interactions*](#)

- Viruses elicit T cell responses. This project aims to study in detail the mechanisms by which this occurs.

Ralph Baric UNC Chapel Hill – \$3.79M, 2017–2019

[*Broad-spectrum antiviral GS-5734 to treat MERS-COV and related emerging COV*](#)

- Tat-Beclin 1 is an autophagy-inducing peptide with broad-spectrum anti-infective activity in vivo. It is being moved forward by Casma Therapeutics.

Anne Moscona Columbia University Health Sciences – \$3.7M, 2015–2019

[*Engineering protease-resistant alpha-beta peptides for broad spectrum antivirals*](#)

- Broad-spectrum antiviral strategy that focuses on inhibiting fusion during viral entry
- Uses lipid-conjugated peptides

Beth C Levine (2) UT Southwestern – \$2.0M, 2018

[*Autophagy-inducing peptides and target identification for treatment of viruses*](#)

- Recently developed a autophagy-inducing peptide (Tat-Beclin 1) which has broad in vitro antiviral and antibacterial activity (e.g. chikungunya and west nile virus).
- Beth Levine is a Howard Hughes Medical Institute investigator, director of the center for autophagy research at UT Southwestern, and was previously director of virology at Columbia (1994–2004). She is a member of the National Academy of Sciences.

UT Southwestern – \$1.5M, 2019

[RP1: Targeting Beclin 1 complexes for broad-spectrum anti-infective therapeutics](#)

- Tat-Beclin 1 is an autophagy-inducing peptide with broad-spectrum anti-infective activity in vivo. It is being moved forward by Casma Therapeutics.
- Knock-in studies of Beclin 1 in mice appear to show increased autophagy, that autophagy is safe, and that it induces reduced susceptibility to tuberculosis and chikungunya virus. West nile virus and zika virus will be tested next.

John Huibregtse

UT Austin – \$3.1M, 2011–2019

[Mechanism and function of ISG15](#)

- Type 1 interferon is part of our immune response to viral infection
- ISGs (interferon stimulate gene products) mediate broad-spectrum antiviral effects

Herbert W Virgin (2)

Washington University – \$1.6M, 2018

[Genes/pathways for ATG gene-dependent inhibition of viruses & parasite infection](#)

- Autophagy and ATG genes increase the efficacy of host pathways that are active against a wide range of organisms, including viruses and parasites.
- This project aims to screen compounds for ATG stimulation capacity.

UT Southwestern – \$985K, 2019

[RP3: Targeting ATG gene dependent immunity for novel anti-infective therapies](#)

- Pharmacologically targeting intracellular immune mechanisms utilizing autophagy genes to control infection and inflammation

Eric Poeschla

University of Colorado Denver – \$2.3M, 2017–2019

[Novel approaches to innate immunity against HIV-1 and other co-infection viruses](#)

Martin Dorf

Harvard Medical School – \$2.1M, 2016–2019

[Interferon-induced IFITM recruitment of ZMPSTE24 blocks viral endocytic entry](#)

George Belov

University of Maryland, College Park – \$1.5M, 2016–2019

[Role of host protein GBF1 in organizing enterovirus replication complexes](#)

Stacy Remiszewski

Forge Life Sciences, LLC – \$1.2M, 2014–2019

[A single antiviral to treat multiple opportunistic infections](#)

Meike Dittmann

NYU – \$867K, 2019–2020

[ELF1 – Molecular mechanisms of a novel transcription factor with broad antiviral activity](#)

Elke Lipka

TSRL Inc. Ann Arbor – \$202K, 2018–2019

[New prodrug strategies for cidofovir designed for mitigating first-pass metabolism](#)

Lela Vukovic

UT El Paso – \$150K, 2019–2020

[Computational modelling of broad-spectrum non-toxic antiviral nanoparticles](#)

National Institutes of Health – Small Business SBIR/STTR Program

Active grants by the [NIH Small Business Innovation Research and Technology Transfer Programs](#)

Dates: All

Search terms: broad, spectrum, anti, viral, antiviral

Exclusion criteria: Narrow-spectrum antivirals, defined as active against a specific family, genus or species, as determined by review of grant abstract.

Total funding: ~\$2.1M

TSRL Inc. – \$597K, 2013

[Broad spectrum antiviral nucleoside phosphonate analogs](#)

- Acyclic nucleoside phosphates are antiviral agents but have been limited by lack of bioavailability
- TSRL has created a general approach to address the lack of oral bioavailability of these drugs

Kineta Inc. ~ 1.5M, 2016

[Development of novel isoflavone drugs as broad spectrum antivirals](#)

- A novel class of broad spectrum small molecule antivirals
- Working with Prof Michael Gale Jr of the University of Washington

Biomedical Advanced Research and Development Authority (BARDA)

Grants made by BARDA towards antiviral efforts (since 2011)

Per publicly available press releases⁸⁰

Dates: All available (2011–2018)

Sept 25, 2018

[HHS sponsors new formulation of world's first approved smallpox drug](#)

Oct 3, 2017

[HHS, Regeneron partner on portfolio of treatments for pandemic influenza, emerging infectious diseases \(MERS/Ebola\)](#)

Sept 29, 2015

[HHS advances development of novel drug to treat influenza](#)

Sept 28, 2015

[HHS sponsors development of drug for hospitalized influenza patients](#)

Sept 21, 2015

[HHS advances development of new monoclonal antibody drug for Ebola](#)

July 20, 2015

[HHS partnership advances experimental Ebola drug](#)

March 31, 2015

[HHS contracts to develop new Ebola drug](#)

⁸⁰ "MCM Procurements and Grants – PHE.gov."

<https://www.phe.gov/newsroom/Pages/mcm-procurements.aspx>. Accessed 3 Oct. 2019.

Sept 29, 2014

[HHS funds drug to treat severe infections and prevent cytokine storm](#)

This is the only potential broad-spectrum antiviral drug to date (per public data) that BARDA has funded. The potential drug, AB103, combats “cytokine storm”, a complication of severe infection whereby host cells overreact to infection, releasing a surge of cytokines, which results in tissue and organ damage (SIRS: systemic inflammatory response syndrome, and sepsis).

This complication occurs in infections of all types, including bacterial and viral. However, the company developing the drug is seeking an indication for necrotizing soft tissue infections, a bacterial infection.

To develop this drug, HHS contracted Israeli biotechnology company Atox Bio for 1.5 years, for \$4.4 million dollars. As of Sept 25, 2018, AB103 (reltecimod) was in Phase 3 clinical trials with a planned completion of the study in 2019⁸¹.

Sept 2, 2014

[HHS contracts with Mapp Biopharmaceuticals to develop Ebola drug](#)

Department of Defense (DOD)

Grants opportunities posted by the Department of Defense

Per publicly available posts on [Grants.gov](#)

Dates: Active grants (awarded & as yet unawarded)

Search terms: anti + viral, antiviral, countermeasure

Inclusion criteria: Grants posted by the DoD only

DoD USAMRMC FY18–FY22 Broad Agency Announcement for Extramural Medical Research

Opportunity #: [W81XWH18SBAA1](#)

Posted 10/01/2017

Supplemental documents for this grant describe it as supporting a Medical Biological Defense Research Program that includes “antiviral, antibacterial, immunomodulatory, or antitoxin activities, with emphasis on compounds that provide broad, non-specific protection against viruses, bacteria, and toxins as described above.

FY2011 – 2016 Basic Research for Combating Weapons of Mass Destruction (C-WMD) Broad Agency Announcement (BAA)

Opportunity #: [HDTRA1-11-16-BRCWMD-BAA](#)

Posted 3/1/2019

Supplemental documents show this grant covers a broad range of WMD research. It includes awards for research pertaining to:

- “Understanding the viral elements that contribute to species jumping events” which “may ultimately contribute to the development of preventive measures”
- “Understanding of the differences between fully virulent Select Agent viruses and closely related low virulence/avirulent neighbors”
- “Investigation of Factors Enabling Viral Evolution and Emergence” in RNA viruses
- “Understanding how changes in the chemistry of the host-cell environment affect key enzymes in the pathogen may provide insights about potential drug-targets that minimize human side effects”

⁸¹ "Atox Bio Announces Independent Safety Monitoring"

<http://www.atoxbio.com/wp-content/uploads/2018/09/Press-release-September-2018-DSMB-200.pdf>. Accessed 3 Oct. 2019.

Conduct of Clinical Trials to Facilitate the Development and Approval of Novel Countermeasures (vaccines, devices, drugs) for Use by the Warfighter

Opportunity #: [N62645-PA-20-01](#)

Posted 10/9/2019

- Phase 2 through 4 clinical trials
- “Malaria, diarrheal diseases, influenza, dengue fever, Zika virus, chikungunya and other arboviral infections, wound infections, respiratory infections, urinary tract infections and sepsis due to multidrug resistant bacteria and neglected diseases, such as leishmaniasis, are a known threat to military operations and readiness.”
- No mention of broad-spectrum in particular

NRL Long Range Broad Agency Announcement (BAA) for Basic and Applied Research

Opportunity #: [N00173-19-S-BA01](#)

Posted 9/6/2019

- Sensing and diagnostics focused, no antivirals mentioned

Biological Technologies

Opportunity #: [HR001119S0048](#)

Posted 4/23/2019

- “Developing new technologies to treat, prevent, and predict the emergence and spread of infectious diseases that have the potential to cause significant health, economic, and social burden.”
- No mention of broad-spectrum in particular

Young Faculty Award

Opportunity #: [DARPA-RA-19-01](#)

Posted 8/28/2019

- “The DoD has a need to develop effective medical countermeasures (MCMs) for the warfighter in a timely manner. There are currently many challenges along the MCM development pipeline from initial MCM identification, manufacturing, formulation, potency, delivery, safety, pharmacokinetic and pharmacodynamic profiles. Specifically for biologic (protein or nucleic acid) MCMs, there is an opportunity to use advanced analytic approaches based on the sequence information to streamline the MCM development process. Previous investment in DNA or RNA vectored protective monoclonal antibodies has begun to address some of these challenges, but many questions remain around the ability of the nucleic acid to express the desired antibody to sufficient high levels in vivo. DARPA seeks to develop algorithms to address the ability to predict the translation efficiency of a monoclonal antibody from a nucleic acid construct in vivo. “

CONCLUSION

This report serves as a preliminary overview of global & United States policy and practice, as well as United States R&D, towards the development of effective broad-spectrum antivirals. These drugs “should be pursued given their potential value, even if the likelihood of identifying such medicines remains low”⁸².

Impression: There are none-to-few international policies regarding the development of broad-spectrum antivirals, despite earlier interest following the SARS and H1N1 outbreaks. Broad-spectrum antivirals remain less prioritized than vaccines and diagnostics on the international stage. This is likely due to the current lack of effective BSAVs.

Recommendation: Continued work to publicize the importance of broad-spectrum antivirals may be helpful. BSAV language should be included in the Global Health Security Agenda, for example. However, greater effort should be made towards R&D efforts, versus international policy, at this time.

Impression: Within the United States, the National Institute of Allergy and Infectious Disease has made over ~\$245M worth of grants towards broad-spectrum antiviral development (~\$25M in the year 2019, when this report was written, representing ~1% of eligible funding in the *emerging infectious disease* and *biodefense* categories). Of active funding announcements for *health security medical countermeasures* by the NIH, 7% pertain to broad-spectrum antivirals.

Recommendation: NIAID appears well-aware of the importance of broad-spectrum antivirals, however there appears to be an opportunity to increase the % of their budget going to this area. It would also be worthwhile to direct other funders (e.g. philanthropists) to support these NIAID funded and vetted researchers/laboratories.

⁸² "Center for Health Security: Characteristics of Pandemic" 10 May. 2018, http://www.centerforhealthsecurity.org/newsroom/center-news/2018/2018-05-10_characteristics-of-pandemic-pathogens.html. Accessed 15 Oct. 2019.

Impression: The US National Institutes of Health, via mainly NIAID, are actively funding research into broad-spectrum antiviral drugs..

Recommendation: Students and early-career researchers interested in broad-spectrum antivirals should consider working with laboratories who have been awarded NIAID grants in this space.

Impression: Within the US, the Biomedical Advanced Research and Development Authority has substantial influence and funding capability for antiviral drug development. However, they currently prioritize broad-spectrum antibiotic development due to concern for antimicrobial resistance. Only 1.5% (1/67) of their publicly listed grants/investments to date have been for broad-spectrum antivirals (broad-spectrum as defined per this report). BARDA is also significantly restricted in their ability to fund broad-spectrum initiatives, as some of their funding is tied to specific pathogens (e.g. Ebola, Zika).

Recommendation: Work to provide BARDA with consistent levels of annual funding that is not tied to a specific pathogen or emergency Congressional approval would do much to allow the agency to fund broad-spectrum drugs. Lobbying the agency to increase their focus on broad-spectrum antivirals could move substantial funding resources into the area. Ability to add these drugs to the Strategic National Stockpile would follow.

Next Steps: Further research is required into research & development efforts taking place in other countries, such as Japan, China, and the United Kingdom.

APPENDIX

The United Nations (other than the World Health Organization/Assembly)

The Biological Weapons Convention (BWC) is the first multilateral disarmament treaty banning biological weapons⁸³. It was signed in 1972. It prohibits the development, production and stockpiling, and use of biological weapons. It also aims to build trust among member states in order to improve international cooperation in the field of “peaceful biological activities”. Under the agreement, member states must provide annual reports on specific activities related to the BWC including:

- Data on research centres and laboratories
- Information on vaccine production facilities
- Information on national biological defence research and development programmes
- Declaration of past activities in offensive and/or defensive biological research and development programmes
- Information on outbreaks of infectious diseases and similar occurrences caused by toxins
- Publication of results and promotion of use of knowledge and contact
- Information on legislation, regulations and other measures

In 2004, the United Nations passed Security Council Resolution 1540, which requires all States to refrain from providing support to non-State actors that use nuclear, chemical or biological weapons⁸⁴.

Neither the BWC nor Resolution 1540 require member states to actively fund countermeasures. The United Nations does act to counter pandemics, as was the case during the Ebola outbreak of 2013–2016, during which the UN created the UN Mission for Ebola Response (UNMEER)⁸⁵. The aim of such an initiative is to “leverage the existing presence and expertise of UN country teams”. Health strategy and advice instead falls under the purview of the World Health Organization, a specialized agency of the UN.

⁸³ "Biological Weapons – UNODA – the United" <https://www.un.org/disarmament/wmd/bio/>. Accessed 7 Aug. 2019.

⁸⁴ "UN Security Council Resolution 1540 (2004) – UNODA." <https://www.un.org/disarmament/wmd/sc1540/>. Accessed 12 Aug. 2019.

⁸⁵ "making a difference – Global Ebola Response – the United Nations." 4 Jan. 2015, https://ebolaresponse.un.org/sites/default/files/ebolaoutlook_full.pdf. Accessed 7 Aug. 2019.

World Bank Group

The World Bank has previously provided emergency financing to countries that are affected by epidemics. In their role as an international financial institution with the mission of reducing poverty⁸⁶, it falls within their goals to provide loans to countries economically impacted by epidemics.

In 2017, the World Bank launched the Pandemic Emergency Financing Facility (PEF), known as “pandemic bonds” designed to transfer pandemic risk in low-income countries to the financial markets⁸⁷. The PEF provides upwards of \$500M to cover developing countries against the risk of pandemic outbreaks. The AIR Pandemic Model provides expert risk analysis. Funding is triggered when an outbreak reaches publically available WHO epidemic criteria.

PEF covers the following viruses:

- Orthomyxoviruses (Influenza A)
- Coronaviruses (SARS, MERS)
- Filoviridae (Ebola, Marburg)
- Other Zoonotic disease (Lassa fever, Rift Valley Fever, Crimean Congo Hemorrhagic Fever)

PEF is not a governing institution with authority for fast decision making nor is it a pandemic coordinating body. These decisions are deferred to the WHO and WHA, as guided by the International Health Regulations.

Under PEF, investors receive 13% annual interest to compensate for the risk that a pandemic occurs and ‘insurance’ payouts will occur. Otherwise, cash returns to investors at the date of bond maturity. It is possible for the World Bank to mobilize funds for pandemics independently of PEF, as was the case for the Ebola outbreak. Of note, PEF has been criticized for the low likelihood of insurance payout⁸⁸, such as the requirement for the pandemic to cause at least 20 deaths in a second country. “Tragically, current triggers guarantee that payouts will be too little because they kick in only after outbreaks grow large” says Olga Jonas, formerly of the World Bank and now Research Scientist at Harvard Global Health Institute⁸⁹.

⁸⁶ "A Stronger, Connected, Solutions World Bank Group : An Overview of" 7 Oct. 2013, <https://openknowledge.worldbank.org/handle/10986/16093>. Accessed 16 Aug. 2019.

⁸⁷ "World Bank Launches First-Ever Pandemic Bonds to Support \$500" 28 Jun. 2017, <https://www.worldbank.org/en/news/press-release/2017/06/28/world-bank-launches-first-ever-pandemic-bonds-to-support-500-million-pandemic-emergency-financing-facility>. Accessed 16 Aug. 2019.

⁸⁸ "Pandemic bonds: designed to fail in Ebola - Nature." <https://www.nature.com/articles/d41586-019-02415-9>. Accessed 16 Aug. 2019.

⁸⁹ "Pandemic bonds: designed to fail in Ebola - Nature." <https://www.nature.com/articles/d41586-019-02415-9>. Accessed 16 Aug. 2019.

Public Health and Social Services Emergency Fund

PUBLIC HEALTH AND SOCIAL SERVICES EMERGENCY FUND**FY 2018 ALL PURPOSE TABLE**

(Dollars in Millions)

Program	FY 2016	FY 2017	FY 2018	
	Final	Annualized CR	President's Budget	+/- FY 2017 Annualized CR
Assistant Secretary for Preparedness and Response (ASPR):				
Preparedness and Emergency Operations.....	24.654	24.607	24.607	--
Office of Emergency Management only (non-add).....	19.654	19.617	19.617	--
National Special Security Events (NSSE) (non-add).....	5.000	4.990	4.990	--
National Disaster Medical System (NDMS).....	49.904	49.809	49.809	--
Hospital Preparedness.....	254.555	254.071	227.201	-26.870
Hospital Preparedness Program (HPP) Grants (non-add).....	228.500	228.500	204.500	-24.000
Medical Reserve Corps.....	6.000	5.989	5.989	--
Biomedical Advanced Research and Development Authority (BARDA).....	540.080	510.727	511.700	+0.973
Advanced Research and Development (non-add).....	288.080	259.206	259.700	+0.494
Combating Antimicrobial Resistance (non-add).....	192.000	191.635	192.000	+0.365
Operations and Management (non-add).....	60.000	59.886	60.000	+0.114
Project BioShield.....	510.000	509.030	510.000	+0.970
Office of Policy and Planning.....	14.877	14.849	14.849	--
Operations.....	30.938	30.879	30.879	--
Pandemic Influenza				
No-Year Pandemic Influenza.....	40.000	39.924	174.924	+135.000
Annual Pandemic Influenza /1.....	27.991	27.938	27.938	--
Subtotal, Pandemic Influenza	67.991	67.862	202.862	+135.000
Subtotal, ASPR Program Level	1,498.999	1,467.824	1,577.896	+110.072
Subtotal, ASPR Budget Authority	1,498.999	1,467.824	1,577.896	+110.072
Other Office of the Secretary:				
Pandemic Influenza.....	4.009	4.001	4.001	--
Annual funding (non-add).....	4.009	4.001	4.001	--
Cybersecurity /2.....	50.860	50.763	72.223	+21.460
Office of Security and Strategic Information (OSSI) /2.....	7.470	7.456	8.496	+1.040
Subtotal, Other Office of the Secretary.....	62.339	62.220	84.720	+22.500
PHSSEF Total:				
HHS Pandemic Influenza Budget Authority.....	72.000	71.863	206.863	+135.000
No-Year Pandemic Influenza (non-add).....	40.000	39.924	174.924	+135.000
Annual Pandemic Influenza (non-add).....	32.000	31.939	31.939	--
All Other Budget Authority.....	1,489.338	1,458.181	1,455.753	-2.428
Total, PHSSEF Program Level.....	1,561.338	1,530.044	1,662.616	+132.572
Total, PHSSEF, Budget Authority	1,561.338	1,530.044	1,662.616	+132.572
FTE				
ASPR	612	612	612	--
OGA	5	5	5	--
OSSI	35	40	40	--
Cybersecurity	82	93	123	+30
Total FTE, PHSSEF	734	750	780	+30

1/ Includes \$3.0 million for Office of Policy and Planning International Influenza Activities

2/ The FY 2018 President's Budget reflects a realignment of \$1.040 million between Cybersecurity and OSSI for cyber threat activities.