Policy Brief

Viral Families and Disease X: A Framework for U.S. Pandemic Preparedness Policy

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Executive Summary

The threat of future pandemics is intensifying as globalization, urbanization, and encroachment on animal habitats cause infectious outbreaks to become more frequent and severe. To prepare for these future risks, the United States should proactively build a pipeline that encompasses the lifecycle of medical countermeasure development.

While the virus that causes the next viral pandemic has not likely yet emerged, we have identified seven viral families—groups of related viruses—that share pandemic-causing characteristics and are likely to yield the next pandemic virus. We assess that recognizing and prioritizing families of viral pathogens of pandemic potential (VPPPs), instead of individual viruses, will enable the United States to be better prepared. This approach would allow U.S. government officials and researchers to anticipate future threats, develop broad medical countermeasures (MCMs), and put in place foundational basic and applied research that can be used in a crisis.

We examined research publications, clinical trials, and the U.S. Food and Drug Administration-approved medical countermeasures to evaluate U.S. pandemic preparedness for VPPPs. Our key findings include the following:

The United States is not prepared to counteract a pandemic due to two factors: a lack of MCMs, and vulnerabilities in the manufacturing supply chain. Without pre-approved medical countermeasures—and the ability to rapidly produce and deploy them—the American public will not have essential therapies during an emergency.

- Only 43 MCMs are approved for all seven families of VPPP, and these include vaccines, small-molecule drugs, and antibody therapies.
- United States VPPP MCM manufacturing is vulnerable to supply chain disruptions due to limited domestic manufacturing and a lack of manufacturing redundancy; 30 percent of the MCMs are only manufactured abroad and 51 percent of MCMs are only manufactured at a single site.

There is inadequate VPPP research and development (R&D) to provide a foundation for pandemic preparedness, representing a system that reacts to—rather than prepares for—major outbreaks. The United States will lose valuable time during an outbreak if fundamental basic research and clinical developments are not already in place.
The number of research publications and clinical trials peak after major outbreaks and then decline after the public health emergency has passed. VPPP publications have plateaued over time, even as total viral research increased. VPPPs make up only 14 percent of all virus-related research publications and 20 percent of all virus-related clinical trials despite presenting the greatest pandemic risk.

Based on our analysis, we propose that the United States government enact the following policy recommendations:

1. **Include families of VPPP in pandemic preparedness strategies**: We recommend including the seven viral families as priority pathogens for research funding and clinical trials to drive understanding and development of MCMs for pandemic preparedness.

2. **Prioritize research and clinical trials for VPPPs in government-funding mechanisms in advance of public health emergencies**: New public-private initiatives, like the Antiviral Program for Pandemics, created in 2021 and overseen by the National Institutes of Health and Biomedical Advanced Research and Development Authority (BARDA), are a good start for a forward-looking and multidisciplinary approach to VPPP R&D. Such initiatives should be continued and expanded.

3. **Create a market for novel medical countermeasures to incentivize drug development**: The federal government can drive MCM development by creating a market for MCMs to help balance private sector interests with national security needs. Many of these MCMs may not be used if an outbreak does not occur. U.S. programs should incorporate strategies to advance MCM candidates with early clinical testing and then pause development until the therapy is needed.

4. **Onshore medical countermeasure manufacturing**: The United States government should incentivize onshoring MCM manufacturing to protect the public’s access to critical therapies. Such priorities are already reflected in policy initiatives, such as the CHIPS and Science Act of 2022 and an executive order to expand biomanufacturing.

5. **Build redundancy into the medical countermeasure supply**: The United States government should incentivize diversifying MCM manufacturing across multiple sites to protect against supply chain disruptions that can occur when all production is at a single site.
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Scope Note

This paper is focused on the steps that the United States can take to prepare for a future pandemic, while recognizing that solutions may not align with traditional market forces. We acknowledge that framing medical countermeasure (MCM) development as a national security concern is at odds with viewing medical products in the market context of supply and demand. In the United States, MCM development is primarily driven by the private sector, which focuses on products with a large existing market to capture a high return on the investment that it takes to develop a new drug. This is not unique to the pharmaceutical industry; it is in line with most industries that operate in a market-based economy. However, pandemic preparedness is not just a matter of business interests—it is a matter of national security that affects human health and the ability of society to function. The United States will be at a disadvantage if market forces alone dictate the speed of MCM development, as a profitable market for pandemic MCMs will not exist until an outbreak has already taken root and spread.

Regardless of past efforts to build a foundation for pandemic preparedness, the COVID-19 pandemic highlights how reactionary responses have limitations that result in impacts on global health and economics. This will happen again if a different approach is not taken. How can the United States ensure its preparation for a future pandemic, while acknowledging that private industry is motivated by market-driven competition rather than national security? This is the moment for the United States to design policies and incentives that place MCM development and pandemic preparedness squarely in the realm of national security.

We recognize that viral surveillance and diagnostic testing are a critical part of any pandemic preparedness program but are beyond the scope of this report, as is an in-depth risk assessment to compare the different viral families.

*Some government programs exist to develop MCMs for infectious diseases but are limited to certain pathogens (for example, the Biomedical Advanced Research and Development Authority focuses on influenza and emerging infectious diseases; chemical, biological, radiological, and nuclear medical countermeasures also known as CBRN; and the NIH biodefense program prioritizes a select list of priority pathogens). We recognize ongoing effort from these agencies, but recommend a more holistic strategy that encompasses a variety of pathogens that could cause a pandemic. National Institute of Allergy and Infectious Diseases, “NIAID Emerging Infectious Diseases/ Pathogens,” [https://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens](https://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens); and Administration for Strategic Preparedness and Response, “Biomedical Advanced Research and Development Authority,” [https://aspr.hhs.gov/AboutASPR/ProgramOffices/BARDA/Pages/default.aspx](https://aspr.hhs.gov/AboutASPR/ProgramOffices/BARDA/Pages/default.aspx).
Introduction

Pandemic threats are increasing as new viruses emerge and old viruses return. Both urbanization and a changing global climate push people into closer contact with animals and one another, raising the risk of zoonotic events. As a result, new viruses can spread rapidly as globalization carries viruses across borders to new communities. As we look to the future, a proactive approach to preventing and combating pandemics will be essential to safeguard public health and economic interests. However, this approach may not align with traditional market forces, and will necessitate that the government set priorities and incentives to reframe pandemic preparedness as a matter of national security.

The lifecycle of pandemic preparedness begins with foundational basic scientific research and culminates in approved therapies. This report assesses this entire lifecycle, and the level of the United States' preparedness, by examining research publications, clinical trials, and the U.S. Food and Drug Administration (FDA)-approved medical countermeasures (MCMs). We identified critical gaps in this pipeline that reveal that the United States is ill-prepared for both current and future viral threats. This comprehensive look at the depth and breadth of research, clinical development, and MCM supply can help inform actionable strategies to prepare for future viral outbreaks and pandemics.
A New Approach to Pandemic Preparedness: Focus on Viral Families

Accurately predicting the next viral pandemic—and which virus will cause it—is highly unlikely given the emergence of new viruses and the complex interactions between viruses and immune systems. However, we can be better prepared for the next pandemic by examining the factors that would contribute to the rapid spread and societal impact of related viruses. Focusing on groups of related viruses—also known as viral families—that have a combination of characteristics that can cause a pandemic will accelerate research and development (R&D) timelines when new viruses emerge from these families and will enable researchers to develop broad-reaching MCMs based on foundational basic research.

Using foundational assessments on viral families from Johns Hopkins University, we identified seven viral families that are viral pathogens of pandemic potential (VPPPs), as seen in Table 1, (because they contain viruses that spread through the respiratory system such as by sneezing or coughing). These viruses are most likely to cause a pandemic because they spread easily from person-to-person and can travel and persist in the air. Almost every major historical epidemic and outbreak has been caused by respiratory viruses including diseases such as influenza, polio, smallpox, measles, mumps, rubella, and those caused by coronaviruses. Annual recurrent influenza and other viral outbreaks highlight the persistence of respiratory viruses.

Some of the seven families containing VPPPs have additional characteristics that could also contribute to a pandemic: an RNA genome that confers high mutability and zoonotic potential.

**RNA genome**

RNA is genetically less stable than DNA, so viruses that use RNA as genetic material are more likely to mutate. These mutations can give RNA viruses more opportunities to acquire new characteristics that enhance transmissibility, evade immune responses, or expand host ranges (see zoonosis). For example, influenza is an RNA virus that mutates frequently, and new vaccines must therefore be produced every year to counteract the newest influenza strains.

**Zoonotic potential**

Many viruses that newly infect humans originate in animals through zoonosis. Zoonotic viruses are especially risky for several reasons including: people’s immune
systems have never encountered them before, viruses with a breadth of hosts are more likely to be able to infect humans, and MCMs have not been developed. The risk of a new virus entering the human population is increasing as people come into contact with animal habitats more often. Additionally, climate change is altering the habitat ranges of animals, potentially pushing them into closer contact with humans.\textsuperscript{9} Previous zoonotic epidemics or pandemics include influenza pandemics.\textsuperscript{10} 

The combination of respiratory transmission, mutability, and zoonotic potential suggests that the following viral families that share these characteristics are of pandemic potential. Each of these families contains viruses that have infected humans and others that are currently only circulating in animal populations.

Table 1: Viral Pathogens of Pandemic Potential Characteristics

<table>
<thead>
<tr>
<th>Viral Family</th>
<th>Notable Viruses</th>
<th>Mode of Transmission*</th>
<th>Genetic Material</th>
<th>Confirmed Zoonotic Transmission**</th>
<th>Family Size***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoviridae</td>
<td>Adenovirus 7, 14</td>
<td>Respiratory, Fecal-oral</td>
<td>DNA</td>
<td>Yes</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Coronaviridae</td>
<td>SARS-COV-2, SARS-COV, MERS</td>
<td>Respiratory, Fecal-oral, Surface contact</td>
<td>RNA</td>
<td>Yes</td>
<td>50-100</td>
</tr>
<tr>
<td>Orthomyxoviridae</td>
<td>Influenza</td>
<td>Respiratory, Water</td>
<td>RNA</td>
<td>Yes</td>
<td>&lt;10 (hundreds of subtypes)</td>
</tr>
<tr>
<td>Paramyxoviridae</td>
<td>Measles, Mumps</td>
<td>Respiratory</td>
<td>RNA</td>
<td>Yes</td>
<td>50-100</td>
</tr>
<tr>
<td>Viral Family</td>
<td>Virus</td>
<td>Transmission Routes</td>
<td>Viral Type</td>
<td>Zoonotic Transmission</td>
<td>Number</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------------------</td>
<td>---------------------</td>
<td>------------</td>
<td>------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Picornaviridae</td>
<td>Poliovirus, Foot-and-Mouth Disease Virus</td>
<td>Respiratory, Surface, Contact</td>
<td>RNA</td>
<td>None confirmed</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Pneumoviridae</td>
<td>Respiratory Syncytial Virus (RSV)</td>
<td>Respiratory</td>
<td>RNA</td>
<td>None confirmed</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Poxviridae</td>
<td>Smallpox</td>
<td>Respiratory, Surface Contact</td>
<td>DNA</td>
<td>Yes</td>
<td>50-100</td>
</tr>
</tbody>
</table>

* By at least one virus within the viral family.
** See Tables 1-7 in the Appendix for examples of zoonotic transmission.
*** The number of viruses in each family relates to the potential risk and will be discussed later in the paper.

Source: International Committee on Taxonomy of Viruses.
Methodology

As a way to assess current preparedness, we looked at the following factors that we consider to be part of the preparedness lifecycle: basic research, clinical trials, and medical countermeasures using a viral family taxonomy. No one factor alone contributes to preparedness, but a broad foundation of research and manufacturing capabilities would allow a country to quickly develop therapies during an outbreak.

Taxonomy Development: We developed this taxonomy, available at [https://github.com/georgetown-cset/viral-families](https://github.com/georgetown-cset/viral-families), using virus names established by the International Committee on Taxonomy of Viruses,¹¹ and keywords from the National Library of Medicine’s Medical Subject Headings (MeSH).¹² We used this taxonomy to query publications, clinical trials, and MCMs.

Publications:

To characterize the current state of global respiratory viral family research, we investigated the R&D landscape using CSET’s merged corpus of publication open-source data holdings. CSET’s merged corpus of scholarly literature includes Digital Science Dimensions, Clarivate’s Web of Science, Microsoft Academic Graph, China National Knowledge Infrastructure, arXiv, and Papers With Code.¹³ We further analyze this body of research by country and year to examine trends in virus R&D, highlighting the focus on different viral families over time. We looked at years 2000-2019 to assess the state of pandemic preparedness in the United States prior to the COVID-19 pandemic, and to avoid a large data skew in the coronaviridae family.

Clinical trials: Data on clinical trials were queried using the viral taxonomy on [https://www.clinicaltrials.gov/](https://www.clinicaltrials.gov/). We excluded any trials that were not part of the viral taxonomy.

Identifying FDA-approved therapies for VPPPs: The viral taxonomy terms were used to query the “Indications and Usage” labeling section of human therapies in the FDALabel database.¹⁴ This analysis is focused on FDA-approved therapies, so therapies labeled “unapproved” were excluded. We manually verified that each therapy is approved for one of the queried viruses by inspecting the drug label and excluding misidentified therapies—for example, the search term “influenza” identified therapies to treat infections caused by the bacteria haemophilus influenzae and were excluded. Vaccines were identified by cross-referencing the list of FDA-licensed vaccines.¹⁵ For the orthomyxoviridae family, analysis included the nine vaccines that
were approved for the 2022-2023 flu season. Additional analysis includes therapies granted Emergency Use Authorizations (EUA) for the COVID-19 pandemic and mpox outbreak. The analysis includes therapies that were approved as of November 2022.

**Manufacturing analysis:** This analysis is specifically focused on drug products—the finished dosage form that has been mixed with other active or inactive ingredients, packaged, and is ready for consumption or injection. This does not take into account the manufacturing landscape of key starting ingredients, drug substances, or active pharmaceutical ingredients (APIs).

For small-molecule drugs and biologics, we obtained application numbers (NDA, ANDA, or BLA)* for all generic and name-brand formulations on the Drugs@FDA database and codes from the FDA’s National Drug Code for each application were obtained from the NDC Directory. The NDC code was used to find each product’s label, patient insert, and prescriber packet on DailyMed as of November 2022. Each of these documents was manually inspected to identify the disclosed manufacturer and manufacturing location. For the purposes of this analysis, we only assigned a manufacturing location if it was clear that the location corresponded to drug product manufacturing and not drug substance manufacturing. If this was unclear, the manufacturing site was assigned as “undetermined.” In some cases, we called the product’s customer service line to inquire about the manufacturing location. If we were still unable to identify the manufacturing location, or if a product had an active application but did not have a corresponding NDC, the manufacturing status was classified as “undetermined.”

For vaccines, manufacturers were identified by downloading all documentation from the “Product Information” and “Supporting Documents” sections of the list of approved vaccines as of November 2022. Where available, we inspected each vaccine’s package insert, approval letter(s), and Summary Basis for Regulatory Action(s), each of which may contain information about manufacturing. “Unidentified” indicates that the manufacturer was not disclosed, the manufacturing location(s) were redacted, or that we were otherwise unable to confirm a manufacturing site.

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* NDAs, ANDAs, and BLAs are the applications that are submitted to the FDA for approval before a drug can be marketed or sold in the United States. NDAs (New Drug Applications) pertain to new drugs, ANDAs (Abbreviated New Drug Applications) pertain to generic drugs that are based on an already-approved drug, and BLAs (Biologics License Applications) pertain to biologic products.
Reactionary Research and Uneven Development

We chose to assess pandemic preparedness by focusing on families of VPPPs that share potentially risky characteristics, because the viruses within these families are closely related, and building a foundation of R&D for known viruses will also help prepare us for the next ones that emerge from these families. While this approach does not take every possible threat into account, it allows us to prioritize the highest-risk families of viruses and provides a way to explore pandemic preparedness based on the lifecycle of basic research, clinical trials, and therapy development.

Medical Countermeasures Limited Availability

Pandemic response requires rapid production and deployment of critical medical countermeasures, including preventative vaccines and therapies to combat viral outbreaks. A diverse pipeline of MCMs is useful for both current and future viral threats; MCMs for one virus can be repurposed or modified to treat closely related viruses.* However, our analysis of MCM availability and manufacturing indicates that MCM options for VPPPs are limited and that the supply is vulnerable to manufacturing disruptions.

Currently, there are only 43 MCMs approved by the FDA to treat or prevent viruses from the seven viral families that we have prioritized.† These countermeasures include vaccines, drugs, and antibody therapies and are outlined in Figure 1 and Table 2. While most of the seven families of VPPP have vaccines to prevent disease outbreaks, a few are no longer used after disease eradication or are only used in military settings.21

The MCMs that do exist are not equally distributed among the VPPP families, with some having very few approved treatment options. For example, no vaccines are

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* Due to similarities between the orthopoxviruses smallpox and mpox, the smallpox antiviral drug tecovirimat was made available under an expanded access protocol during the 2022 mpox outbreak. See Centers for Disease Control and Prevention, “Expanded Access IND Protocol: Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola orthopoxvirus Infections in Adults and Children,” https://www.cdc.gov/poxvirus/monkeypox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf; and Centers for Disease Control and Prevention, “Tecovirimat (also known as TPOXX, ST-246),” https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html#anchor_1655488284069

† This does not include drugs that are used off-label or that treat secondary symptoms.
currently approved for respiratory syncytial virus of the pneumoviridae family,* despite the fact that RSV hospitalizes over fifty thousand children each year in the United States.²² Additionally, the only Adenoviridae MCM is used exclusively by the military and not available for public use.²³

Our research showed that MCMs are often developed in response to a public health emergency. For example, no vaccines had been approved by the FDA for viruses within the coronaviridae family until the emergence of COVID-19. While the clinical testing and approval of COVID-19 vaccines were reactionary to the outbreak, the novel vaccines were built on decades of basic research into coronaviruses and mRNA vaccines and highlight the value of foundational basic R&D.²⁴ Similarly, multiple formulations of the flu vaccine of the orthomyxoviridae family exist to combat the ever-evolving and prevalent disease.²⁵ These examples, and the overall low number of MCMs for VPPPs, highlight the fact that the United States does not proactively develop MCMs for future viral threats.

Figure 1. FDA-Approved Medical Countermeasures for Viral Pathogens of Pandemic Potential (VPPPs)

Source: CSET Analysis of FDA Documentation.

* Several RSV vaccines are under clinical development and may be approved as early as 2023. Palivizumab (Synagis) is a monoclonal antibody that can help protect high-risk infants from RSV infection, but is not a vaccine and does not provide long-term protection.
Table 2. Viral Pathogens of Pandemic Potential with FDA-Approved Medical Countermeasures

<table>
<thead>
<tr>
<th>Family</th>
<th>Vaccine(s) or Preventative Immunoglobulins</th>
<th>Therapeutic Treatment(s)</th>
<th>Prominent Family Members without Approved MCMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoviridae</td>
<td>Adenovirus types 7 and 14</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Coronaviridae</td>
<td>SARS-CoV-2 (COVID-19)</td>
<td>SARS-CoV-2 (COVID-19)</td>
<td>SARS-CoV, MERS-CoV</td>
</tr>
<tr>
<td>Orthomyxoviridae</td>
<td>Influenza (including seasonal H1N1, seasonal Influenza B, and H5N1)</td>
<td>Influenza (including seasonal H1N1, seasonal Influenza B, and H5N1)</td>
<td>None</td>
</tr>
<tr>
<td>Paramyxoviridae</td>
<td>Rubeola virus (Measles), Mumps virus</td>
<td>Rubeola virus (Measles)</td>
<td>Nipah virus, Hendra virus</td>
</tr>
<tr>
<td>Picornaviridae</td>
<td>Poliovirus, Hepatitis A virus</td>
<td>Poliovirus Hepatitis A virus</td>
<td>None</td>
</tr>
<tr>
<td>Pneumoviridae</td>
<td>Respiratory Syncytial Virus (RSV)*</td>
<td></td>
<td>RSV (vaccine)**</td>
</tr>
<tr>
<td>Poxviridae</td>
<td>Variola virus (Smallpox)</td>
<td>Variola virus (Smallpox) Vaccinia virus</td>
<td>Monkeypox virus***</td>
</tr>
</tbody>
</table>

* Palivizumab (Synagis) is a monoclonal antibody that can help protect high-risk infants from RSV infection, but is not a vaccine and does not provide long-term protection.
** Several RSV vaccines are under clinical development and may be approved as early as 2023. Palivizumab (Synagis) is a monoclonal antibody that can help protect high-risk infants from RSV infection, but is not a vaccine and does not provide long-term protection.
*** A smallpox vaccine (JYNNEOS) has been granted emergency use authorization for mpox, and a smallpox drug (Tecovirimat) has been made available under a non-research Expanded Access Investigational New Drug (EA-IND) protocol.

Source: FDALabel database.
Medical Countermeasure Manufacturing Deficiencies

The capacity to domestically manufacture and distribute MCMs is as important as having approved therapies, but the United States does not produce all of its own VPPP MCMs. Analysis of MCM manufacturing locations indicates that only 47 percent of the MCMs have at least one domestic manufacturing site, with another 30 percent only manufactured abroad (Figure 2).

The United States also lacks redundancy in its supply chain of MCMs. Of the total identified VPPP MCMs, 51 percent are only manufactured at one site (Figure 2). This introduces vulnerabilities into the MCM supply chain if the entirety of U.S. supply comes from a single facility, as one natural disaster, contamination issue, or attack can incapacitate the MCM supply.
Figure 2. Manufacturing Analysis of Viral Pathogens of Pandemic Potential (VPPPs)

**MCM Domestic Manufacturing**

- No domestic manufacturers (30%)
- At least one domestic manufacturer (47%)
- Undetermined (23%)

**MCM Manufacturing Redundancy**

- More than one manufacturing site (21%)
- Single manufacturing site (51%)
- Undetermined (28%)

Source: CSET Analysis of FDA Documentation.
Research and Development is Reactionary

MCMs are built on decades of basic research and clinical development, and prior R&D on existing viruses will accelerate the speed of MCM development when new, related viruses emerge. Despite the importance of foundational research on a wide range of viruses, our investigation shows that instead of steady or increasing research on these VPPPs, R&D from 2000 to 2019* (Figure 3) was reactionary to major viral outbreaks. For example, both Orthomyxoviridae publication numbers and clinical trials dramatically increased after the 2009 H1N1 influenza pandemic that caused at least 150,000 worldwide deaths.28 Interestingly, Coronaviridae publications, but not clinical trials, increased following the 2002-2004 severe acute respiratory syndrome (SARS-CoV) pandemic. This might be due to better containment and thus fewer deaths by SARS.29

Picornaviridae has the most clinical trials in our analysis for every year except for 2009, even though there was no significant increase in viral outbreaks (Figure 3). This could be because Hepatitis A clinical trials make up more than two-thirds of Picornaviridae clinical trials, likely due to a high global health burden.30 Initiatives to eradicate polio, also in the picornaviridae family, gained prioritization and funding in the mid-2010s.†

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* We did not include data during the ongoing COVID-19 pandemic, as the axis on the graphs are skewed, and we cannot yet evaluate the status of research and development of the Coronaviridae because the pandemic is ongoing

† In 2012, the WHO declared polio eradication to be a global health priority. The United States and organizations including The Global Polio Eradication Initiative and Bill and Melinda Gates Foundation pledged billions of dollars towards eradicating polio in the 2000s.
Figure 3. Viral Pathogens of Pandemic Potential (VPPPs) Publications and Clinical Trials over Time, 2000-2019

VPPP Publications
2000-2019

VPPP Clinical Trials
2000-2019

Source: CSET Merged Corpus and clinicaltrials.gov.
Trends in Research and Development are Uneven Among the Viral Families

VPPPs make up a small percentage of all research publications about viruses despite the fact that they are the most likely to cause a pandemic (Figure 4). In addition, the number of VPPP publications has plateaued over the same time period that total viral research has increased. This indicates that there will be limited foundational understanding that could be used to develop MCMs if a VPPP causes an outbreak.

Figure 4. Total of Viral Pathogens of Pandemic Potential (VPPPs) Publications and All Viruses over Time, 2000-2019

Clinical trial data also reveals limited preparation for a future pandemic. VPPPs only make up about one-fifth of all viral clinical trials (Figure 5b). These clinical trials are not distributed amongst the VPPPs similarly to publications and instead are predominated by just two viral families (Figure 5b). This indicates that many of the VPPPs we identified do not have a coordinated pipeline of clinical research that could lead to MCMs.
Figure 5. Viral Pathogens of Pandemic Potential (VPPPs) Publications and Clinical Trials Family Distribution, 2000-2019

VPPP Publications

<table>
<thead>
<tr>
<th>Virus Family</th>
<th>Total Publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Viruses</td>
<td>992,622</td>
</tr>
<tr>
<td>Total VPPPs</td>
<td>138,105</td>
</tr>
</tbody>
</table>

Total VPPP Publications by Virus Family

VPPP Clinical Trials
Total clinical trials from 2000-2019.

<table>
<thead>
<tr>
<th>Virus Family</th>
<th>Total Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Viruses</td>
<td>26,728</td>
</tr>
<tr>
<td>Total VPPPs</td>
<td>5,444</td>
</tr>
</tbody>
</table>

Total VPPP Clinical Trials by Virus Family

Source: CSET Merged Corpus and clinicaltrials.gov.
**Conclusion**

The United States reacts to—rather than prepares for—major outbreaks. A proactive approach to pandemic preparedness should include development across the entire lifecycle from basic research to clinical development to MCM approval and manufacturing. The United States will lose valuable time during the next pandemic if the ecosystem of researchers, clinicians, manufacturers, and regulatory agencies have not already been established prior to a public health emergency.

The viral families that are most likely to cause a pandemic—VPPPs—are not uniformly prioritized in R&D even though they potentially present the greatest public health risk. The combination of ease of spread, frequent mutation, and transmission between humans and animals means that VPPPs could cause rapid and global outbreaks. If a new virus emerges from one of these families, the United States preparedness lifecycle for these VPPPs is disjointed between basic research, clinical trials, and MCM development. This disconnect could reflect the different priorities of actors in the process—researchers may have academic or public health interests while the companies that fund clinical trials and produce MCMs have financial interests.

Lack of MCMs and vulnerabilities in manufacturing them also leave the United States vulnerable to the next pandemic. Rapid MCM distribution is critical in the early days of an outbreak; however, some viral families lack vaccines or effective treatment options. A lack of MCMs gives the outbreak time to spread while new drugs undergo the lengthy development and approval process. While some of the viral families do have multiple treatment options, a reliance on foreign manufacturers and a lack of manufacturing redundancy means that the American public may not be able to access these MCMs in the event of an emergency.
Policy Recommendations

The vulnerable MCM supply and lack of foundational research for families of VPPP highlights the necessity of government support for strategic industries, particularly when commercial markets do not align with national interests. Based on our analysis, we propose that the United States government enact the following policy recommendations:

1. **Include families of VPPP in pandemic preparedness strategies.**

Viral families with pandemic-causing characteristics pose a major public health risk and should be the focus of preparedness efforts. However, current national strategies predominantly focus on individual viruses instead of related families. We therefore recommend including the seven viral families as priority pathogens for federal research funding and clinical trials to drive understanding and development of MCMs for pandemic preparedness.

2. **Prioritize research and clinical trials for VPPPs in government-funding mechanisms in advance of public health emergencies.**

VPPP research and clinical trials should be proactive to prepare for future pandemics. New public-private initiatives in reaction to the COVID-19 pandemic, like the Antiviral Program for Pandemics created in 2021 brought together NIH institutions and BARDA to prioritize R&D of viral pathogens of pandemic potential. The APP funds early clinical trials of antiviral candidates, aiding in MCM development that will allow these therapies to be more rapidly scaled up in the event of an outbreak. Programs like these are a good start for a forward-looking and multidisciplinary approach to VPPP R&D, and should sustain and expand funding from all agencies.

3. **Create a market for novel medical countermeasures to incentivize drug development.**

MCMs are critical during the first days of a pandemic and should be developed in advance of an outbreak. However, MCMs for a future outbreak may not have a commercial market—and therefore incentives for private industry to invest in R&D—until an outbreak occurs. We recommend that the federal government drive MCM development by creating a market and incentives for MCMs—either by guaranteeing purchase for the national stockpile, creating a subscription model similar to the proposed PASTEUR Act for antimicrobials, or incentivizing development. For example,
programs like Project Bioshield, BARDA funding for pandemic influenza and emerging infectious disease, and public-private partnerships like the Coalition for Epidemic Preparedness Innovations (CEPI) could be used as models for future efforts.\footnote{33} We recommend implementing programs that can advance MCM candidates through early clinical trials and then pause development until an outbreak occurs based on the Department of Health and Human Services’ Integrated Technology Readiness Levels for Medical Countermeasure Products.\footnote{34} These efforts will help to balance investment levels with the fact that the therapy may not be needed.

4. \textit{Onshore medical countermeasure manufacturing.}

The U.S. government should prioritize onshoring MCM manufacturing to protect the public’s access to critical therapies. This effort will require significant government infrastructure investments and workforce development initiatives. Such priorities are already reflected in policy initiatives, such as the CHIPS and Science Act of 2022 and an executive order to expand biomanufacturing. However, successfully reshoring pharmaceutical manufacturing will be an ongoing effort. In line with recent recommendations from the U.S. Government Accountability Office, we suggest that a study of risks, challenges, and goals be established for the new domestic manufacturing program BioMaP in order to maintain a manufacturing capacity reserve in a future public health emergency.\footnote{35}

5. \textit{Build redundancy into the medical countermeasure supply.}

The U.S. government should prioritize diversifying MCM manufacturing across multiple sites to protect against supply chain disruptions that can occur when all production is at a single site. Some solutions could be for the federal government to incentivize companies to produce MCMs at more than one manufacturing site or to build and equip flexible manufacturing facilities for rapid deployment in a pandemic.
Appendix: Viral Family Pandemic Characteristics

As described previously, our analysis uses a virus family-based approach (Table 1). The following sections detail an in-depth look at each viral family of pandemic potential and include key viruses, major outbreaks, and implications.

**Adenoviridae**

Currently, the only FDA-approved therapy is a vaccine against adenovirus types 4 and 7. This vaccine is only available to the military, where respiratory adenovirus infections spread in close-quarter and specific environmental conditions.

**Appendix Table 1. Adenoviridae**

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
</table>
| Types 3, 4, 7, and 14 | Humans       | Endemic, sporadic cases and outbreaks | · Type 7 is associated with more severe outcomes  
· Types 4 and 7 can spread in bodies of water  
· Zoonotic; Type 4 shares most of its genetic sequence with the chimpanzee adenovirus sequence | Vaccine (Type 4 and 7 only) |
<p>| Types 8, 19, 37, 53, and 54 | Humans       | Endemic, sporadic cases and outbreaks | · Causes epidemic keratoconjunctivitis                                           | None                       |</p>
<table>
<thead>
<tr>
<th>Types 40 and 41</th>
<th>Humans</th>
<th>Endemic, sporadic cases and outbreaks</th>
<th>Causes gastroenteritis, especially in children</th>
<th>None</th>
</tr>
</thead>
</table>
| Canine Adenovirus 1 (CAV-1) and 2 (CAV-2) | Canines | Endemic in canines | CAV-1: infectious canine hepatitis  
CAV-2: infectious tracheobronchitis (kennel cough) | Animal Vaccines |
| Avian adenoviruses | Birds including chickens, quails, and pheasants | Endemic in birds | Avian adenoviruses cause inclusion body hepatitis, bronchitis, and marble spleen disease | Animal Vaccines |
Coronaviridae

Prior to the COVID-19 pandemic, there were no MCMs against viruses in the Coronaviridae family. As a result of a coordinated effort by researchers, clinicians, pharmaceutical companies, and regulatory agencies, FDA-approved therapies now include two vaccines, the antiviral drug Veklury (remdesivir) and the immune modulating drug Olumiant (baricitinib).\textsuperscript{37}

Appendix Table 2. Coronaviridae

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV</td>
<td>Humans</td>
<td>2002-2003</td>
<td>• ~8,000 infections, nearly 800 deaths.</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Only 8 cases were confirmed in the United States, and none after 2004.</td>
<td></td>
</tr>
<tr>
<td>MERS-CoV</td>
<td>Camels, humans</td>
<td>2012</td>
<td>• Zoonotic; has reached 27 countries and caused over 800 deaths since 2012.</td>
<td>None</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Research is ongoing</td>
<td>2019-Present</td>
<td>• Not fully captured yet</td>
<td>Vaccines, drugs</td>
</tr>
<tr>
<td>Common Human Coronavirus: HCoV types 229E, NL63, OC43, HKU1</td>
<td>Human</td>
<td>Endemic</td>
<td>• Mild to moderate upper-respiratory tract illness, similar to the common cold</td>
<td>None</td>
</tr>
<tr>
<td>Virus/Microbial Pathogen</td>
<td>Host(s)</td>
<td>Geographical Distribution</td>
<td>Symptoms/Impact</td>
<td>Vaccine Type</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>----------</td>
<td>---------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Canine Coronavirus</td>
<td>Canines</td>
<td>Endemic, worldwide</td>
<td>Highly contagious in dogs</td>
<td>Animal vaccines</td>
</tr>
<tr>
<td>Infectious bronchitis virus</td>
<td>Chickens</td>
<td>Endemic, worldwide</td>
<td>Highly contagious in chickens, causes lowered egg production</td>
<td>Animal vaccines</td>
</tr>
<tr>
<td>Bovine Coronavirus</td>
<td>Cattle</td>
<td>Endemic, worldwide</td>
<td>Extreme dehydration in calves</td>
<td>Animal vaccines</td>
</tr>
</tbody>
</table>
Orthomyxoviridae

Influenza contains four viral types: A, B, C, and D, some of which are further broken down into subtypes or lineages. Seasonal influenza is caused by circulating influenza types A and B. New strains are created frequently, both through mutations to existing strains over time and combination of two influenza A strains into a new virus.³⁸

As new strains emerge, influenza A is further classified into subtypes based on the hemagglutinin (HA) and neuraminidase (NA) proteins on the virus’s surface and are indicated as Influenza A(H#N#). Influenza B is split into two lineages (B/Yamagata and B/Victoria) and further categorized into types and subtypes. Novel strains have characteristics unfamiliar to the immune system, so additional MCMs are needed to combat them.

Selected members of the four influenza viral types are presented here.³⁹

Appendix Table 3. Orthomyxoviridae

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
</table>
| Influenza A (H1N1)    | Birds, pigs, humans | 1918; 2009; Endemic disease (seasonal outbreaks) | • 1918: infected approximately one-third of the world’s population and caused at least 50 million deaths  
  • 2009: first detected in California, contained elements of the H1N1 virus that had transferred between birds, pigs, and humans, CDC estimates at between 150,000 and 600,000 deaths | Vaccines |
| Influenza A (H2N2) | Birds, humans | 1957-1958 | - 1957 Pandemic: approximately 1.1 million deaths worldwide  
- Not currently circulating | None |
| Influenza A (H3N2) | Pigs, birds, canines, humans | 1968; Endemic disease (seasonal outbreaks) | - 1968: approximately 1 million deaths worldwide  
- Zoonotic; Caused by reassortment between human and avian viruses  
- Influenza A(H3N2) still circulates today and contributes to seasonal flu | Vaccines |
| Influenza A (H5N1) | Birds, pigs, canines, felines, humans | Endemic in birds | - Worldwide: 864 reported cases in humans and 456 deaths (as of March 2022)  
- Zoonotic; First human case in the US reported in April 2022 | Vaccines |
<table>
<thead>
<tr>
<th>Influenza A viruses of pandemic concern</th>
<th>Birds, Pigs</th>
<th>Not currently circulating in humans</th>
<th>A number of strains have been identified by the CDC Influenza Risk Assessment Tool as having pandemic potential</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other influenza A viruses of pandemic concern</td>
<td>Birds, Pigs</td>
<td>Not currently circulating in humans</td>
<td>A number of strains have been identified by the CDC Influenza Risk Assessment Tool as having pandemic potential</td>
<td>None</td>
</tr>
<tr>
<td>Equine Influenza Virus A (H7N7, H3N8)</td>
<td>Horses, mules, donkeys</td>
<td>Endemic; worldwide except for Australia, New Zealand, and Iceland</td>
<td>Highly contagious among horses</td>
<td>Animal Vaccines</td>
</tr>
<tr>
<td>Influenza B viruses</td>
<td>Humans</td>
<td>Endemic disease (seasonal outbreaks)</td>
<td>Contributes to seasonal flu</td>
<td>Vaccines</td>
</tr>
<tr>
<td>Influenza C viruses</td>
<td>Humans, pigs, dogs</td>
<td>Endemic, worldwide</td>
<td>More mild symptoms than influenza A or B</td>
<td>None</td>
</tr>
<tr>
<td>Influenza D viruses</td>
<td>Cattle, pigs, sheep, goats, possibly humans</td>
<td>Endemic in animal populations</td>
<td>First identified in 2011, limited evidence suggests that the virus can infect humans</td>
<td>None</td>
</tr>
</tbody>
</table>
**Paramyxoviridae**

Several paramyxovirus strains are endemic and cause widespread upper and lower respiratory tract infections. Reinfection is possible, but typically results in less severe symptoms.\(^40\) Major diseases that were prevalent in the United States, such as measles and mumps, have either disappeared or rarely occur due to aggressive vaccine campaigns.\(^41\)

**Appendix Table 4. Paramyxoviridae**

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubeola Virus (Measles)</td>
<td>Humans</td>
<td>Endemic</td>
<td>• 2000: United States declared measles eliminated</td>
<td>Vaccines, antibody therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>disease</td>
<td>• 2019: 1,300 cases reported in 31 U.S. states</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Current: over 100,000 deaths per year globally</td>
<td></td>
</tr>
<tr>
<td>Mumps Virus</td>
<td>Humans</td>
<td>WWI 2005</td>
<td>• Approximately 500,000 cases per year worldwide</td>
<td>Vaccines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(England and Wales)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endemic</td>
<td>• Prior to the advent of the mumps vaccine, mumps was one of the most common causes of aseptic meningitis and hearing loss in children</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>disease,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>including US</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human Parainfluenza Viruses (HPIVs)</td>
<td>Humans, although closely related viruses infect a range of species</td>
<td>Endemic disease</td>
<td>Upper and lower respiratory tract infections</td>
<td>None</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Nipah Virus</td>
<td>Fruit bats, pigs, humans</td>
<td>1999 (Malaysia and Singapore); yearly in some Asian countries</td>
<td>Infections can range from mild to cause brain swelling and death</td>
<td>None</td>
</tr>
<tr>
<td>Hendra Virus</td>
<td>Fruit bats, horses, humans</td>
<td>1994</td>
<td>Zoonotic; 1994 outbreak involved horses and humans</td>
<td>None</td>
</tr>
<tr>
<td>Menangle Virus</td>
<td>Fruit bats, pigs, humans</td>
<td>1997; Endemic in fruit bats in Australia</td>
<td>Zoonotic; 1997: outbreak infected pigs and two humans</td>
<td>None</td>
</tr>
<tr>
<td>Virus Type</td>
<td>Hosts</td>
<td>Endemicity</td>
<td>Clinical Features</td>
<td>Control Measures</td>
</tr>
<tr>
<td>------------</td>
<td>-------</td>
<td>------------</td>
<td>------------------</td>
<td>------------------</td>
</tr>
</tbody>
</table>
| Newcastle disease virus (avian paramyxovirus type 1) | Birds, humans | Endemic in avian populations | • Newcastle disease in avian herds  
• Zoonotic; Occasional infection of humans | Animal vaccines |
| Parainfluenza Virus type 3 | Cattle, sheep | Endemic in animal populations | • Common in livestock | Animal vaccines |
| Canine Distemper Virus (Morbillivirus) | dogs, wolves, foxes, coyotes, raccoons, ferrets, mink, weasels, dingoes, skunks | Endemic in animal populations | • Infection can spread to the central nervous system, which often renders the disease fatal | Animal vaccines |
*Picornaviridae*

Diseases caused by picornaviruses range from the common cold, pneumonia, and fever to severe organ disease and paralysis. Poliovirus specifically has been the subject of global initiatives to eradicate. No cases of wild polio have originated in the United States in over forty years.42

**Appendix Table 5. Picornaviridae**

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poliovirus</td>
<td>Humans</td>
<td>1940s-60s; Endemic disease</td>
<td>· Attacks the nervous system, can cause meningitis and irreversible paralysis</td>
<td>Vaccines, drug</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>Humans</td>
<td>Endemic</td>
<td>· Causes the common cold</td>
<td>None</td>
</tr>
<tr>
<td>Coxsackieviruses</td>
<td>Humans</td>
<td>Endemic in children &gt;5</td>
<td>· Causes hand, foot, and mouth disease*</td>
<td>None</td>
</tr>
<tr>
<td>Enterovirus D68 (EV-D68)</td>
<td>Humans</td>
<td>2014; endemic disease</td>
<td>· Can cause acute flaccid myelitis (AFM) in some cases</td>
<td>None</td>
</tr>
<tr>
<td>Enterovirus A71 (EV-A71)</td>
<td>Humans</td>
<td>Endemic disease</td>
<td>· Causes hand, foot, and mouth disease*</td>
<td>None</td>
</tr>
</tbody>
</table>

· Can rarely cause meningitis, encephalitis,
### Viral Infections

<table>
<thead>
<tr>
<th>Virus/Microorganism</th>
<th>Hosts</th>
<th>Disease Characteristics</th>
<th>Prevention/Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A</strong></td>
<td>Humans</td>
<td>Endemic disease</td>
<td>Sporadic outbreaks linked to contaminated food or water</td>
</tr>
<tr>
<td><strong>Foot-and-mouth disease virus</strong></td>
<td>Cattle, swine, sheep, goats, deer, water buffalo</td>
<td>Endemic diseases</td>
<td>Can cause significant livestock losses</td>
</tr>
<tr>
<td><strong>Tremovirus A (Avian encephalomyelitis virus)</strong></td>
<td>Chickens, pheasants, turkeys, quail</td>
<td>Endemic, widespread distribution</td>
<td>Average 20% mortality in young birds</td>
</tr>
</tbody>
</table>

*Hand, foot and mouth disease affects humans and should not be confused with foot-and-mouth disease, which affects animals.*
**Pneumoviridae**

While there are multiple RSV vaccine candidates currently under development, no FDA-approved options exist as of November 2022. Palivizumab (Synagis) is a monoclonal antibody that can help protect high-risk infants from RSV infection. However, because palivizumab is not a vaccine and does not provide long-term protection, it must be readministered monthly.\(^\text{43}\)

**Appendix Table 6. Pneumoviridae**

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory syncytial virus (RSV)</td>
<td>Humans; closely related animal viruses include bovine RSV and pneumonia virus of mice (PVM)</td>
<td>Endemic disease</td>
<td>• Infects nearly all children by the age of two and causes approximately 160,000 deaths per year globally</td>
<td>Antibody therapy*</td>
</tr>
<tr>
<td>Human metapneumovirus (HMPV)</td>
<td>Humans; closely related viruses in birds</td>
<td>Endemic disease</td>
<td>• Similar to the common cold</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Estimated to cause approximately 10-12% of respiratory illnesses in children</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Assumed to have evolved from avian metapneumovirus following a zoonotic</td>
<td></td>
</tr>
</tbody>
</table>
event, but has not been observed

| Bovine respiratory syncytial virus | Cattle, sheep, goats | Endemic in cattle populations; worldwide | Livestock mortality can approach 20% | Animal vaccines |

*Several RSV vaccines are under clinical development and may be approved as early as 2023.*
Poxviridae

Poxviruses include both viruses with a strict host range (for example, variola virus) and viruses that can infect a range of hosts (monkeypox, cowpox). Viruses with a large host range are especially prone to zoonosis, and human encroachment on natural habitats is increasing this risk (see Zoonosis section). Since widespread smallpox vaccination ended in the United States in the 1980s after the World Health Organization’s (WHO) declaration that smallpox was eradicated, most of the population under 40 is susceptible to poxviruses.

Appendix Table 7. Poxviridae

<table>
<thead>
<tr>
<th>Notable Virus</th>
<th>Known Host(s)</th>
<th>Outbreaks</th>
<th>Implications</th>
<th>MCMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variola virus</td>
<td>Humans</td>
<td>Sporadic; usually associated with civilization growth and exploration</td>
<td>• 1980: declared eradicated by WHO</td>
<td>Vaccines, drugs</td>
</tr>
<tr>
<td>(smallpox)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccinia virus</td>
<td>Humans, unknown origin</td>
<td>Sporadic outbreaks</td>
<td>• Closely related to variola virus, which is why the vaccinia virus is used to immunize for smallpox</td>
<td>Antibody</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Infection is typically mild, infrequent but potentially severe vaccine-associated side effects can be managed with a</td>
<td></td>
</tr>
<tr>
<td>Virus Name</td>
<td>Hosts</td>
<td>Year/Description</td>
<td>Characteristics</td>
<td>Treatment</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Monkeypox virus</td>
<td>Rodents, primates, humans</td>
<td>2022; circulates in West and Central African forest regions</td>
<td>· Zoonotic&lt;br&gt;· July 2022: declared a Public Health Emergency of International Concern (PHEIC) by the WHO&lt;br&gt;· Over 29,000 cases have been reported in the U.S. as of December 2022</td>
<td>Vaccine, drug*</td>
</tr>
<tr>
<td>Cowpox virus</td>
<td>Rodents, cattle, felines, canines, elephants, ungulates, primates, humans</td>
<td>Endemic in animals in Europe and northern and central Asia</td>
<td>· Zoonotic; humans have been infected from contact with dairy cows, domestic cats, rodents, and elephants&lt;br&gt;· Closely related to variola virus (smallpox); used in the first smallpox inoculation efforts</td>
<td>None</td>
</tr>
<tr>
<td>Virus/Pathogen</td>
<td>Hosts</td>
<td>Endemicity</td>
<td>Zoonotic</td>
<td>Vaccine</td>
</tr>
<tr>
<td>----------------</td>
<td>-------</td>
<td>------------</td>
<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td>Orf virus (also called contagious ecthyma virus or sore mouth infection)</td>
<td>Sheep, goats, humans, may be spread by insects</td>
<td>Endemic in animal populations</td>
<td>· Zoonotic</td>
<td>Animal vaccine</td>
</tr>
<tr>
<td>Fowlpox virus</td>
<td>Birds; several closely related viruses that infect a range of avian species, can be spread by mosquitoes</td>
<td>Endemic in bird populations</td>
<td>· Highly contagious in infected flocks</td>
<td>Animal vaccines</td>
</tr>
<tr>
<td>Leporipoxviruses including myxoma virus and shope viruses</td>
<td>Rabbits, hares, squirrels, spread by mosquitoes</td>
<td>Endemic in animal populations</td>
<td>· Was used in Australia in an attempt to eradicate feral rabbits</td>
<td>None</td>
</tr>
</tbody>
</table>

*The CDC is making tecovirimat available for mpox infections under a non-research expanded access Investigational New Drug (EA-IND) protocol, although this indication has not been approved by the FDA.*46
**Authors**

Caroline Schuerger and Steph Batalis are biotechnology research fellows at CSET, where Katherine Quinn is a data scientist. Amesh Adalja is an infectious disease physician and a senior scholar at the Johns Hopkins Center for Health Security, and Anna Puglisi is the director of biotechnology programs and a senior fellow at CSET.

**Acknowledgments**

The authors would like to thank Amesh Adalja for his input when conceptualizing this project and Katherine Quinn and Sara Abdulla for their data work. For their feedback and assistance, the authors would like to thank Catherine Aiken, Vikram Venkatram, James Dunham, Amy Chao, and Jacob Feldgoise. The authors are especially grateful to Michael Imperiale and Larry Kerr for their comprehensive reviews. Finally, we thank Matt Mahoney for his fact-checking and Lynne Weil and Shelton Fitch for their editorial support.

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Endnotes


9 Carlson et al., “Climate Change Increases Cross-Species Viral Transmission Risk.”

10 Centers for Disease Control and Prevention, “Influenza (Flu) - Past Pandemics,” https://www.cdc.gov/flu/pandemic-resources/basics/past-pandemics.html; Seth D. Judson and Peter M. Rabinowitz, “Zoonoses and Global Epidemics,” Current Opinion in Infectious Diseases 34, no. 5 (October


3. Data sourced from Dimensions, an interlinked research information system provided by Digital Science (http://www.dimensions.ai). All China National Knowledge Infrastructure content is furnished for use in the United States by East View Information Services, Minneapolis, MN, USA.


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