A scientific framework for epidemic and pandemic research preparedness

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BACKGROUND

The Constitution of the World Health Organization (WHO) delineates one of its key roles: the promotion, conduct, and coordination of research in the health domain. Current critical activities, including deliberations on the Pandemic Treaty/Accord/Instrument, prioritization exercises for Viral and Bacterial families, and R&D Blueprint for Epidemics collaborative platform establishment across all research areas, contribute significantly to shaping a safer future.

Since 2015, the WHO has implemented a comprehensive global research strategy and preparedness plan known as the WHO R&D Blueprint for Epidemics. A centrepiece of this work is the WHO pathogen priority list which ensures research efforts are concentrated on diseases with epidemic or pandemic potential where medical countermeasures are and limited or non-existent. Since November 2022, a new approach has been implemented, focusing on entire classes of viruses or bacteria rather than individual pathogens.

Research activities that are fundamental to Pandemic Preparedness include Bio-surveillance and viral discovery, fundamental research (pathogenesis, immunology, antigen design, delivery, reagents, and assays), Research and Development of vaccines, therapeutics and diagnostics, and infrastructure and systems to produce and rapidly deploy interventions on a global scale.

Many have proposed a variety of approaches including promoting basic research, translational research, coordination of access to data, and development of prototype vaccines among others. Coordinating and accelerating global research must promote universal values.

WHO’s global prioritization exercise.

More than 200+ scientists from 53 countries are independently evaluating the evidence related to 30 viral families; one core group of bacteria, and “Pathogen X” – an unknown pathogen with potential for triggering a severe global epidemic. This new approach will help identify representative viruses (or prototypes) within a viral family as a guide for generating evidence and filling knowledge gaps that will facilitate the development of countermeasures for other pathogens in the same family or functional group.

As a global community, we need to openly explore the scientific challenges that differ by location, culture, and economic status; outline the various potential actions and what problem(s) each action will address; and reach consensus on global and regional scientific solutions that can be tracked and documented. A series of three consultations were conducted to discuss these matters.
To review state-of-the-art technologies and define the scientific opportunities and challenges.

To outline what cross-cutting scientific actions are needed (globally and at the country level) to address the challenges of MCM development.

To discuss and clarify the utility and feasibility of establishing generalizable approaches for MCM development within and across viral families or functional pathogen groups.

Because of the focus on research needs, specific national or international initiatives or global governance were not discussed.

Improved pandemic research preparedness can be achieved by proactively managing emerging virus threats focused on four areas of work using currently available tools: discovery and surveillance; targeted basic research; translational research including development of reagents and tools and product development, and clinical trial infrastructure and vaccine production and deployment capacity.

Research activities that are fundamental to pandemic preparedness include bio-surveillance and viral discovery; fundamental research (pathogenesis, immunology, antigen design, delivery, reagents, and assays); research and development of vaccines, therapeutics, and diagnostics; mechanisms to produce and deploy rapid interventions on a global scale.

Swiftly advancing technology provides the opportunity to keep pandemic preparedness at the state of the art—but also requires attention to ensure that scientific approaches are diverse and updated as new technologies enable discoveries and improved outcomes. The invaluable lessons drawn from the COVID-19 pandemic underscore the paramount importance of continued investment in basic, clinical, and implementation research, technology development, and engineering innovation. The collaborative endeavours facilitated by the WHO exemplify the remarkable outcomes achievable when researchers unite to coordinate a global research response.
Substantial and sustained funding for basic science emerges as a requisite, aligning its importance with the enhancement of public health infrastructure.

This synergistic approach aims to achieve equitable healthcare on both local and global scales, recognizing that equity in access to effective MCMs and equity in regional research capabilities must be foundational values in any research initiative.

Equitable distribution of discovery science and manufacturing is critical to address regional problems before they become global.

Coordination and collaboration are essential if we are to optimize efforts towards pandemic prevention and response.

**WHO is working on several initiatives to strengthen the global architecture for health emergency preparedness and response.**

The following WHO initiatives aim to ensure that the global response will be high quality, equitable and trusted:

- **Expansion of critical research capacity** via the **WHO R&D Blueprint for Epidemics**
- **Contributing to enhanced governance** via the **Pandemic Agreement and Amendments to international Health Regulations**
- **Enhanced financing via The Pandemic Fund**
- **Enhancing local vaccine production capability** via the **mRNA Technology Transfer Hub** and via WHO’s Health Technology Access Pool
- **Improving surveillance via the WHO Hub for Pandemic and Epidemic Intelligence**
- **Increasing accountability via the Universal Health and Preparedness Review**
- **Facilitating the sharing of samples via the WHO BioHub**
- **Establishing the necessary workforce via the Global Health Emergency Corps**
- **Promoting collaboration regarding countermeasures via I-MCM-net interim coordination mechanism**

The collaborative endeavours facilitated by the WHO exemplify the remarkable outcomes achievable when researchers unite to coordinate a global research response.

Pandemic research preparedness stands as a cornerstone for an optimal pandemic response, necessitating collaboration for effective research pre- and post-pandemics.

Substantial and sustained funding for basic science emerges as a requisite, aligning its importance with the enhancement of public health infrastructure.

This synergistic approach aims to achieve equitable healthcare on both local and global scales, recognizing that equity in access must be a foundational value in any research initiative. Science and technology can help solve many problems but we need accord on global coordination, communication, and governance.

Equitable access to research knowledge, distribution of discoveries, and manufacturing is critical to addressing local problems before they become global. Coordination and collaboration are essential if we are to optimize efforts towards pandemic prevention and response.

We find ourselves in a period of relative enlightenment post-pandemic, armed with the scientific tools and opportunities essential for achieving rapid and equitable access to high-quality and trusted medical countermeasures in future pandemics. It is not merely an aspiration; it is our historical duty, and together, it can and must be accomplished.
**THE VIRAL AND BACTERIA FAMILY APPROACH**

The discovery of new human pathogens continues, now numbering approximately 150 with potential for person-to-person spread that exhibit pandemic potential. While new pathogens, especially viruses, continue to be discovered, the number of virus families considered to pose a pandemic risk has remained constant at 26. Thus, by focusing on virus families, we can assure that there will be relevant knowledge even as new potential pandemic pathogens arise from within these families.

Emerging infections thus represent a large but finite problem. Focusing on prototype pathogens within each family is intended to create knowledge to inform the identification of generalizable solutions across entire pathogen families, toward the goal of improved pandemic preparedness. This approach also facilitates the potential creation of vaccines effective against multiple related viruses within the same family that roughly corresponds to functional pathogen groups that share mechanisms of entry and immunity.

In the context of pandemic preparedness, prototype pathogens act as models or representative examples in scientific research and preparedness planning. These pathogens are selected based on specific criteria, promoting fundamental research that enhances preparedness for emergent threats.

Certain priority pathogens may also function as prototype pathogens (e.g., the Ebola virus), but these classifications are not inherently synonymous. For instance, the Zika virus within the Flaviviridae family causes human morbidity but may not be considered an ideal prototype for developing medical countermeasures for other Flaviviridae family members. There is a crucial need to promote research across all viral and bacterial families, irrespective of perceived pandemic potential.

Understanding key viral proteins is pivotal for vaccine design and the identification of targets for effective therapeutics. Developing animal models aids in comprehending disease progression and assessing MCM efficacy. In immunology, designing serological assays is critical for evaluating MCM effectiveness, enhancing technologies related to immunological assays, and genetic examination for understanding emerging infectious diseases. Repositories facilitating access to viral stocks, convalescent serum, antibodies, and animal models play a critical role in scientific advancements.

**GENERALIZABLE RESEARCH STRATEGIES APPLICABLE TO ALL PATHOGENS, REGARDLESS OF PERCEIVED PANDEMIC POTENTIAL**

Viruses within the same family share genome characteristics, protein functions, entry mechanisms, and often tissue tropism. While differences in cell tropism, receptors, and antigenicity will make the development of broadly protective vaccines across an entire virus family uncommon, it may occasionally be possible as in the case of poxviruses.

However, similarities in target antigen organization and function and mechanisms of immunity may provide a blueprint for rapid antigen design during a pandemic response, as demonstrated by rapid COVID-19 vaccine development.

Some concepts can be generalized across virus families like the finding that stabilizing class I fusion protein trimers in the native prefusion conformation results in more effective vaccine antigens. This was critical for the development of COVID-19 vaccines.

It is likely there are similar generalizable principles that would facilitate vaccine development for non-enveloped viruses and enveloped viruses with Class II and Class III fusion proteins. For some pathogen groups, basic immunology questions still need to be answered about immunodominance, B cell memory phenotypes, and induction of mucosal immunity.

Breakthroughs may come from studying pathogens that are not perceived to have high pandemic potential.

It is important to perform key activities on prototype viruses from all pathogen families, regardless of pandemic potential. Another way to maintain surge capacity would be to invest in clinical development of products for prototype pathogens that are regional problems but not perceived to be current global threats. This would require new business models to make small market biologics feasible and at least cost neutral. This would potentially result in products to address regional problems like Lassa, Rift Valley fever, Crimean Congo Hemorrhagic fever, MERS, Ross River, Mayaro, and other viral diseases.

Laboratory, clinical, and manufacturing infrastructure and activity needed to provide surge capacity for rapid pandemic response could in part be maintained with sustained collaborative work on prototype pathogens including those in families that are not considered to have high pandemic potential.

In addition, while some pathogen families may not currently be perceived to have high pandemic potential, there are plausible scenarios for pathogens from all 26 virus families under scrutiny to become a pandemic threat.
Pathogen discovery and surveillance

Continued discovery of new pathogens, and surveillance of known pathogens, are essential for monitoring existing and future pandemic risks.

Recently, new non-specific techniques in genomic sequencing have increased our capacity to discover and identify new viruses. Because these techniques do not rely on the full sequence of the virus, they can detect even as-yet undiscovered viruses. The sensitivity of these methods can be further increased by using capture sequencing, in which viral sequences are further enriched.

Capture sequencing can identify a pathogen within 8 hours from sample receipt and has been used to discover several new pathogens.

New advances in developing agnostic serological assays, for example, using microarrays and multiplex phage display, allow detection of the footprint of past infections in the immune systems of people or animals, supporting non-targeted surveillance within populations, to determine whether new pathogens are arising or if the incidence of infections is changing.

Research on monoclonal antibodies is at the nexus of key immunological goals and high-throughput serological analysis using properly folded proteins, including cellular responses.

"Smart surveillance" focuses on spillover risks at the human-animal interface, including wildlife, communities, wastewater, and screening patients with fever and rashes of unknown origin in clinics in places where the risk may be increased.

It is also recognized that animal reservoirs are not completely known for all viruses, and thus, more comprehensive screening of viral reservoirs in animals and vectors with potential for transmission is also important.

Regardless of the methods employed, improved implementation of discovery and surveillance will require increased focus on samples from people and animals likely to provide information about the potential emergence of pandemics.

Recognizing that many new human pathogens come from animals, "Smart surveillance" focuses on spillover risks at the human-animal interface, including wildlife, communities, wastewater, and screening patients with fever and rashes of unknown origin in clinics in places where the risk may be increased.

Animal reservoirs and vectors of transmission is also important. The advantages of "Smart surveillance" include: it can be cost-effective, rapid, convenient, flexible, wider net at high-risk interfaces, biosafety, biosecurity, and, animal welfare. The disadvantages include potential poor sensitivity, sample types, no individual level (meta/epi) data, bioinformatics, PCR inhibition, sample degradation, and the need for Standardized Operating Procedures.

Basic research (microbiology, pathogenesis, and immunology)

New technologies to define the atomic-level details of surface proteins allow the selection of likely vaccine targets. AI/ML combined with high-throughput screening is allowing accelerated development of vaccine antigens for important human pathogens.

The study of cellular tropism and its impact on pathogenicity requires an atomic-level understanding of interactions between cellular receptors and viral receptor-binding domains. Currently, this may be studied by co-precipitation, which can allow prediction of how viral mutations affect binding to cellular receptors.

Study of other early steps in viral infection, including how viruses overcome innate cellular defenses, will aid in understanding how viruses cause disease, improve animal model development, and may provide additional targets for disease prevention.

Understanding the roles of different arms of the immune system in protection, and how to induce immune responses with particular specificities and memory phenotypes, has the potential to lead to more effective pandemic vaccines. Rapid detection and isolation of human monoclonal antibodies is at the nexus of reagents needed for developing vaccines and diagnostics and the development of potential therapeutic MCMs.

Basic research is critical

The needs include improved understanding of pathogen microbiology (i.e., virology and bacteriology), pathogenesis (e.g., virulence, pathogen-host interactions) and immunology (including protective immune responses against different types of pathogens). Improved high-throughput tools to apply cutting edge science to pandemic research will increase its impact.
Applied research (antigen design, vaccinology, advanced manufacturing, and development of reagents and tools)

Induction of a protective immune response requires the presentation of the right target antigen in the right conformation delivered in the right modality to induce a protective immune response in vaccine recipients. Recent advances in structural biology allowing atomic-level understanding of antigenic sites have been used to increase the likelihood of obtaining protective immune responses to vaccine antigens. High-resolution cryo-electron microscopy and electron microscopy-based polycrystalline epitope mapping are improving our ability to rapidly define the antigenic landscape of pathogen surface proteins likely to be vaccine targets and to visualize immunodominant epitopes in polyclonal immune responses. Indeed, it was the application of these strategies to the non-pandemic respiratory syncytial virus that provided a proof-of-concept for structure-based antigen design that was applied to rapidly select the most effective SARS-CoV-2 vaccine antigens.

Artificial intelligence strategies are being used to accelerate the identification and engineering of vaccine antigens for important human pathogens. Further research is expected to improve predictions of how genetic sequences lead to pathogenicity and antigenicity (termed “functional viromics”). These methods combined with high-throughput synthetic biology will enable rapid execution of design-build-validate cycles to aid in designing antigens that will induce the desired immune responses. Broadly protective vaccines likely will require the development of multiple antigens from within or between pathogen families or genera.

While mRNA vaccines showed their value in the COVID-19 pandemic, it is important to keep working on other vaccine platforms for the delivery of vaccine antigens. Key goals are to identify strategies for inducing more broadly protective immune responses (which could allow a single vaccine to cover several pathogens or an increased number of variants) and to identify improved ways to target different arms of the immune system—especially mucosal immunity which is believed to play a key role in preventing many viral infections. Self-assembling nanoparticle display, mRNA, live vaccines, vectored vaccines, molecular adjuvants, DNA vaccines, computational protein design, and AI/ML all deserve additional investment to expand our repertoire of versatile platforms. Broadly accessible adjuvants play a crucial role in increasing antibody titers and the breadth of response, with goals including reducing vaccine doses, enabling immunization in weakened immune systems, and adjuvant stockpiling. Other goals include improving thermostability, efficiency and scalability of existing platforms, and understanding how different platforms might be used together to achieve improved immune responses.

Expanding local production, diversifying vaccine delivery platforms, establishing a centralized adjuvant facility, and balancing incentives and risks for manufacturers are crucial for sustainable vaccine manufacturing. Advances in the manufacture of vaccines, including increased automation, will enhance the portability and scalability of vaccine manufacture.

These approaches may first be proved for non-pandemic pathogens, but generalizability to platforms likely to be useful for pandemics will greatly improve global pandemic preparedness and equity.

Progress towards pandemic preparedness will be facilitated by the development of tools and reagents. Some of these tools may effectively be developed in the context of needs for non-pandemic pathogens, and some will have value in completely different disciplines.

Although there is hope that in vitro methods will eventually be able to replicate key steps needed to support pandemic vaccine development, it seems likely that animal models will be needed in the foreseeable future to mimic human susceptibilities and responses, and to mitigate risk.

Animal models enable study of viral pathogenesis and vaccines in live organisms containing the full range of cell and organ types, including the diverse elements of the immune system.

Recently available technologies have enabled the creation of animal models that contain key human components, including receptors for viruses, human tissues, and increasingly humanized immune systems. Examples include the engrafment of SCID mice with human tissues including stem cells, using of CRISPR/CAS-9 to allow precise targeting and gene modifications that alter interferon expression to more closely mimic human responses or alter cellular receptor expression to allow viral infection or replace parts of the innate immune response that pathogens have evolved to inhibit.

Organ-on-chip systems, which are microfluidic devices containing living engineered substructures, enable the recapitulation of organ dynamics, functionality, and responses in vivo. They are valuable for screening and understanding critical factors of human infection.

Recent progress includes development of autologous immunocompetent chips, bone marrow on chip, vasculature, and lymph node on a chip, enabling multi-organ systems that begin to replicate the complexity of animals. Single-cell analysis has also seen recent advancements.
For all pathogen families, a WHO pathogen family-specific target product profile (TPP) will help to guide research directed toward the development of one or more prototype vaccines. These TPPs will emphasize research needs that may be generalizable both within and outside of a pathogen family.

Prototype pathogens will be selected based on the likelihood that their study will yield generalizable information of relevance to pandemic response, while also considering public health and market needs.

These pathogen family-based TPPs are to be distinguished from TPPs that are developed for products intended to address individual pathogens of high public health interest.

Nonetheless, the importance of maintaining warm vaccine development, infrastructure, and manufacturing bases around the world suggests that even for vaccine families with lower pandemic potential, ongoing vaccine development efforts are an important part of pandemic preparedness.

Target Product Profiles and vaccine development

Prioritization is a critical component of pandemic response. While development of prototype vaccines for all vaccine families will likely be useful, the importance in pandemic response of vaccines for pathogen families considered likely to have higher pandemic potential implies that those vaccines should have higher priority.

Research infrastructure

Pandemic preparedness depends in part on overall healthcare system resilience around the globe.

WHO identifies five key components of resilient health systems, including collaborative surveillance, community protection, safe and scalable care, access to countermeasures, and emergency coordination.

Improved global vaccine safety systems will provide a basis for enhanced trust in both pandemic and non-pandemic vaccines.

Critical infrastructure needs for vaccine development include clinical trial site preparedness, availability of laboratories to perform assays, regulatory preparation, and manufacturing capacity.

Where feasible, infrastructure should be developed in such a way as to support the evaluation and production of vaccines that are important for pandemic preparedness.
Data, reagents, CORE protocols, and candidate vaccine sharing

All of the proposed strategies will be effective only if mechanisms for data, reagent and candidate vaccine sharing are maintained and improved.

While collaboration during a pandemic is essential, collaboration before a pandemic is equally important.

Data can effectively be shared through working groups such as the WHO animal models and assays groups convened by WHO early in the COVID-19 pandemic to discuss CORE protocols, progress, and results on animal models and assays.

Existing biorepositories played a critical role in reagent sharing during the COVID-19 pandemic, but non-scientific considerations sometimes interfered with the shipping of reagents across national boundaries.

The importance of collaboration was exemplified by the development of the VSV-vectored Ebola vaccine. The vaccine was made available to collaborators around the world to collect data in numerous studies, which ultimately led to the demonstration of efficacy in the pivotal Guinea trial.

Further improved strategies are needed.

To facilitate access to key reagents, including standards, viral stocks, convalescent serum and other clinical samples, antibodies, animal models and candidate vaccines could play a critical role in scientific advancements.

SPECIFIC ADDITIONAL RESEARCH STRATEGIES FOR INDIVIDUAL PATHOGEN FAMILIES WITH HIGH PANDEMIC POTENTIAL

In addition to the strategies listed above, additional priority activities are important for pathogen families considered to have high pandemic potential.

Pathogen discovery and surveillance

Because of the increased risk of crossover events from animals to humans, increased surveillance at this interface, including in animal reservoirs (to be identified, if not already known), is recommended.

Basic research

According to current thinking, induction of mucosal immunity has the best chance to prevent infection at mucosal surfaces and thus reduce transmission efficiency.

Humoral responses (especially neutralizing responses) can also prevent and attenuate respiratory infections and length of shedding but usually are not sufficient to completely prevent infections. Cellular responses tend to be longer-lived and more cross-reactive, and thus play a role in the breadth of protection and in reducing severe disease as has been observed in virus infections by many viral families, including flaviviridae, arboviruses, togaviridae, paramyxovirdae, arenaviridae, and picorna/enterovirdae.

Cell-mediated responses may also play a role in clearing persistent disease (as may occur in Ebola infections). Non-neutralizing (Fc dependent) humoral responses appear to play a critical role in protection against Ebola, as well.

For pathogen families with more immediate pandemic potential, there should be an increased focus on microbiology and immunology.

Immune mechanisms of protection, including the role of innate, mucosal, humoral, and cellular components, which could ultimately lead to biomarkers useful for prioritizing and evaluating vaccines, are a key area of interest.

In addition, strategies to obtain broader immune protection against multiple members of a pathogen family are emphasized. This work would be facilitated by the advanced development of pathogen-specific animal models.

Thus, for many viruses, inducing combined responses encompassing all arms of the immune system may deliver optimal protection. In cases where pre-existing immunity to related pathogens may exist, new strategies to subvert immunodominance may be needed to achieve effective vaccines.

Evaluation of vaccines for pathogen families with pandemic potential will be facilitated if immune markers that are predictive of protection are available. To the extent that information from prototype pathogens can be extrapolated to other, related pathogens, this could further facilitate pandemic preparation.
Induction of broader immune humoral immune responses that could protect against multiple pathogen family members is made more difficult by antigenic diversity within virus families and weaker vaccine immune responses among the most vulnerable.

Nonetheless, cross-reactive immunity for pathogens (as is observed between CHIKV and EEV or among poxviruses) implies that this may be achievable for some viral families. It is also important to consider the goal of broadly protective vaccines—vaccines that induce broad cellular immunity may be sufficient to protect against severe disease, while protecting against milder disease or transmission may be more difficult. Strategies currently under consideration for antibody-mediated protection include vaccines with mosaic antigen display, serial immunization with diverse antigens, mixed antigen cocktails, development of broadly reactive antigens, inclusion of conserved regions in vaccines, and combined platforms. Development of broad immune responses may require the administration of vaccines against multiple-related pathogens (i.e., more than just a single prototype).

**Applied research**

Key viral proteins involved in viral attachment and fusion have already been identified as vaccine target antigens for many virus families with pandemic potential and represent potential vaccine candidates.

Critically, not all antigens are able to induce desired responses. For example, as shown for other viruses with class I fusion proteins, the Lassa fever glycoprotein complex must be presented in its native pre-fusion conformation in order to induce neutralizing antibodies (which is feasible despite heavy glycosylation).

An overemphasis on speed rather than scientific understanding and precision antigen design could lead to ineffective or poorly effective vaccines and miss the opportunity to identify generalizable approaches.

Further work on vaccine platforms, and in particular, identification of vaccine platforms that induce the types of immune responses likely to be important for members of an individual pathogen family, could help to maximize protective responses.

For pathogen families with immediate pandemic potential, the development and sharing of appropriate tools and reagents will facilitate vaccine development. These tools and reagents will need to address the range of high-priority pathogens within each family.

Ideally, there would be simultaneous development of animal models refined for each of the known high-risk groups of pathogens along with simultaneous development of micro-physiological systems that may complement or support in vivo approaches. This will require coordination and would benefit from policies and a governance structure.

There is also a need to understand protection, vaccine effect, and population immunity, which require high-quality assays. A basic understanding of SARS-CoV-2 immunology facilitated the rapid development of reagents to measure immune responses including across variants.

**Research infrastructure**

Key regulatory considerations include immunobridging and extrapolation of data from related products, within or across platforms.

Recognizing high levels of collaboration among regulators during COVID-19 and Ebola vaccine development efforts, additional inclusive conversations among all regulators regarding lessons learned from COVID-19 and future pandemic preparedness could be helpful.

There is a need for prospective development of strategies and CORE protocols to simplify the implementation of first-in-human studies for pandemic pathogens and make provisions for rapidly advancing to phase 3 (in part using data that can be collected before a pandemic is declared).
Vaccine development

Finding mechanisms to make small-market vaccines economically feasible and sustainable would be a more productive way to have vaccines readily available for future potential pandemic threats.

GMP material is needed in order to perform clinical studies, and it is considered important to fund and study candidate vaccines for pathogen families with pandemic potential, even if short-term public health need is less clear.

The ultimate goal (and pre-pandemic stopping point) of vaccine development for each pathogen family will need to be individually considered. For example, if regulators indicated that phase 1 or phase 2 data for a prototype vaccine could support going directly into phase 3 with a pandemic vaccine, this could be an argument for obtaining phase 1 or phase 2 data before the next pandemic.

Decisions about performing phase 3 studies would likely depend on the breadth of protection and potential vaccine markets. Independent expert evaluation of various candidate vaccines will contribute to achieving this.

Decisions to develop vaccines for a given viral family should take into account the availability of antivirals and other countermeasures.

Unless there is substantial progress on broadly protective vaccines (though it’s unlikely that an effective vaccine will be on the shelf when a pandemic occurs), stockpiling of candidate vaccines is unlikely to be highly successful or cost-effective.

ADDITIONAL RESEARCH STRATEGIES FOR PATHOGEN X

Furthermore, additional priority research activities are critical to prepare for the emergency of a pathogen X causing an epidemic.

In the context of pandemic preparedness, prototype pathogens act as models or representative examples in scientific research and preparedness planning. These pathogens are selected based on specific criteria, promoting fundamental research that enhances generalizability and preparedness for emergent threats.

Certain priority pathogens may also function as prototype pathogens (e.g., the Ebola virus), but these classifications are not inherently synonymous. For instance, the Zika virus within the Flaviviridae family causes human morbidity but isn’t an ideal prototype for developing medical countermeasures for other Flaviviridae family members.

There is a crucial need to promote research across all viral and bacterial families, irrespective of perceived pandemic potential.

Depending on what Pathogen X turns out to be, there may be gaps in the pre-pandemic research and activities outlined in the foregoing sections. It will be important to fill these gaps as soon as possible.

In a subsequent pandemic, even closer collaboration among the global scientific community, public health authorities, and developers could achieve better results in support of the key values for countermeasure development of quality, equity, trust, speed, and cost.

Key areas where facilitated collaboration would be useful include 1) animal models and basic research (microbiology, pathogenesis and immunology), 2) technological tools, assays and reagents, including research on surveillance and early detection and diagnostics to support early pandemic response, 3) vaccinology including antigen design, 4) clinical trials and vaccine development and evaluation, and 5) convergence.

WHO-mediated international collaborations on animal models, assays, and CORE protocols and several other areas, and the lessons learned from COVID-19 underscore the need for continued global coordination and collaboration.
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