World Health Organization

# Meeting summary

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Scientific Strategies from recent Outbreaks to help us prepare for Pathogen X
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R&DBlueprint
Powering research
to prevent epidemics

# Goals for Pathogen X preparation and response



Equity and access (within and across countries)

- Pandemic-specific and in non-pandemic times (health equity disparities are accentuated by pandemics)

Individual and public health outcomes

- Prevent spread
- Prevent disease
- Provide care

Desire to learn from and improve on previous outcomes

# Key Strategies: General principles



Partnerships build and maintain trust and speed response, and promote equity

- Collaboration >> competition
- High income countries do not have a great record in sharing critical public health resources during the COVID pandemic. Plans to incentivize sharing in the next pandemic may help, but self determination is most likely to be successful in supporting global equity. Move away from the “charity model” of action and toward full collaboration..
- Data sharing, using online platforms and preprints. Sharing increased pace of discovery (not just by providing information but also facilitating replication of key results)

# Key Strategies: General principles (2)



Preparation

- Sense of urgency with need to consider both long and short term commitments
- Build on existing systems: surveillance, analysis tools, etc.
- Build capacity (“access to opportunities”) & collaboration around the world: communities, research, labs, production. More reliable data focused on global research needs and global access

Perform work in parallel rather than sequentially

Work at risk where that could speed results

including using prototype pathogen family approach

Use existing expedited regulatory pathways where feasible. Coordinated scientific & regulatory advice can also be useful. Ethics committee harmonization could be helpful. Surge regulatory and advice capacity (e.g., at WHO) is important in a pandemic.

# Key Strategies: Innovation



Drive incorporation of innovations into public health response, as appropriate to meet critical individual and public health needs

New technologies can help to democratize data collection and research

Role of research to show impact

Flexibility of regulatory process to accommodate innovations and specific needs during pandemics

# Key Strategies: Coordination & Collaboration



Specific areas for coordination and collaboration

- Pandemic detection and predictions
- Diagnostics as an essential enabler for everything else
- Other cross cutting enabling activities
- Priority and prototype pathogen-centered approach
- Antivirals
- Vaccines

- Communication among stakeholders is critical

# Key insights: Innovations in pandemic detection and prediction



Needs: More rapid identification of pandemics as they evolve. Improved predictions about likely pathogens and needed response. Viruses & bacteria evolve in response to immune pressure.

Solutions: Need proper data inputs and robust software tools including improved surveillance networks in humans (especially people at greater risk, including identifying them) and animals (including potential spillover risk). Pathogen X will likely spill over from animals supporting OneHealth approach focusing on monitoring wildlife trade and detection of spillover and spillback at human-animal interfaces (and measuring effectiveness of measures). Banked sera over age groups can help to identify susceptibles. Clinicians identify clusters of unusual illnesses to allow diagnostic & discovery techniques to be applied– can we improve on syndromic surveillance? Study past pandemics to learn & apply lessons about conditions that enable high threat pathogen emergence (including VoCs).

Innovations: novel (including genomics & exon-capture based) pathogen discovery & detection, syndrome identification

Implementation: Must be world-wide– new pandemic pathogens may arise in LMICs where the capacity to continuously implement these solutions is feasible and essential.

# Key insights: Diagnostics enable almost everything else



Needs: Decentralization and globalization with data consolidation. Accurate, point of care, rapid diagnostics. NAT kits, rapid Ag tests, POC molecular assay. Multiplex assays that allow new pathogens to be rapidly added would be very useful. Tools for surveillance (e.g., in sewage).

Solutions/Innovations: drones for diagnostics distribution, early warning diagnostics, point of care systems,, high throughput serology, improved aggregation of data via technology, photonic biosensors, transistor based sensors (binding to DNA probe, antigen, or antibody changes current for high sensitivity without amplification), rapid isothermal amplification with CRISPR cleavage, using taste as a biosensor, artificial intelligence

Implementation: Rapid availability of diagnostics early in a pandemic provides the best chance for early control. Find ways to speed their evaluation and dissemination.

# Key insights: Cross-cutting activities are an essential enabler for therapeutics and vaccine development

Needs: animal models, immunology and virology, translational work (i.e., assays and standardization), epidemiology, clinical understanding, “platform” adaptive clinical trials

Challenges: biosecurity, sample sharing across borders

Solutions/enablers: Collaboration and coordination. New biorepositories, shared data systems

Implementation: WHO-coordinated workgroups to enable discussion and data sharing

# Key insights: Antivirals/antimicrobials



Needs: Antivirals tend to work better earlier in disease, and have important uses early in disease. We need a larger arsenal of family-specific drugs that can go straight to testing. Antibody-based therapeutics are a critical component of the response. TPP: safe, effective, available-but will depend on how novel pathogen X is and how it behaves, and when antivirals are given in course of illness. AMR is already a pandemic-scale problem.

Challenges: Biosafety/biosecurity, export control, and differences in stakeholder perspectives (including academics, companies, policymakers [who in some cases drove use of ineffective COVID therapies], regulators). For monoclonals and small molecules, rapidly changing pathogens will lead to resistance (could be reduced with multi-agent treatment). Increasing reliance on academic labs.

Solutions/enablers: clinical data and epidemiology, virology, structure/modeling/biochem, discovery/chemistry, pharmacology, animal models, coordinated human testing (a few large trials are much more useful than many small trials and real world data often overestimates therapeutic efficacy), and global coordination. Randomized trials are an essential component of product evaluation. Role and utility of human challenge studies to be defined. Systems to consolidate and share clinical data. Strategies for developing monoclonals are well-known. Convalescent plasma is easy to collect but use case may be limited. Molecular surveillance is essential for detecting AMR.

Innovations: human organoid systems, broadly neutralizing antibodies, candidate sharing (e.g., “pathogen box”), improved drug selection and screening strategies, artificial intelligence as a tool to identify and screen antivirals, genomics and improved trial design, including for AMR

Implementation: Can regulatory approaches keep up with clinical needs as the virus evolves? ICMRA discussions, guidance documents and confidentiality agreements facilitate harmonization, but there isn’t yet a clear consensus on how to use in vitro data even as clinical data collection becomes impossible or lags.

# Key insights: Vaccines



Needs: Rapid development of vaccines that safely prevent severe disease, mild disease, transmission, long-term sequelae with adequate breadth. Rapid onset & duration of protection. Available and readily deployable as critically important attributes to consider up front. Rigorous evaluation of safety and efficacy.

Challenges: new variants (or evolution of vaccine resistance), efficacy against mild disease or transmission, deployment. Trust. Maintaining manufacturing base in the interpandemic period.

Solutions/Innovations: Many enablers in common with antivirals, plus importance of understanding immunity at the portal of entry and inducing broad immune responses (antibodies are sufficient but not necessary. Neutrophils play an important role; but later on, memory B and T cells make a big difference– hybrid immune people also have mucosal responses). Use existing platform-based vaccines, new platforms (including mucosal vaccines) & other strategies to meet additional needs. Coordinated adaptive trial designs with appropriate success criteria. Innovations in R&D (including assays), manufacturing (transportable strategies, automation & plant-based production), stability, delivery schemes may further speed development and/or vaccine availabilty. Artificial intelligence for antigen design and predictions (yield, variants, etc.). Importance of investing in multiple platforms and promoting innovation.

Implementation: critical importance of clear communication of reliable scientific results to support public trust. Make early vaccines available for comparison with next-gen vaccines. Immunobridging criteria can be developed with appropriate comparators and understanding of immunology, but may be challenging for the first pathogen X vaccine (nothing to bridge to)

# Other key insights



We’ve focused mostly on science to support product development, but there is a lot more to pandemic response, e.g.

Infection Prevention and Control measures can reduce transmission and slow spread of pandemic, reduce likelihood of AMR.

Organizing logistics of manufacturing capacity and response is complex. Innovations in manufacturing including automation could increase portability and scalability.

Clear and accurate communication are needed to maintain trust in science and public health infrastructure. All participants can play a role.

Social sciences are also critically important, along with political support and community engagement

Strengthening health care and research infrastructure around the world

The worldwide collaboration must continue! We can celebrate the amazing successes so far, but know much more work is yet to be done to fulfill WHO’s vision.