White Paper: MetaBridge

Why Metagenomic Surveillance Requires Investment in Decision-making Support, Not Just Technology

SHIELD Initiative

Executive Summary

New metagenomic technologies are poised to be a significant advance in pathogen detection, but technology alone does not prevent pandemics. Without parallel investment in supporting decision-makers at the front lines of public health, we risk repeating the mistakes of past efforts that focused only on alerting rather than on action. Decision frameworks, response protocols, workforce capacity, and evaluation systems must be built concurrently with the pathogen detection technology, not after it comes online. Effective public health decision-making capacity and coordination among multiple healthcare and public health stakeholders will determine whether these advanced technologies become a transformative early-warning system or an expensive data generator.

I. When the Alarm Sounds: Deciding on Metagenomic Triggers

Consider this scenario. Biothreat Radar (BTR) or another novel system detects an unexpected respiratory pathogen sequence in wastewater samples from three major metropolitan areas. The sequence shows 15% divergence from known influenza strains. An interpretation by an artificial intelligence scan flags it as a potential novel threat. The metagenomic data is available within 24 hours.

Now what? Who interprets whether this is a lab contaminant, environmental noise, or the next pandemic? What threshold triggers which response? Who has the authority to act? What do we tell the public? This is the challenge facing every metagenomics-based surveillance system currently in development or deployment, from wastewater networks to port-of-entry screening to hospital-based environmental surveillance. This gap between signal and action is what MetaBridge addresses.

> *“The technology right now is out in front of public health’s resources and expertise to manage it efficiently. What we present is the need for a decision-support approach that allows the non-tech public health leader to wade through the information in a sequencing risk assessment, ask useful questions, and make the best decision.”*
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> ***- Key Informant, CORI interviewee***

Metagenomics in Context

Metagenomics enables the detection and sequencing of all genetic material in a sample, such as a wastewater stream, a nasal swab, or air from a ventilation system, regardless of the pathogen being sought. Unlike traditional tests that ask, *‘Is influenza present?’*, metagenomics asks, *‘What is present?’* This pathogen-agnostic approach can detect novel threats, known pathogens in unexpected places, and potentially engineered sequences, all at once. Promising advancements include mSCAPE in the UK and Biothreat Radar, a program recently requested in the U.S. President’s budget. The proposed Biothreat Radar program is an innovative biothreat detection system that will rapidly detect novel pathogens with a 24-hour turnaround. This system will expand the Traveler-Based Genomic Surveillance (TGS) and Advanced Molecular Detection (AMD) work coordinated by the Centers for Disease Control and Prevention (CDC).

While this represents a transformative development, generating data is not the same as preventing pandemics. The question is not whether such technology works, but whether public health systems are prepared to use the insights it produces. Early detection only matters if public health systems can act on it wisely and swiftly (Nascimento de Lima et al., 2024).

Metagenomics surveillance without robust implementation infrastructure and decision support risks two failure modes: **paralysis**, where data without actionable protocols leads to inaction, and **overreaction**, where false alarms consume resources and erode trust. Addressing these risks requires two complementary investments that must advance alongside the technology itself: implementation infrastructure to translate metagenomic signals into public health action, and baseline applied research to understand what those signals mean in real-world settings. The most pressing need is to address the paralysis mode, which means developing the operational systems, including decision frameworks, risk assessments, workforce capacity, and partnerships such as those with healthcare, needed to act on signals effectively (Liang et al., 2023).

II. The Implementation Challenge: From Signal to Action

The Decision Gap

As metagenomic technologies become more widely used, public health and government officials will encounter information in ways that may be unfamiliar to them, presented at a technical level that does not support effective decision-making (Awan et al., Health Security 2024). Metagenomic sequencing will generate data showing novel sequences, known pathogens in unexpected locations, and potentially engineered-looking sequences. No standardized frameworks currently exist to answer the two fundamental questions every public health leader will face: *'Should I be worried?'* and *'What should I do?'*

The recent NASEM workshop on Accelerating the Use of Pathogen Genomics and Metagenomics in Public Health (NASEM 2025) confirmed that while pathogen genomics applications are vast and evolving, cross-domain implementation capacity remains a critical challenge.

What Decision-Makers Will Receive & What They Will Need

Currently, metagenomic results are delivered as technical reports of environmental samples that do not facilitate decision-making. For those assessments to be useful, they need to be understandable and guide proportionate action. Specifically, they should answer key questions that determine the next steps: how and from where the sample was collected; what specimen type was tested and its implications for interpretation; what testing method was used and what are its limitations; what is the overall level of concern when all factors are combined; and what actions are appropriate based on the findings. Only then can they interpret the result by combining all inputs to assess the level of concern and identify suitable interventions.

Context is everything. The same pathogen detected in different contexts demands fundamentally different responses. For example, anthrax detected in wastewater from Uvalde, Texas, can be expected to be ubiquitous in the environment. Japanese encephalitis virus in Miami, Florida, wastewater is unexpected and warrants investigation. Nipah virus in Nashville, Tennessee, is likely a lab error that requires retesting before action. Engineered sequences within an H5N1 genome require rapid expert sequence assessment as a high priority. Currently, no standardized system exists to make these distinctions in real time. Decision-makers need tools that integrate geographic, epidemiologic, and laboratory contexts to triage signals appropriately. Integrating these tools with existing surveillance systems will provide vital context for understanding public health threats and enhancing response efforts.

Case Example

In 2025, a contractor performing routine metagenomic sequencing of U.S. municipal wastewater flagged a sequence containing both SARS-CoV-2 spike protein fragments and apparently synthetic elements, noting they could not rule out something malicious. The report, delivered to public health leadership on the eve of a holiday weekend, contained unmarked phylogenetic trees and technical jargon without context on collection methods or testing purposes. It took several days and urgent expert consultation to determine that the finding was a laboratory contaminant introduced during sequencing. The episode consumed senior leadership time and attention, not because of an actual threat, but because no structured framework existed for signal assessment, issue escalation, or proportionate characterization of concern.

Decision Frameworks and Risk Assessment

What decision-makers need is not just more data. They also need a structured approach to interpret and act on the data they will receive. This includes tiered risk assessment protocols that classify signals by level of concern and map each tier to a defined set of actions. It should also include clear escalation pathways that specify who is notified, who has authority to act, and at what speed. Finally, decision makers also need risk communication templates that allow officials to explain findings to the public in plain language, including when a signal turns out to be benign or erroneous. Equally important is the reverse flow: clinicians encountering unusual clinical presentations at the bedside represent a critical signal source that can corroborate or contextualize environmental detections. Decision frameworks must be bidirectional from population-level surveillance down to clinical action, and from clinical encounters back up to surveillance systems (Elbehiry & Abalkhail; 2025).

A well-designed MetaBridge framework would enable a non-specialist public health leader to receive a metagenomic alert, understand its significance through a structured risk assessment, and initiate a proportionate response, all without requiring personal expertise in bioinformatics or genomic sequencing. This is the core implementation investment that determines whether metagenomic systems, such as Biothreat Radar, produce actionable intelligence or distracting noise.

Past efforts with other frameworks may be relevant for the current development need. Those include the Pathogen Genomics in Public Health Surveillance Evaluation (PG-PHASE) Framework (Ferdinand et al., 2021) and the Value of Information (VOI) framework (Awan et al. 2024). Internationally, frameworks for translating genomic surveillance into public health action are already being developed (ECDC, 2023; WHO, 2022). For a greater return on implementation investment, these decision-support tools should go alongside training for state and local officials to effectively use these resources. Establishing standard operating procedures for various detection scenarios will prepare officials for different situations. Sustained trust with state and local partners, particularly in light of inevitable false positives, is equally essential.

Workforce and Coordination

Implementation infrastructure requires skilled interdisciplinary professionals. Very few public health professionals have training in metagenomic interpretation. The field requires interdisciplinary teams spanning healthcare, bioinformatics, epidemiology, laboratory science, and decision science. The AMD Roadmap for Nonlaboratorians (Ricaldi et al., EID May 2025 Supplement) underscores this gap: public health practitioners need foundational literacy in advanced molecular detection to ask the right questions when presented with sequencing data. Without designated liaisons at state and local levels trained in interpretation, without joint exercises conducted before real detections occur, and without clear prospective roles and authorities, even the best decision frameworks will fail in practice. Training programs, consultation infrastructure, and workforce development are essential components of any implementation investment, especially to strengthen the connection with healthcare for bidirectional data sharing to support real-time actions.

Evaluation Systems

Preventing a repeat of past surveillance failures requires accountability built into the system from day one. This means metrics assessing system performance, mandatory federally funded after-action reviews to reduce the burden on jurisdictions, continuous improvement loops, and public transparency about system performance. A recent scoping review of evidence-to-decision frameworks in public health (Bracchiglione et al., Euro Surveillance 2025) reinforces the need for structured, evidence-informed approaches to public health decision-making, particularly in the context of infectious disease. Evaluation should be a core design requirement.

III. Lessons from the Past

The history of U.S. biosurveillance shows that detection technology needs proper implementation infrastructure to be effective. The BioWatch program has faced significant criticism for over two decades, highlighting that even with substantial investment, the lack of operational frameworks and coordination results in value that fell well short of its investment (GAO-16-99, 2015). False positives eroded trust with state and local partners (National Academies, 2011), and the absence of decision protocols has hindered effective responses (Bipartisan Commission on Biodefense, 2021). This pattern is starting to emerge with current metagenomic capabilities, as noted in insights from public health leaders from the Case Example.

Similarly, in the 2024 H5N1 dairy cow outbreaks, several sites reported sudden H5 detections that triggered resource-intensive public health investigations. The technology to detect and report “H5 present” was ahead of any structured public health response. Current wastewater techniques cannot differentiate between human and animal sources, and fecal shedding patterns for H5N1 in humans are not well understood. Investigations eventually revealed that the signals did not come from human infections but from milk processing facilities and farm vehicle washdowns entering the sewer system (Honein et al., 2024).

These cases illustrate a common pattern: molecular detection methods can now surface highly specific findings quickly, but public health officials lack standardized, decision-ready frameworks to translate those findings into proportionate, explainable actions. Independent analyses have concluded that ‘the barrier to effective metagenomic surveillance is not technology’ but the commitment to build and sustain the operational systems around it (Global Biodefense, 2025).

Whole genome sequencing (WGS) is an example of what this may look like. When WGS for foodborne disease surveillance was introduced through the PulseNet network, the technology was paired with standardized methods, shared data systems, and trained workforces at the state and local level. The phased rollout allowed decision protocols to develop in step with detection capacity. This resulted in an estimated 270,000 illnesses prevented and $500 million saved annually (MMWR 2016, 65). Countries with pre-existing sequencing infrastructure and trained workforces were able to leverage this for COVID-19. While WGS targeted known pathogens, its rollout process offers valuable lessons for metagenomics. MetaBridge can break this cycle.

IV. Recommendations

1. Establish a MetaBridge “implementation infrastructure” in parallel with technology deployment, not sequentially.
2. Develop decision-support tools and interpretation frameworks designed for non-specialist public health and government leaders.
3. Invest in implementation science that evaluates and develops best approaches for assessing risk and making decisions using environmental baselines and technical surveillance data.
4. Build evaluation and performance metrics into system design from day one, with regular performance evaluation and reporting.
5. Develop training scenarios and exercises to provide continuous learning for public health and government leaders.
6. Partner with external experts and academic institutions to develop and validate operational protocols before full-scale deployment.
7. Establish bidirectional data-sharing protocols between public health surveillance systems and clinical diagnostic laboratories to ensure that clinical signals inform environmental surveillance interpretation, and vice versa.

V. Conclusion

Metagenomics can transform infectious disease surveillance and clinical detection. Metagenomic sequencing offers capabilities that would have been unimaginable a decade ago: pathogen-agnostic detection, complete genomic characterization, and near real-time data sharing. But detection without interpretation is data, not intelligence. And data without a decision infrastructure is noise, not an early warning.

The choice is between a system that generates unprecedented volumes of genomic data that overwhelm existing public health capacity, and a system that translates early detection into timely, proportionate, and effective public health action with clinical benefits.

The difference lies entirely in whether implementation infrastructure is built alongside the technology. This decision frameworks that enable non-specialist leaders to act confidently on complex signals; a trained workforce prepared to interpret metagenomic data; coordination mechanisms tested before the first real detection; strengthened public health and healthcare connections to drive meaningful progress; and the implementation science research to support all of it.

The technology is ready to sound an alarm. The question is whether we will be ready to move from alarm to action.

Alternative Short Title

MetaBridge

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