The world is in the midst of an unprecedented technology-enabled transformation, unparalleled in pace and complexity that will have profound implications in how the US will defend against known and unknown biological threats. To protect the civilians and warfighters, biodefense stakeholders must be able to foresee possible technological trends that can affect threat assessment. However, there are significant flaws in how we prioritize countermeasure needs. As biotechnology becomes increasingly de-skilled and less expensive, the potential proliferation of a new generation of biological weapons can now be achieved by state, non-state actors and even individuals. Given this situation, it will take years before the intelligence community identify and fully understand the new bioterror landscape and even more years for the scientific community to develop effective countermeasures against them. Therefore, a reliable biosurveillance approach supporting a diversity of stakeholders can provide not only early warnings about the emergence of natural and manmade pathogen, but can facilitate the identification of vulnerable countermeasures and propose the most appropriate solutions. However, a series of errors in stored pathogen genomic records, narrow-scope databases and the lack of standards and interoperability across different detection and diagnostic devices continue to restrict the multidimensional biothreat assessment. The fragmentation of different approaches have resulted in few attempts to propose the technical foundations required to implement a biosurveillance enterprise that is reliable, realistic and that avoids a warning that might come too late. Our discussion focus on the medical intelligence and laboratory response network issues in order to prioritize and improve a nationwide capability to manage investments to allow biosurveillance enterprises to track emerging, reemerging and novel microbial health threats. The talk will summarize the development of a modular and extensible genomic-based enterprise to systematically address the collection, integration, disambiguation and translation of pathogen DNA information into operational biosurveillance.