



**The First FAO/WHO/AU International Food Safety Conference
Addis Ababa, 12-13 February 2019**

**Whole-genome sequencing: Paving the way forward globally to better
understand food systems**

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1. Shifting horizons

The advent of whole genome sequencing (WGS) has brought about a revolution in public health microbiology. At the apex of molecular typing resolution, it has immense power in field applications and research— some readily realised, and yet more untapped.

Tectonic shifts are underway in the global food safety landscape, with WGS representing a potent tool for phylogenetics, epidemiologic surveillance, transmission studies, food testing and monitoring, outbreak and traceback investigations, source tracking and attribution, and root cause analysis. Additional information on virulence and antimicrobial resistance (AMR) markers garnered through *in silico* analysis, has important surveillance and research uses.

WGS has the potential to replace many phenotypic and genotypic methodologies currently used in a typical microbiology laboratory, into a single workflow. Isolate preparation is identical for all bacterial pathogens, and the 'wet laboratory' components (DNA extraction, library preparation and sequencing reactions) are quick and easy to perform. With the cost of WGS declining, it is fast becoming a cost-effective technology for foodborne pathogen speciation and subtyping.

Expert bioinformatics analysis is critical to interrogation and interpretation of WGS data. A major advantage to WGS data is electronic portability and ease of data sharing, allowing for a global inter-laboratory comparison of bacterial strains. A proliferation of open access on-line analysis pipelines facilitates rapid analytics and data sharing.

Complementary epidemiologic and WGS datasets provide the ultimate tool to delineate outbreak events, whether localised or trans-continental.

The use of WGS during the South African listeriosis outbreak of 2017-2018 was invaluable in guiding the successful outbreak investigation and eventual source identification. This was a landmark event for both the country and the African continent, proving that even resource-limited countries can ably implement this technology and gain tremendous benefit.

2. Strategic areas for focus

For all the potential power and application of WGS to be realised in the global context, key strategic requirements need to be considered.

• WGS alone is not enough

WGS data must be partnered with robust epidemiologic data for foodborne disease surveillance, and outbreak detection and investigation. The WHO landscape paper on WGS for foodborne disease surveillance¹ states that it should be implemented for public health purposes only where there is already a basic epidemiology, surveillance and food monitoring and testing infrastructure in place; this is undeniably the single greatest challenge for less developed countries.

WGS for foodborne bacterial pathogens typically requires bacterial isolates. Therefore, the capacity, infrastructure and expertise of diagnostic microbiological laboratories in clinical, food and veterinary sectors is critical and should be prioritised. Whilst culture-independent metagenomics analysis (analysis of genetic material of all microbial DNA in a given sample) holds much promise and its potential uses in food safety are being explored, it is not able to replace routine culture-based diagnostic testing and WGS at present.

Basic foodborne disease epidemiology is either lacking or minimal in most developing countries, with a shortage of skilled epidemiologists and existing public health systems and infrastructure not designed or able to support basic surveillance or outbreak detection, investigation and response. The importance of foodborne disease surveillance and outbreak response must be elevated within public health agencies and health ministries; in the face of a multitude of competing health priorities and severe resource constraints, foodborne disease has typically been neglected.

- Collaborations

Institutions/agencies with WGS capacity and expertise should be identified as 'hubs' and form a network to share knowledge and data. Such hubs could serve as regional reference centres, performing WGS on isolates from clinical, veterinary and food laboratories throughout the region. The Establishing Next Generation Sequencing Ability for Genomic Analysis in Europe (ENGAGE) project showed that it is possible to implement WGS and the use of bioinformatics tools in laboratories through multijurisdictional partnerships incorporating public health, food and veterinary sectors. This model could be adapted in other regions, with inter-country and international partnerships and collaborations providing a platform for training and capacity development.

- Data quality and analysis

Current challenges with WGS implementation worldwide include standardising both the quality of data generated and subsequent bioinformatics analysis of the data. This is essential to enable appropriate data interpretation for epidemiological purposes, and for meaningful inter-laboratory data comparison. If we are to use WGS to better understand and investigate food systems on a global scale, these are fundamental priorities for the global food safety community.

There are several international initiatives which aim to enable and support global platforms for data quality, analysis and storage. Their purpose is to facilitate rapid, robust WGS data analysis and allow comparison to large international datasets for surveillance and outbreak investigation purposes.

- PulseNet International (PI)² is a global network dedicated to laboratory-based surveillance and investigations of foodborne diseases. The network comprises national and regional laboratory networks in Africa, Asia Pacific, Canada, Europe, Latin America and the Caribbean, the Middle East and the United States. The network promotes standardised methodology for molecular epidemiological investigations of foodborne bacterial pathogens, resulting in molecular data which is comparable between laboratories and allows for global comparison. PI's vision is that public health laboratories worldwide transition to WGS which will replace all existing phenotypic and molecular methodologies, and support of foodborne disease preparedness and response. WGS data analysis and sharing will take place using standardised PI on-line analysis pipelines, which are publicly available and open access. These pipelines will operate in a similar way to existing WGS pipelines such as Enterobase and BIGSdb. Such pipelines simplify WGS data analysis dramatically; the user requires little to no bioinformatics expertise, as the pipelines are automated and no user intervention (command line coding) is required.
- The Global Microbial Identifier (GMI)³ consortium is developing a global, interoperable analytical platform with standardised pathogen genome databases, typing systems and bioinformatics analysis tools that will be made accessible to all nations with basic laboratory infrastructure. The platform is envisioned to utilise standardised epidemiological, clinical and laboratory metadata using a Minimal Data for Matching (MDM) standard to facilitate data exchange that enables multinational outbreak investigations to be conducted in real time whilst minimising the legal risk of public data sharing. Standardised analytical systems using automated pipelines are under investigation, and a proficiency testing framework is under development.

- Data sharing and metadata

Critical to the success of using WGS data for surveillance, outbreak detection and investigation is being able to compare against data from One Health sectors, within the country and between countries – the so-called 'open data' model. Clearly, such data access and sharing is very sensitive and needs to address a range of issues at country and global levels –including intellectual property rights; legal, jurisdictional, and regulatory

frameworks; and the participation of the food industry. This requires considered, inclusive consultation with all stakeholders and political support.

- One Health in practice

The current state of food safety and burden of foodborne disease in low- and middle-income countries also reflects on the absence or weakness of a One Health approach. Whilst funding for new programs is a constant challenge, countries should actively drive small-scale initiatives to overcome practical, regulatory and inter-agency obstacles to facilitate sharing of knowledge, data, epidemiological and laboratory skills and capacity. Political commitment and support is paramount to enable effective multijurisdictional collaboration across public health, veterinary and food sectors. The food industry needs to be an active participant and take responsibility for its role in a collective effort to improve food safety and foodborne disease surveillance both at the local level and worldwide.

3. Looking ahead

Data is the currency of science, and has the power to influence policy, law, trade and public opinion. WGS provides the ultimate One Health data platform for foodborne disease surveillance and outbreak response. This technology should be embraced globally, leaving no country behind, if we are to transform the food safety landscape, facilitating a safer food supply and preventing foodborne disease. A collective approach is key, encompassing public health, veterinary and food sectors. WGS is becoming less expensive, and an increasing number of countries and laboratories around the world will implement the technology. Meanwhile, there is no time to lose and we should leverage on existing WGS capacity and create hubs and a network for data sharing and expertise that can support training and WGS implementation as One Health and food safety gain traction across the the globe.

REFERENCES

1. Whole genome sequencing for foodborne disease surveillance, landscape paper. Publication date: 30/04/2018. https://www.who.int/foodsafety/publications/foodborne_disease/wgs_landscape/en/
2. PulseNet International: <http://www.pulsenetinternational.org/>
3. Global Microbial Identifier: www.globalmicrobialidentifier.org

Keywords

Sequencing
Collaboration
Surveillance
Epidemiology
Outbreak