



Food and Agriculture Organization
of the United Nations

Workshop proceedings

Drafting the technical paper on Applications of Whole Genome Sequencing (WGS) for Food safety Management

**Food and Agriculture Organization of the United Nations
(FAO) in collaboration with World Health Organization
(WHO)**

7-8 December 2015

Executive summary

The expert workshop on practical applications of Whole Genome Sequencing (WGS) for food safety management was held to develop a paper with concrete case studies on the use of WGS for food safety management in the regulatory frameworks at the national level. The experts presented different case studies, practical applications and lessons learnt from implementing WGS for food safety management. WGS could be an effective tool that allows the identification and characterization of microorganisms with a high level of precision not previously possible. The experts stated that WGS could be a cost-efficient alternative for countries with existing subtyping capabilities or countries that have existing infrastructure and want to implement WGS.

Through the case studies presented by the experts, along with various benefits and potential drawbacks, it was recognized that there are several regulatory and technical challenges associated with the actual implementation of WGS in food safety management. Interpretation of data and validation, comfort level among partners on appropriate use of data, intellectual property, and isolate ownership can be drawbacks related to implementation of the technology. Another challenge that needs to be addressed, especially in developing countries is the confidence in the use of databases and fear of trade barriers.

At the end of the workshop, the first draft of the technical background paper was successfully developed. All key elements identified on the first day were incorporated into the paper and some suggestions were made for FAO and WHO for the next steps.

Key words

Whole genome sequencing, WGS, food safety management, data sharing, FAO, WHO

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Acronyms

FAO	Food and Agriculture Organization of the United Nations
NGS	Next Generation Sequencing
PFGE	Pulsed-field gel electrophoresis
WGS	Whole Genome Sequencing
WHO	World Health Organization
GMI	Global Microbial Identifier
DTU	Technical University of Denmark
CDC	Centers for Diseases Control and Prevention
FDA	Food and Drug Administration
USDA FSIS	Food Safety and Inspection Service, United States Department of Agriculture
PHE	Public Health England
ANSES	French Agency for Food, Environmental and Occupational Health and Safety
PHAC	Public Health Agency of Canada
KMRI	Kenya Medical Research Institute
LATU	Technological Laboratory of Uruguay
ITGRFA	International Treaty on Plant Genetic Resources for Food and Agriculture
GLIS	Global Information System on Plant Genetic Resources for Food and Agriculture
PUID	Permanent Unique Identifiers
OIE	Organization for Animal Health
DOI	Digital Object Identifier
NCBI	National Center for Biotechnology Information
EMBL	European Molecular Biology Laboratory
DDBJ	DNA Data Bank of Japan
MLST	Multilocus Sequence Typing
SSI	Statens Serum Institut

Acknowledgement

FAO/WHO would like to express its appreciation to the international experts who participated in the workshop, namely Frank Møller Aarestrup (Chair), Marc Allard, John Besser, Sabah Bidawid, Tim Dallman, Stephanie Defibaugh-Chávez, John N. Kiiru, Ana Maria Maquieira, Paula Mussio, Celine A. Nadon (Vice chair), Eva Møller Nielsen and Sophie Roussel. The workshop was organized by Masami Takeuchi (FAO) under the overall guidance of Markus Lipp and Renata Clarke (FAO). Technical contributions from FAO/WHO colleagues including Sarah Cahill (FAO), Francisco López (FAO), Gwenaëlle Dauphin (FAO) and Amy Louise Cawthorne (WHO) are also gratefully appreciated.

1. Introduction

1.1. Background

Unsafe food, beyond direct effects on health, causes significant social and economic costs resulting from loss of income, loss of employment and reduced market access. Additionally, one large-scale food safety incident can create a food insecurity situation. Advances in genome sequencing technology and techniques, have the potential to change the way we conduct food safety management. In the area of food microbiology, it allows the identification and characterization of microorganisms with a very high and accurate level of precision.

For the last decade, the costs in practically utilizing the techniques based on genomics are rapidly declining with the recent development of the Next Generation Sequencing (NGS) techniques. However, the level of understanding of the concepts and potential use of such techniques varies among countries. Particularly for developing countries, there are capacity implications, regulatory implications, and resource implications to be considered. While several industrialized countries advance with the technologies, it is FAO's role to keep its Members informed on the latest scientific developments in the food and agriculture sectors and provide technical assistance to those who need it.

In preparation to hold a Technical Meeting on the impact of Whole Genome Sequencing (WGS) on food safety management in conjunction with the 9th meeting of the Global Microbial Identifier (GMI) on 23-25 May 2016, FAO recognized that presenting practical and current applications of genome sequencing data for food safety management and identification of the benefits and potential drawbacks of the technology are the fundamental elements of the Technical Meeting. For that purpose this workshop aimed to develop a technical background paper with concrete case studies on the use of WGS for food safety management in the regulatory frameworks at the national level and the paper will serve as a basis for discussion during the Technical Meeting.



PARTICIPANTS OF THE EXPERT WORKSHOP

1.2. Objective of the expert workshop

The objective of the workshop was to develop the first draft of the technical background paper for the abovementioned Technical Meeting on applications of Whole Genome Sequencing (WGS) in food safety management. The technical paper would assist countries in gaining greater understanding of using WGS for food safety management and enable food safety officials in developing countries to make informed decisions.

1.3. Scope of the expert workshop

The scope of the workshop was on currently available applications of WGS in the area of food safety, and was set within national regulatory frameworks for food safety.

2. Opening session

Mr Markus Lipp (FAO) welcomed all the experts and appreciated their valuable contribution for the development of the technical paper. Following the opening remark, Ms Masami Takeuchi (FAO) provided the introductory presentation. She stated that food safety is an important topic for both

FAO and WHO to achieve their mandates which are food security and public health respectively. WGS can be an effective tool that allows the identification and characterization of microorganisms with a level of precision not previously possible. With the rapidly declining cost of this technology, WGS applications in food safety could contribute to the global goal of consumer protection, trade facilitation, and food security. The full presentation is available at http://tiny.cc/faowgsworkshop_01.

Mr Frank Møller Aarestrup (Chair, DTU, Denmark) explained that Next Generation Sequencing (NGS) data could be very helpful in food safety management if the relevant data are shared globally. He also stated that standardization/harmonization of the technology, easy access to obtained data and protocol exchange are the key issues to be further discussed in order to consider successful WGS implementation world-wide. The full presentation is available at http://tiny.cc/faowgsworkshop_02.

3. Practical applications – success stories and lessons learned

Ms Eva Møller Nielsen (SSI, Denmark) introduced a case of the WGS application for food safety investigation in Denmark and stated that WGS could be a cost-efficient alternative for countries with existing subtyping capabilities or countries that have existing infrastructure and want to implement WGS. She highlighted that WGS is a highly sensitive method and can contribute to cluster detection and outbreak investigations as well as improved source tracing. However, actual implementation in a country/region requires a respective local infrastructure, thus, Ms Nielsen emphasized on the importance of inter-governmental/cross-sector collaboration in employing WGS at regional/national level. The full presentation is available at http://tiny.cc/faowgsworkshop_03.

Mr John Besser (CDC, USA) discussed a case in the USA and highlighted the importance of root cause analysis and investigation during a disease outbreak. Since the start of the outbreak investigation, the number of outbreaks has increased but the incidence of the disease has gradually dropped due to the regulatory changes made in response to the outbreak. Through a case study on outbreak investigation of *Listeria monocytogenes*, Mr Besser explained that real time surveillance can be very useful for inclusion/ exclusion of individual cases in clusters.

Mr Marc Allard (FDA, USA) introduced the GenomeTrakr database and its progression and stressed that to fully utilize the database, it is important to have a well characterized environmental isolates with good metadata and geographic information. He also stated that the database helps in earlier intervention in averting illness sooner which reduces the number of food products to be recalled, the number of lawsuits and there is minimal damage to brand recognition.

Ms Stephanie Defibaugh-Chávez (USDA FSIS, USA) stated using WGS has resulted in better strain discrimination, illness cluster detection, and case classification. She highlighted the challenges that FSIS has faced with regards to data storage and transmission, accreditation of Laboratory and bioinformatics. All three experts from the US confirmed the importance of inter-agency and inter-sectoral collaboration in sharing real-time analysis and WGS data. The compiled presentation of US experts is available at http://tiny.cc/faoexpertworkshop_04.

Mr Tim Dallman (PHE, UK) presented a case study of a large multi-national outbreak of *Salmonella* Enteritidis that showed not only the benefit of WGS in revealing the true epidemiology of an outbreak allowing inference about source diversity but also the importance of the availability of data from multiple countries. He explained that WGS fully characterizes the pathogen allows to identify the source of the contamination. The full presentation is available at http://tiny.cc/faoexpertworkshop_05.

4. Challenges and pre-requisite activities

Ms. Sophie Roussel (ANSES, France) stressed that prior to the implementation of WGS, it is important to compare the potential of WGS with the current standard methods used for surveillance and harmonize WGS at each step of the process. As France has not yet officially implemented WGS at regulatory level, she presented a

roadmap for WGS to better manage the food safety, which includes; track and type more strains, design a rational typing scheme, harmonization within clinical and food reference lab, EU-wide harmonization and sharing data. The full presentation is available at http://tiny.cc/faoexpertworkshop_06.

Mr Sabah Bidawid (Health Canada) stated that the process of surveillance/monitoring using WGS is an evolving process and not yet fully functioning, however, Canada is beginning to incorporate WGS in the routine activities. WGS has been started for virulence profiling and bacterial identification, in particular for *Listeria monocytogenes*, *Salmonella*, and *E.coli* since 2013. When new tests are applied during outbreak investigations, they are applied in parallel to the primary tests (PFGE) and are carefully interpreted on a case-by-case basis.

Ms Celine A. Nadon from (Vice-chair, PHAC, Canada) complemented Mr Bidawid's presentation stating that some of the challenges in implementing WGS for surveillance and outbreak investigation in Canada include interpretation of data and validation, comfort level among partners on appropriate use of data, intellectual property, and isolate ownership. In Canada, WGS has been used to support outbreak investigation in real-time and in the near future it is expected that WGS will be used to support real-time surveillance and not just outbreak response. The full presentation is available at http://tiny.cc/faoexpertworkshop_07.

Mr John N. Kiiru (KMRI, Kenya) explained that food microbial safety assessment in Kenya is based on traditional isolation methods and the major challenge is that food safety is low and pathogen diversity and foodborne diseases are very high. Molecular methods including WGS have a potential to provide novel strategies for detection of food-borne pathogens but the penetration level could be very low and the technology is still expensive. Although penetration of WGS is low, sensitizing the government on the potential benefit, possible subsidized equipment and reagents, increased collaboration with institutions and nations already applying WGS are some of the important steps to take. The full presentation is available at http://tiny.cc/faoexpertworkshop_08.

Ms Ana Maria Maquieira (LATU, Uruguay) shared her presentation through video conferencing from Uruguay. She elucidated that in order to implement WGS, some challenges such as knowledge on the benefits of data sharing, resources, cross-sector collaborations still exist. She stressed that key issues regarding confidence in the use of databases and fear of trade barriers need to be addressed. The full presentation is available at http://tiny.cc/faoexpertworkshop_09.

5. Global activities

Ms Takeuchi introduced FAO activities relevant to genome sequencing. At FAO, under the Animal production and Health division, the Animal Health Service branch, Animal Genetic Resources International Treaty on Plant Genetic Resources for Food and Agriculture and Commission on Genetic Resources for Food and Agriculture have been working on the genome sequencing related activities.

Mr Francisco López (International Treaty on Plant Genetic Resources for Food and Agriculture, ITGRFA, FAO) delivered his presentation on the experiences ITGRFA has faced. In 2015, the Governing Body of the treaty adopted the Vision and the first Programme of Work on the Global Information System on Plant Genetic Resources for Food and Agriculture (GLIS). Proposals for the implementation of Permanent Unique Identifiers (PUID) for PGRFA are under development. The features for the PUID are already identified and after several consultations with experts, of all the PUID types available, DOI resulted as the most promising for adoption in GLIS to the plant genetic resources community. He also stated that once analysing DOI as a viable option, the next step is to define the minimum set of metadata-core-fields and currently, guidelines for users on how to identify the descriptors is under development. The full presentation is available at http://tiny.cc/faoexpertworkshop_10.

Ms Gwenaelle Dauphin (FAO) also shared FAO's activities in Animal Health sector relevant to genome sequencing. Genome sequencing in Animal Health is often carried out using Sanger sequencing and not specifically on whole genome sequence. Discussions and activities are ongoing at World Organisation for Animal Health (OIE) on how to integrate sequence information and the possibilities of obtaining sequence information from Member countries when there is an outbreak. Ms Dauphin shared some of the activities of Animal Health Service branch of FAO, which include, provision of Sequencing Service for developing countries,

providing guidelines, access to global information and support, and training. The full presentation the global activities of FAO in the area of Animal health is available at http://tiny.cc/faoexpertworkshop_11.

It was discussed that there are several existing and internationally recognized voluntary databases that host relevant WGS data for food safety. They include but are not limited to the following; NCBI, European Molecular Biology Laboratory (EMBL) and DNA Data Bank of Japan (DDBJ), it was suggested that international organizations could work closely with these databases to ensure easy access to global data.

6. Key stakeholders – global networks, industries and academia-industry partnerships

As a focal point of the PulseNet International, Ms Nadon presented the activities of its global network on genome sequencing. The steering committee of PulseNet International formally discussed the vision for implementation of WGS for global foodborne disease surveillance, replacing existing phenotypic and molecular methods. In addition, the steering committee agreed upon the standardization of WGS –Multilocus Sequence Typing (wg-MLST) methodologies. Presentations on the activities of PulseNet International is available at http://tiny.cc/faoexpertworkshop_12.

7. Drafting the paper

On the second day, following a brief summary by Ms Takeuchi of day 1's presentation, an outline of an FAO paper was developed. The experts were divided into 5 working groups, each of which drafted the paper according to the outline focusing on different topics. By the end of the drafting sessions, all participants identified key elements for the topics and formulated recommendations to be included in the technical paper. The presentation on the summary of day one is available at http://tiny.cc/faoexpertworkshop_13.

8. Final remarks and next steps

By conducting the workshop, the first draft of the technical paper was successfully developed. FAO's paper on the application of WGS for food safety management could provide competent food safety authority officials especially those from developing countries with fundamental factors to consider various aspects relevant to the implementation of WGS for food safety. Key elements identified during the workshop including the potential benefits and possible drawbacks of WGS and data generated from the technology, pre-requisites in employing WGS for routine could enable food safety officials to make an informed decision. Further steps would be to edit the paper and organize a peer review with an aim to publish the technical paper online prior to the Technical Meeting on 22-25 May 2016. Following the outcomes of the discussion sessions, the following are the future steps to be taken:

- The importance of cross-sector collaboration, especially between health and agriculture sectors to apply WGS technology on food safety management at all national, regional and international levels was identified. FAO and WHO to consider this importance for the future relevant activities.
- Technical paper to be presented at the beginning of the Technical Meeting on 23-25 May 2016.
- Experts suggested that the international organizations like FAO and WHO should continue providing a forum for different stakeholders to discuss best practices on the applications of WGS for food safety and the use of global databases that host WGS data for food safety.
- After publishing the technical paper, provision of technical assistance to developing countries in assessing capacity development needs in strengthening national food safety systems (laboratory, epidemiology, food monitoring/testing, health surveillance, policy development and regulatory assistance) would likely be requested to FAO and WHO. FAO and WHO could consider possible means to provide such assistance.

Annex 1: List of participants

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Annex 2: Agenda

MONDAY 7 December 2015		
Opening session		
09:00 – 09:30	Welcome by Senior Officers, Food Safety Unit	Markus Lipp
	Background, objectives and scope of the meeting	Masami Takeuchi
09:30 – 09:45	The use of genome sequencing technology on food safety management	Chair: Frank Møller Aarestrup
09:45 – 10:00	Draft outline of the paper and the expected output	Frank and Masami
Session 1: Practical applications – success stories and lessons learned		
10:00 – 10:30	Applications of genome sequencing technology on food safety management - Denmark	Eva Møller Nielsen and Frank
10:30 – 11:00	Coffee break	
11:00 – 11:45	Applications of genome sequencing technology on food safety management – The United States of America	Marc Allard, John Besser and Stephanie Defibaugh-Chávez
11:45 – 12:15	Applications of genome sequencing technology on food safety management – The United Kingdom	Tim Dallman
12:15 – 13:00	Discussion: success stories and key considerations	All
13:00 – 14:00	Lunch	
Session 2: Challenges and pre-requisite activities		
14:00 – 15:30	Potential usefulness of genome sequencing technology on food safety management	Sophie Roussel (France), Sabah Bidawid and Celine A. Nadon (Canada), John N. Kiiru (Kenya), Ana Maria Maquieira (Uruguay - Remote)
	Discussion: Challenges in employing the technology at the regulatory levels and pre-requisite activities	All
15.30 – 16:00	Coffee break	
Session 3: Global activities		
16:00 – 16:10	Introduction to the relevant FAO activities (Lessons learned)	Masami
16:10 – 16:25	Activities of the International Treaty on Plant Genetic Resources	Francisco Lopez
16:25 – 16:40	Activities of the FAO Animal Health Unit	Gwen Dauphin
16:40 – 17:00	Discussions on Roles of international organizations	
Session 4: Key stakeholders – global networks, industries and academia-industry partnerships		
17:00 – 17:10	Activities by the PulseNet International	Celine
17:10 – 18:00	Discussions on the roles of global/regional networks, industries	
18:00 – 18:30	Setting up the working groups for Day 2	Masami
19:30	Informal Dinner	

TUESDAY 8 December 2015 (Gabon Room)		
08:50 – 09:00	Quick recap of the Day 1	Masami
Session 4: Establishing concrete case studies		
09:00 – 09:30	Key elements for the FAO paper – Draft outline review	Facilitated by Frank
09:30 – 10:00	Discussions and finalization of the outline	All
Session 5: Drafting the paper		
10:00 – 10:30	Introduction to the working groups	Masami
10:30 – 11:00	Coffee break	
11:00 – 13:00	Drafting session (working groups) - Identification of key elements	All
13:00 – 14:00	Lunch	
14:00 – 15:30	Drafting session (working groups) - Identification of key elements	All
15.30 – 16:00	Coffee break	
16:00 – 17:00	Formulating concluding paragraphs and recommendations	Facilitated by Frank
	Adjourn	