



EFSA State of play on NGS and future perspectives in the food safety area

“Science meets Policy” conference:
Modern technologies to enable response to crises: Next
Generation Sequencing to tackle food-borne diseases in the EU,
25 September 2020

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Trusted science for safe food



Disclaimer

The following slides give an overview of the principles, architectural design and processes that have been identified during the planning phase in EFSA for the set up of the new One Health WGS system. Changes to some of these requirements and features can still be made during the implementation phase.

It is well known the great potential that WGS offers in the surveillance and monitoring of emerging health threats and in epidemiological investigations of foodborne outbreaks, BUT.....

we are still facing many challenges



ORGANIZATIONAL

- Legislation
- Regulations
- Silo working
- Infrastructure
- Funding
- Economical drivers
- Prioritization



CULTURAL

- Cross-sector and cross-border collaboration
- Political barriers
- Language barriers
- Resistance to change



TECHNICAL

- Data protection
- Meta-data format
- Data storage
- Data transfer
- Computing power
- Quality management



SCIENTIFIC

- Sequencing platform
- Bioinformatics tools
- Downstream approach
- Training and capacity
- Harmonizing results

- The need to have WGS data quickly available → centralized data collection
- The path towards centralized WGS-based typing data collection
 - Mandates from EC
 - Guiding principles to address some of the challenges identified

Multi-country outbreak of *L. monocytogenes* ST6 linked to frozen corn and other frozen vegetables

November 2017

SUN	MON	TUE	WED	THU	FRI	SAT
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

December 2017

SUN	MON	TUE	WED	THU	FRI	SAT
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

JANUARY 2018

SUN	MON	TUE	WED	THU	FRI	SAT
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

FEBRUARY 2018

SUN	MON	TUE	WED	THU	FRI	SAT
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28			

3/11/2017: Finland launched an UI. Four MS reported matching human isolates.

20/11/2017: EURL Lm launched an inquiry to NRLs network

30/11/2017: MSs reported isolates matching with PFGE. WGS not yet performed.

05/01/2018: EURL reported isolates matching with WGS → 2 from food and 1 from environment

29/01/2018: sequences of the food isolates sent to EFSA

05/02/2018: the relevant MS shared information on the food type of the matching isolates



Hypothesis about



- In 2017, EFSA and ECDC received a joint mandate for expanding the molecular typing data collection to **Whole Genome Sequencing (WGS)** data (feasibility study):
 - Requirements and constraints
 - Evaluate possible solutions
- EFSA and ECDC
 - published in May 2019 the **technical report**¹ comparing potential solutions
 - identified '**Strategic elements**' to guide the decision on the best scenario (WGS roadmap)

Strategic elements identified by EFSA



The IT architecture should allow to develop internal bioinformatic services addressing multiple needs for different risk assessment domains



Guarantee full transparency of the analytical procedures



Engage more with data providers for increasing the attractiveness of the system and therefore the submission of data related to non-human isolates

1. <https://www.efsa.europa.eu/en/supporting/pub/en-1337>

In 2019, EFSA and ECDC received a follow up mandate for **implementing and managing a One Health system** for the collection and joint analysis of **WGS data** from foodborne isolates from human, food, feed, animal and environmental samples

The European Union needs a robust and sensitive tool for rapid detection and management of multi-country foodborne outbreaks with the ultimate purpose of serving public health interests and protecting European consumers. Emphasis will be placed on **full interoperability** of this joint molecular typing system between the food and public health pillars in order to ensure the protection of consumers within the EU single market in the context of a ‘One Health’ system approach.

Requirement from the requestor



Interoperability of the two systems in the public health and the food safety sectors

- **Term of references**

- **ToR 1:** set up in ECDC and EFSA **two interoperable systems for the collection and sharing of WGS data** provided by Member States, allowing the joint analysis of WGS data for at least *Salmonella*, *L. monocytogenes*, and *E. coli* for the purpose of **multi-country outbreak detection and assessment**;
- **ToR 2:** deliver services allowing data providers to interact and query the systems, according to the agreed provisions on the **management of data** on molecular testing of food, feed and animal isolates of selected foodborne pathogens and their use together with molecular typing data on isolates from human infections for public health purposes

- **Deadline June 2022**

■ Requirements



Interoperability



IT architecture



Transparency



Engagement

■ Additional requirements

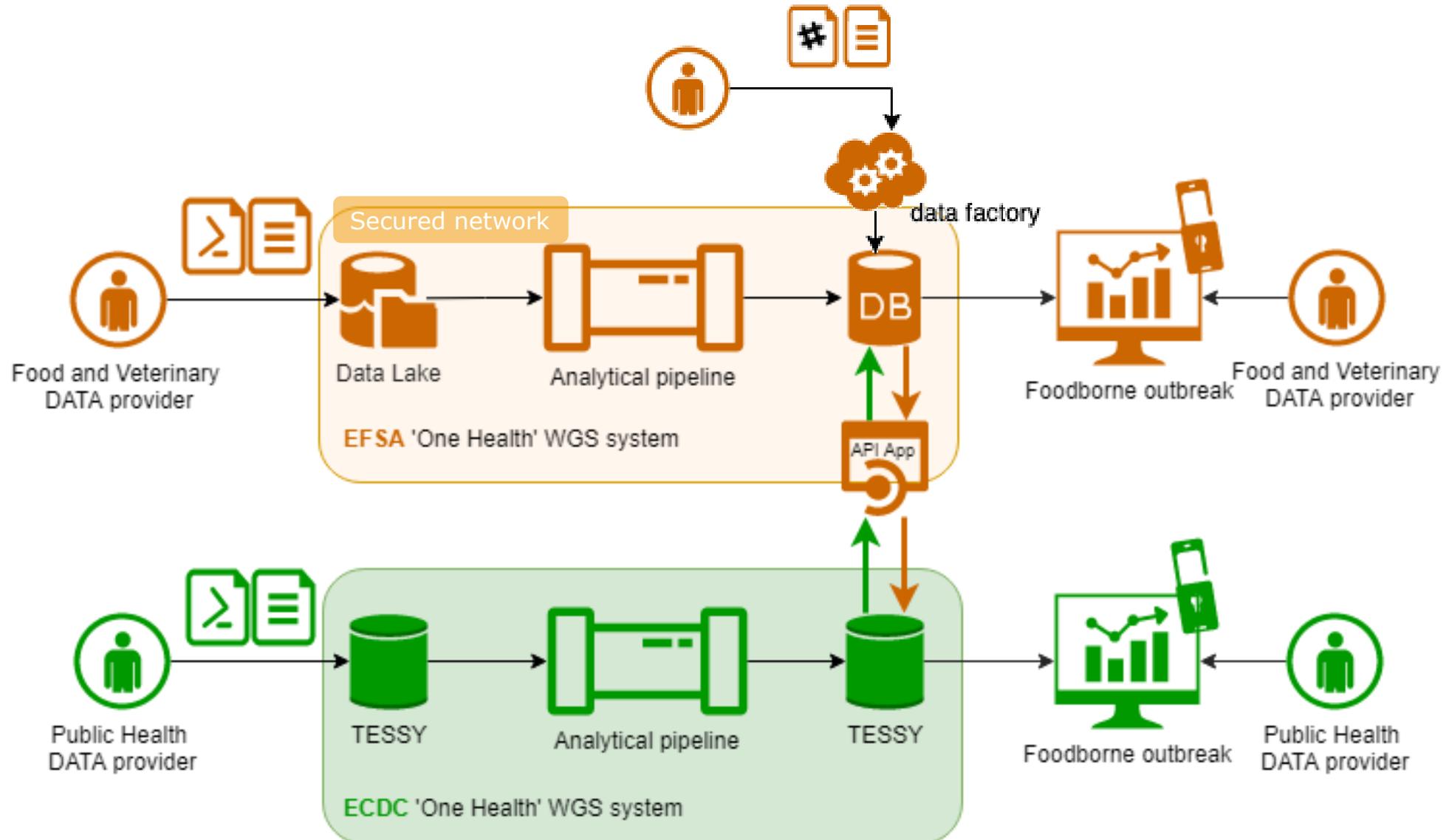


EFSA is not the owner of these data.
Data ownership should be respected.



The system should be able to guarantee the **data confidentiality**.

The foreseen 'One Health' system





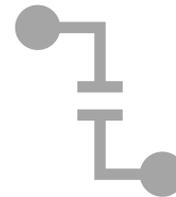
Interoperability



Two interoperating systems

(EFSA and ECDC)

Each system collects and stores the data (i.e. allelic profiles and descriptive data) of the respective data domain.



Cross-sector matches

Databases will be queried, and comparison will be performed live to the data stored, returning any matches (according to business rules)



Machine-to-machine

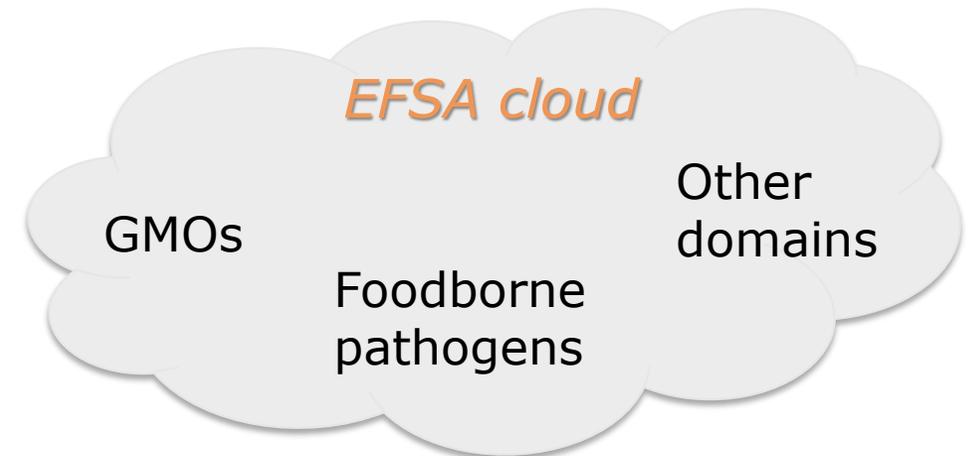
Automatic exchanging of allelic profiles and descriptive data as established in the Collaboration Agreement



IT architecture

■ **Cloud-based** implementation

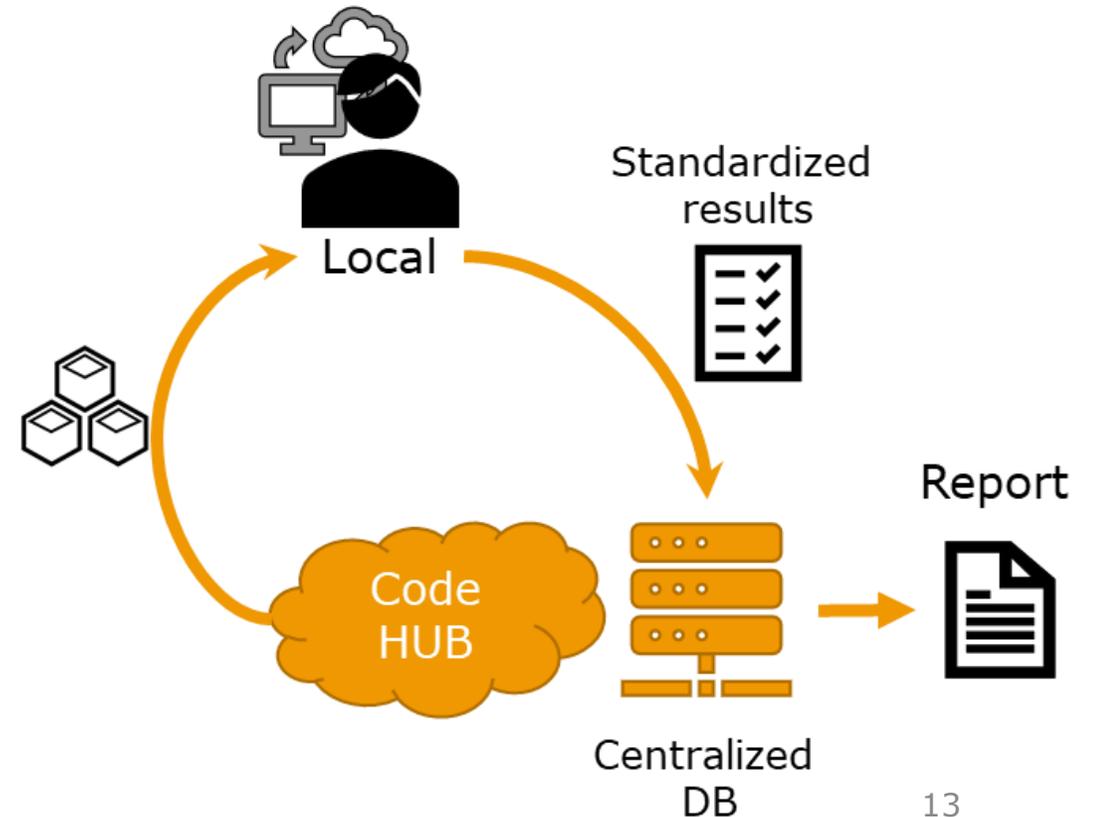
- The EFSA WGS system will be integrated in the EFSA cloud system, that addresses multiple needs for different risk assessment domains.
- Storage located in Western (primary site) and Northern Europe (secondary site).
- Data will be stored and analysed in a system within secured network.





Transparency

- **Open source** analytical pipeline:
 - Written in nextflow (modular)
 - Open source distribution of the pipeline
- **Move-code-to-data**
 - Decentralization of the resources to data providers allowing programmatic submission of WGS-based typing data
 - Raw data can remain at the owner level, if data providers wish (only final results are shared)
 - Capacity building at country level



- **Raw Reads:** FASTQ(s) submitted by data providers or downloaded from public repositories
- **EpiData:** epidemiological data linked to one raw reads submission; always submitted by the data providers
- **Analytical Pipeline Results:** containing data extracted from the raw reads by the analytical pipeline in the EFSA system or at the data provider premises:
 - **Allelic profile**
 - **Accessory data:** statistics of the analysis, QC, Serotype, Pathotype, stx type
 - **Assembly**
 - **AMR profile:** EURL AR official pipeline
 - **Virulence profile:** BLAST search of dedicated reference datasets



Data ownership

- Data provider **is always owner of the submitted private FASTQ**
 - Data submitted by data provider (EpiData, FASTQ or both) and EpiData linked to publicly available FASTQ are considered “**private**”
- The data providers **remain owners of the transformed FASTQ** if data refers to individual isolates
- In case of transformation-results **aggregating several records**, the resulting data are **owned by EFSA**
- The **data providers are allowed to withdraw data** and prevent their use for future searches

- **Physical deletion** of *FASTQ* and *assembly* → remove the data from the database
- **Logical deletion** of the *allelic profile* and *typing data* → data remains in the database, but invisible for future research
- **EpiData cannot be deleted but only updated**
 - Old versions are stored for traceability
 - No check for consistency between versions of EpiData
- In case of **ROA** → '**entries frozen for deletion**'
 - During such freeze-period, the owners/organizations will not be capable of deleting data
 - Maintained by EFSA administration

Linker to FASTQ submission

LocalRawReadsID	data provider's sequence identification code or ENA Accession Number	M/Exp
OwnerOrganization	The organization who owns the RawReads data;	M/Exp
Sample ID	ID of the sample from which the bacteria has been isolated and sequenced and from which the WGS files have been derived.	M
Country of sampling	Country of sampling	M
Date of sampling	Year/month/day	M
Sample Matrix	Description of the sample taken based on FoodEx2 catalogue	M
Isolate ID	ID of the bacteria isolate sequenced and from which the WGS files have been derived.	M
Sampling point	Point where the sample which generates the isolate has been sampled	R
Country of origin	Country of origin of the sample taken	R
Date of isolation	Year/month/day of isolation	O
Area of sampling	Area where the sample was collected	O
Programme type	"Outbreak investigation" (K032A) or "RASFF alert notification" (K033A)	O
Sampler	i.e. "Official sampling" (CX02A)	O
Additional sampling programme information	RASFF notification number, if available.	O



Data confidentiality

- The Collaboration Agreement of the current Molecular Typing Database will be amended to take into account the features and processes of the new system
- This Agreement will stipulate the **visibility of data**

- A **centralized WGS data collection** is needed to support promptly the investigation of multi-country foodborne outbreaks
- In the design of the centralized data collection and analysis system many **key factors** should be considered, keeping the balance between:
 - Openness/ Transparency
versus
 - Data ownership/ Confidentiality/ Engagement
- **Dialogue with all stakeholders** is crucial

Thanks for your attention



EFSA is committed to:

**Excellence,
Independency,
Responsiveness and
Transparency**

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