24th workshop of the NRLs for *Salmonella*

Update on EFSA/ECDC database and EFSA activities on WGS in the area of foodborne pathogens

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BIOCONTAM Unit

Trusted science for safe food

efsa
European Food Safety Authority

Molecular typing database

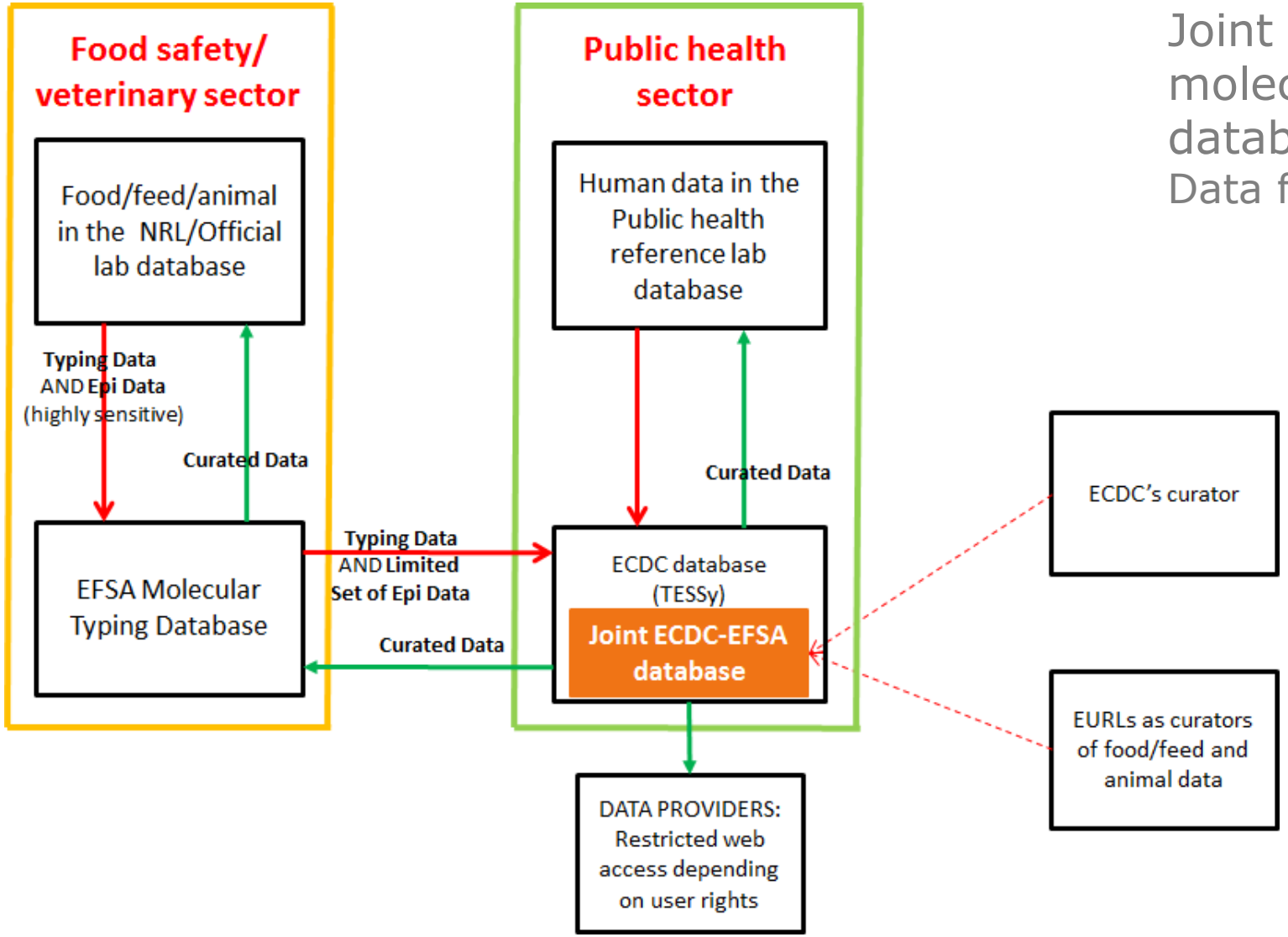
- The Standing Committee on Food Chain and Animal Health (representing all EU Member States) approved in December 2012 the Vision paper on the development of databases for molecular testing of food-borne pathogens in view of outbreak preparedness

- Request for technical assistance:
  - ECDC to collect molecular typing data from food-borne pathogens isolated from human cases (TESSy)
  - EFSA to collect similar data from food, feed and animal isolates, in close collaboration with relevant EURLs (EFSA database)
  - Regular joint data analyses of the data in the joint EFSA-ECDC database (hosted in ECDC), where curation of molecular typing data is carried out by the relevant curators (EURLs).

- The data collection to cover initially:
  - *Salmonella*, VTEC and *Listeria monocytogenes* with PFGE and MLVA (*S*. Typhimurium and *S*. Enteritidis) methods.

Molecular typing database

Joint ECDC-EFSA molecular typing database
Data flow



Molecular typing database

To guarantee **data confidentiality** only a subset of the metadata stored in the EFSA database will be sent to ECDC for storage in the joint EFSA-ECDC database.

The **visibility of data** in joint EFSA-ECDC database depends on the **type of data** (sensitive or non-sensitive) and the **users**.

Data shared in the joint database:

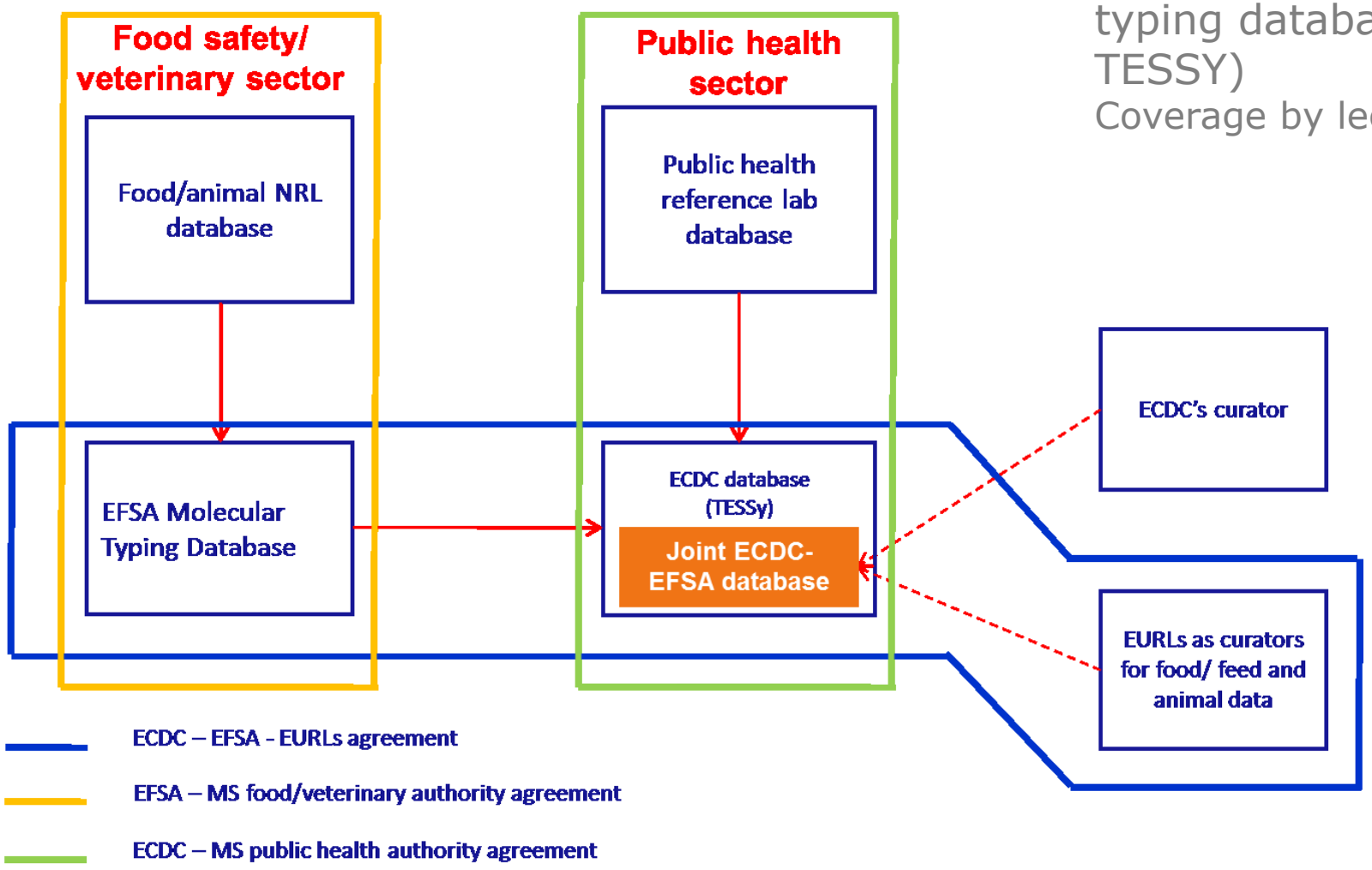
Non-sensitive data:
Microbiological Data, limited to *Molecular Typing Data* and other typing data (*Salmonella* serotype, *Listeria* serotype and STEC serogroup). EFSA Isolate Id, date of sampling, date of receipt of isolate in the reference lab, type of sample (e.g. 'animal', 'food', 'feed', 'environment')

Sensitive data:
Country of sampling, laboratory identification code

Collaboration agreements

Joint ECDC-EFSA molecular typing database (hosted in TESSY)

Coverage by legal agreements



Laboratory engagement procedure

Prerequisites

- Laboratories willing to participate must be compliant with the following prerequisites:
  - The laboratory is an NRL or official control laboratory for *Listeria monocytogens*, *Salmonella* or *E. coli*.
  - The laboratory owns BioNumerics (Applied Maths) version 7.1 or higher or is able to submit data through the EFSA's Data Collection Framework (DCF).
  - The laboratory submits the data according to the EFSA data model.

Official nomination

- The countries willing to participate in the data collection have to:
  - officially nominate their representatives for submitting molecular typing data to EFSA and communicate them to Commission;
  - sign the Collaboration Agreement (Appendix 1).

Download Issue

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EUROPEAN UNION COLLABORATIVE PROJECTS BETWEEN EUROPEAN UNION OR NATIONAL REFERENCE LABORATORIES

The ECDC-EFSA molecular typing database for European Union public health protection

Auteur : Valentina Rizzi, Teresa Da Silva Felicio, Benjamin Felix, Celine M. Gossner, Wilma Jacobs, Karin Johansson, Saara Kotila, Damien Michelon, Mario Monguidi, Kirsten Mooijman, Stefano Morabito, Luca Pasinato, Jonas Torgny Björkman, Mia Torpdahl, Rosangela Tozzoli, Ivo Van Walle

http://euroreference.mag.anses.fr/en

Status of engagement of laboratories

	Human side	Food/ veterinary side
Nominated users	All MSs	**14 MSs***: AT, BE, DK, DE, ES, FI, FR, IE, IT, LU, PT, SE, SK, UK (21 labs**)
Signature of the Collaboration Agreement	**16 MSs**: AT, CZ, DK, EE, DE, EL, HU, LV, LT, MT, NO, RO, ES, SE, NL, SK	**11 MSs**: AT, BE, DE, FI, FR, IE, IT, LU, PT, SE, SK (12 labs)
Transmission of data	**14 MSs**: AT, BE, DK, EL, ES, FR, IE, IT, LU, NL, NO, SE, SI, UK	**8 MSs: BE, DE, FI, IE, IT, LU, SE, SK**
Total number of isolates uploaded	**47,784**	**1,000**

**Salmonella* and STEC: 12 MSs (all except FI and FR) - *Listeria*: all MSs
***3 different users for the 3 pathogens in AT, IE and IT, 2 users for the 3 pathogens in SK

Status of engagement of laboratories

Data on **food isolates** submitted to the joint database, by country (as of 1 May 2019)

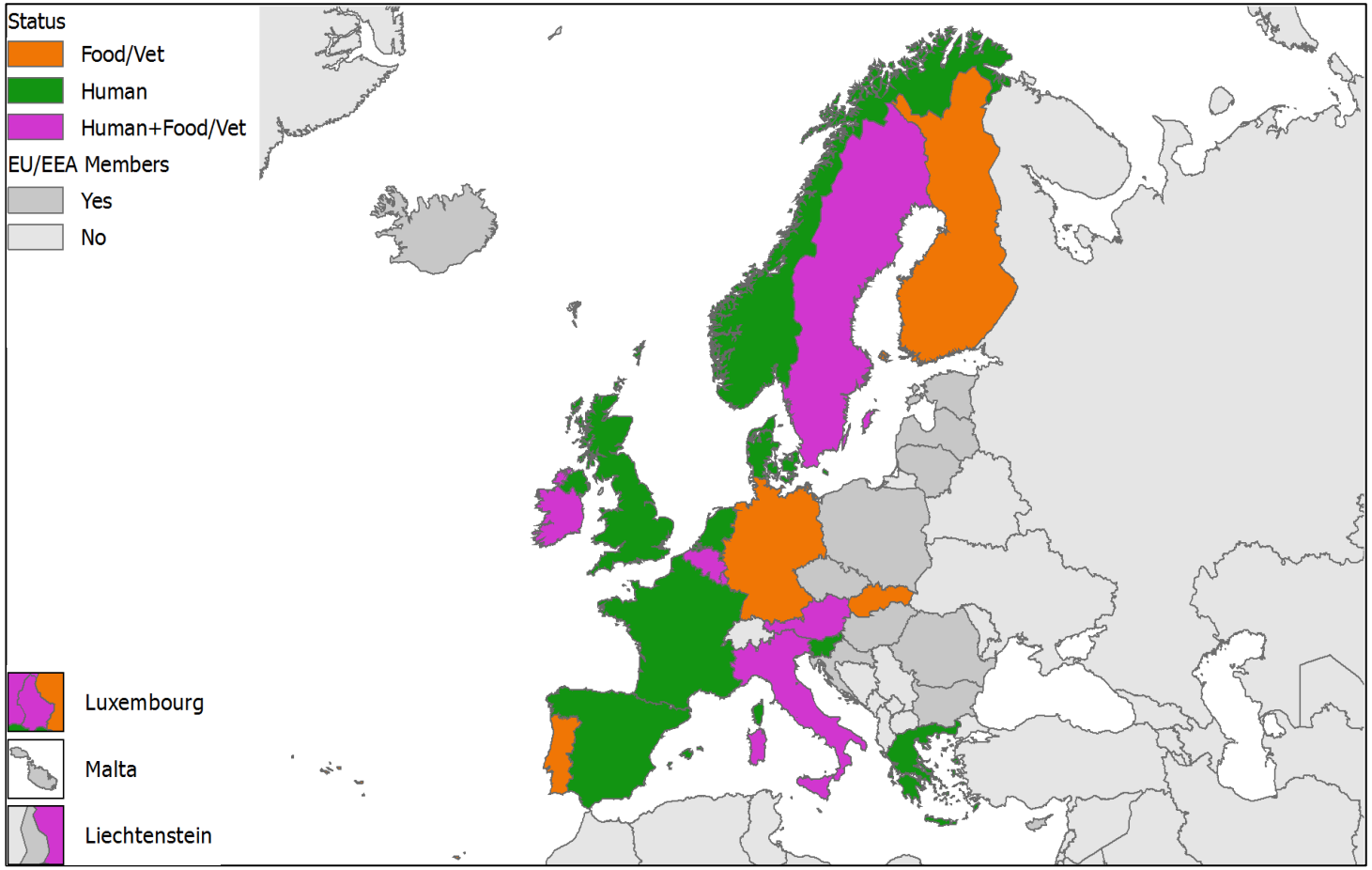
Country	N. isolates	Data transmission to EFSA DB				Data transmission from EFSA DB to Joint DB
		Directly from MS (n. isolates/ comments)		From EURL Lm on behalf of MS (n. isolates/ comments)		
BE	370	330	All *L. monocytogenes* *some of these do not have reference lanes defined or are linked to some possible corrupt images			291
				40	All *L. monocytogenes*	
DE	152			152		152
FI	28			28	All *L. monocytogenes*	28
IE	129			129	All *L. monocytogenes*	129
LU	121	121	118 *L. monocytogenes* and 3 *Salmonella* (PFGE)			121
SE	26			26	All *L. monocytogenes*	26
IT	45	45	All VTEC			45
	91	91	*Salmonella* (MLVA)			91
SK	117	117	110 *L. monocytogenes,* 2 VTEC and 5 *Salmonella* (PFGE)			117
TOTAL		704		375		1,000

Status of engagement of laboratories

Data on **food isolates** submitted to the joint database, by country, and by pathogen (as of 1 May 2019)

Country	*L. monocytogenes*	*Salmonella*	VTEC	N. isolates submitted from EFSA DB to Joint DB
BE	291			291
DE	152			152
FI	28			28
IE	129			129
LU	118	3 (PFGE)		121
SE	26			26
IT			45	45
		91 (MLVA)		91
SK	110	5	2	117
TOTAL	854	99	47	1,000

Status of engagement of laboratories



Human: submitting data. Food/veterinary: collaboration agreement signed.

New mandate on WGS

- Given:
  - the rapid development of WGS in recent years,
  - the growing importance of WGS analysis in recent multinational foodborne outbreak investigations and in surveillance/monitoring fields (including AMR)
  - The gradual increasing WGS capacity of public health and food laboratories

In 2017, EFSA and ECDC received a new joint mandate from EC to expand the molecular typing data collection to **WGS** data.

New mandate on WGS - Terms of reference

In particular, jointly evaluate the **possible solutions** for the **collection and the analysis of WGS** data for at least *L. monocytogenes*, *Salmonella*, *E.coli* by

- ToR1: to analyse **outcome of ECDC and EFSA Surveys on WGS** capacity for foodborne pathogens in MSs (food and PH).
- ToR2: **...** to assess the **state of the art of pipelines** for collecting and analysing WGS data…
- ToR3: … to assess **needs/requirements** for analysis and comparability; interactions among databases; roles and responsibilities.
- ToR4: to prepare a **Technical report**: identification, comparison of potential solutions for a joint EFSA-ECDC

Deadline April 2019

(publication of the report: end May 2019)

WGS data

EFSA is interested in using WGS for:

- Outbreak detection and investigation
- Source trace back investigations
- Source attribution
- Detection and surveillance of emerging pathogens
- Monitoring of antimicrobial resistance

Our main interest is to use the data generated by new Sequencing technologies (WGS, Metagenomics) for Food Safety and Public Health Protection

Cross sectoral working arrangements

MEMBER STATES' BODIES

Molecular Typing database | TESSy | EPIS | Data sharing | EWRS | RASFF

Assessment

Multinational outbreak investigations

Management

ECDC: outbreak investigation, risk assessment for human health, options for response

EFSA: to assess food/animal data, consumers' advice, investigation to source

Joint Rapid Outbreak Assessment

DG SANTE: Based on assessment: measures, trade restrictions, negotiations with third countries

Technical support

EURL network: analytical methods, molecular testing

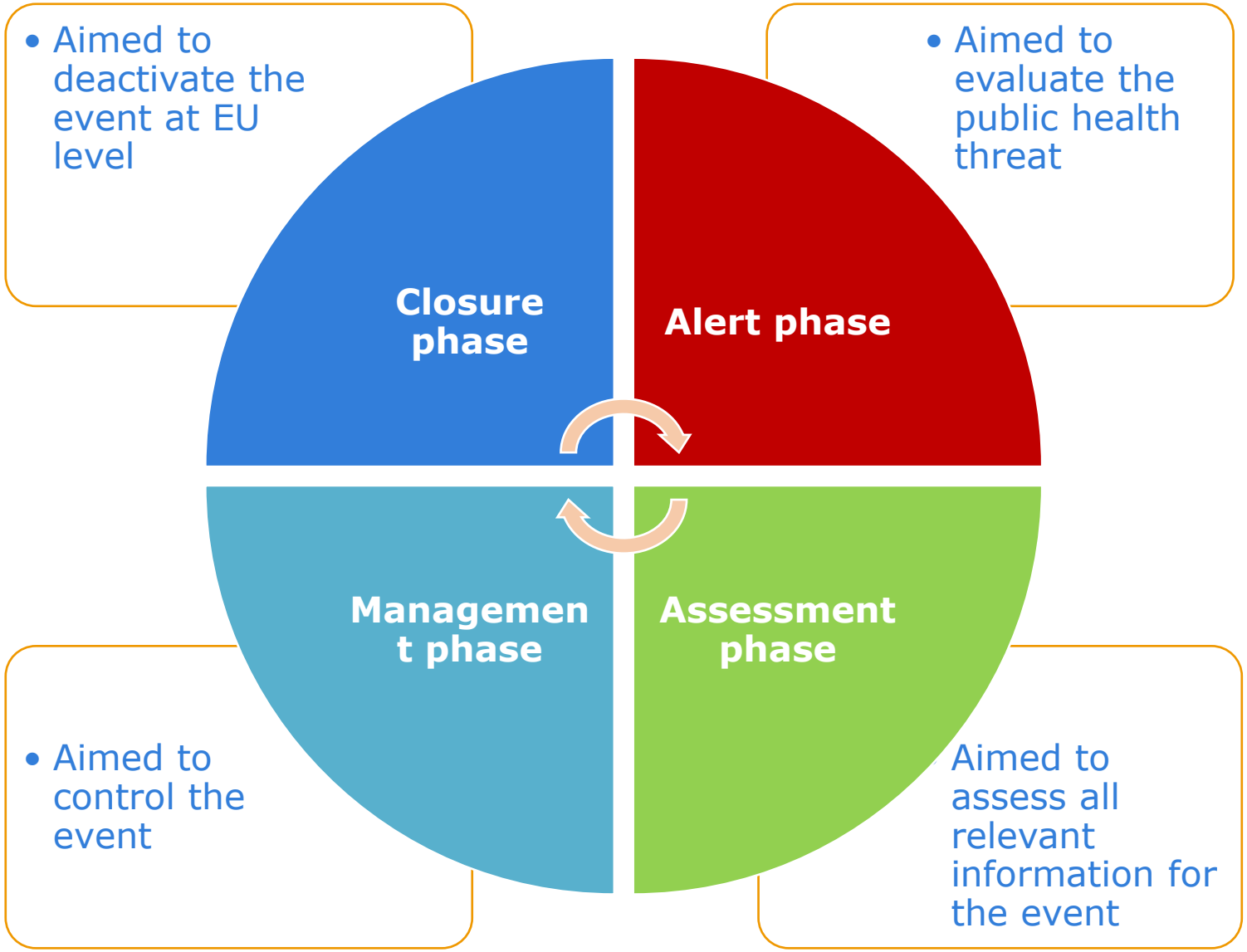
Technical support

Joint ECDC-EFSA Rapid Outbreak Assessment

- Produced when there is need to rapidly communicate about the assessment to MS and EC
- Produced by ECDC, EFSA, EC (DG SANTE) and Member States
- Request from ECDC or EC
- Criteria that trigger the production of a ROA:
  - Multi-country outbreak
  - Foodborne outbreak
  - EWRS notification and/or EC request

Joint ECDC-EFSA Rapid Outbreak Assessment

Phases of actions



Joint ECDC-EFSA Rapid Outbreak Assessment

Production of the joint ROA

- ECDC describes the cases in humans
- EFSA extracts background data (zoonoses database) and assesses data on food and animals shared by countries in RASFF
- ECDC and EFSA draft the assessment
- When relevant, SANTE-G4 contacts the food and animal experts and/or the EURL to collect further information through other networks (e.g. NRLs, PAFF Committee, PAFF's working groups)
- MSs review the content and may add information.

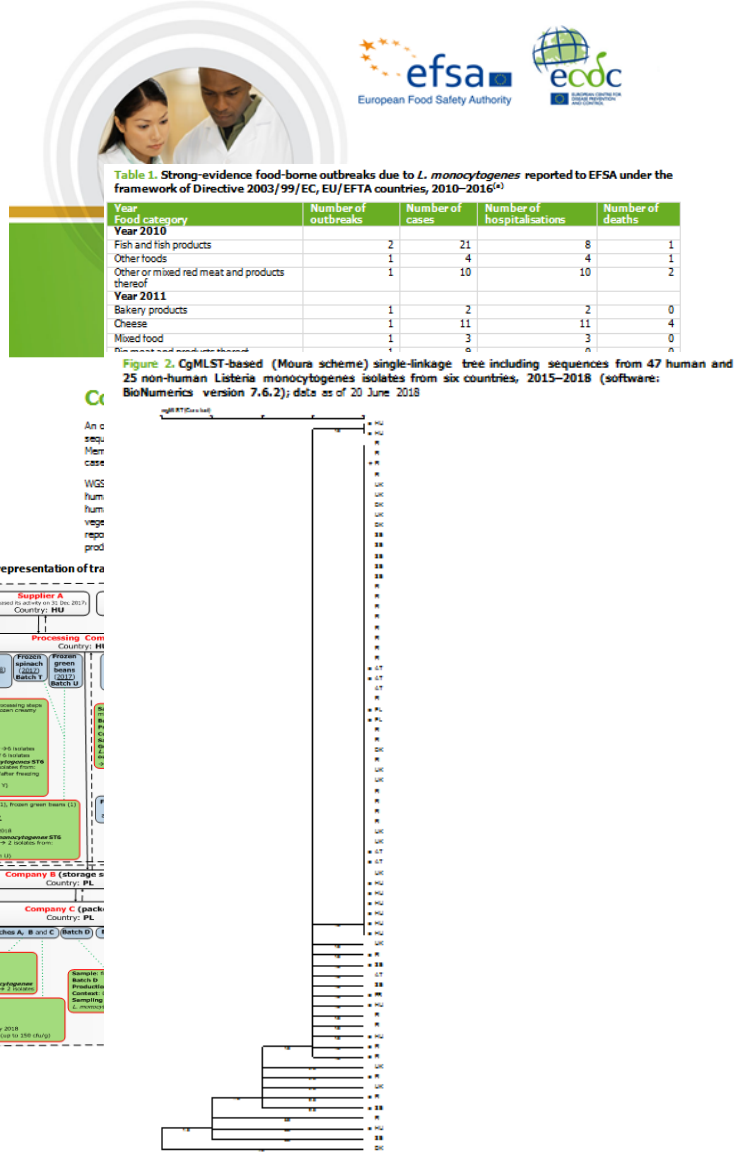


Table 1. Strong-evidence food-borne outbreaks due to *L. monocytogenes* reported to EFSA under the framework of Directive 2003/99/EC, EU/EFTA countries, 2010–2016[a]

Year Food category	Number of outbreaks	Number of cases	Number of hospitalisations	Number of deaths
Year 2010				
Fish and fish products	2	21	8	1
Other foods	1	4	4	1
Other or mixed red meat and products thereof	1	10	10	2
Year 2011				
Bakery products	1	2	2	0
Cheese	1	11	11	4
Mixed food	1	3	3	0

Figure 2. CgMLST-based (Moura scheme) single-linkage tree including sequences from 47 human and 25 non-human Listeria monocytogenes isolates from six countries, 2015–2018 (software: BioNumerics version 7.6.2); data as of 20 June 2018

Figure 3. Graphical representation of tra

Hungary

Supplier A

Country: HU

Processing Com

Poland

Company B (storage

Country: PL

Company C (pack

Country: PL

Joint ECDC-EFSA Rapid Outbreak Assessment Successful stories

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

The hypothesis about the food vehicle was formulated by:

- Searching databases at EU and country level for food isolates matching the human outbreak strain,
- Assessing traceability data.

Confirmation of the food vehicle through:

- Patient's interviews,
- Joint WGS analysis (cgMLST) of human and non-human isolates (done jointly by ECDC, EFSA and the EURL *L. monocytogenes*)

Joint ECDC-EFSA Rapid Outbreak Assessment Successful stories

Multi-country outbreak of *Salmonella* Enteritidis PT8, MLVA 2-9-7-3-2 and 2-9-6-3-2

The case definition of this outbreak was based on typing data.

- WGS provided a more accurate case definition compared to MLVA and resulted in a more conclusive outbreak investigation.

Confirmation of the food vehicle was achieved through

- joint WGS analysis (SNPs) of human and non-human isolates (collaboration between PHE, ECDC, *EURL-Salmonella*, EFSA).

Joint ROAs – A recent example

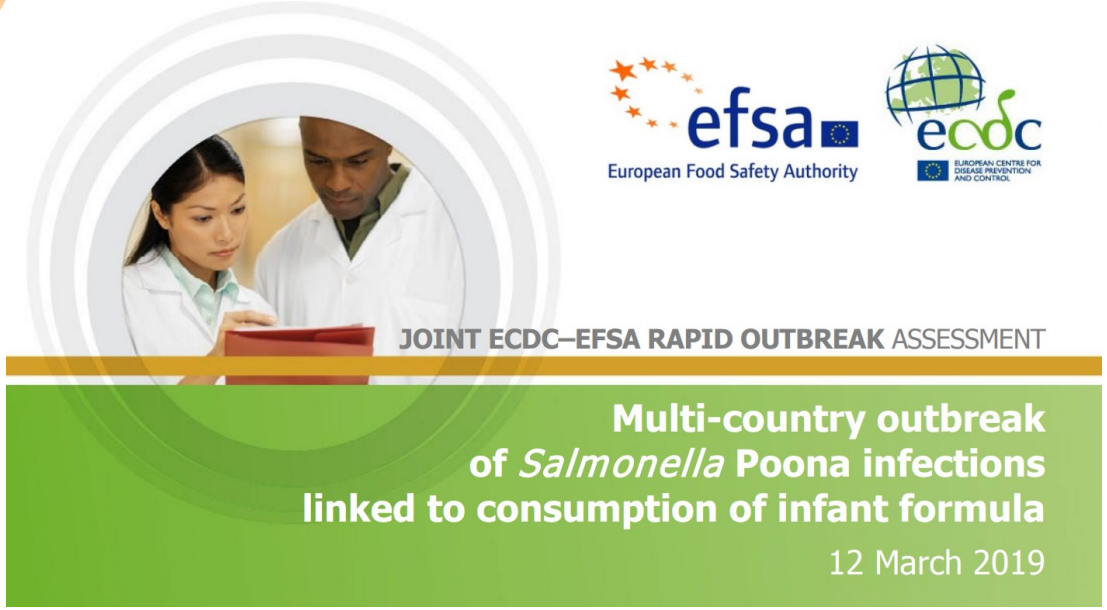
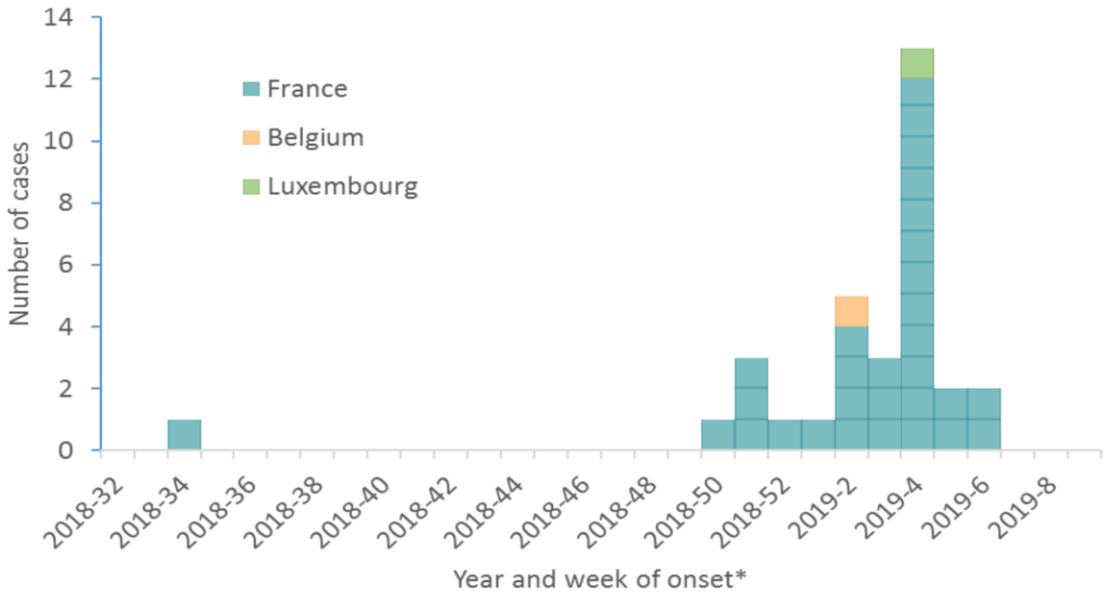


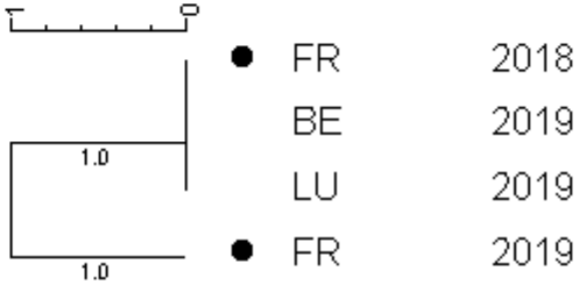
Figure 1. ***S.*** **Poona outbreak-confirmed cases by country and week of onset*, EU, 2018 and 2019, as of 6 March 2019 (n=32)**



- Three EU countries (FR, BE and LU)
- 32 cases reported in infants and young children (symptoms between August 2018 and February 2019)
- Link to three infant formula products based on rice proteins from the same brand manufactured by a Spanish processing company and marketed by a French company.

Joint ROAs – An example

cgMLST-based (EnteroBase scheme) single-linkage clustering analysis including sequences from four human S. Poona isolates from three countries, EU/EEA 2018–2019



The French representative outbreak isolates are indicated with a circle.

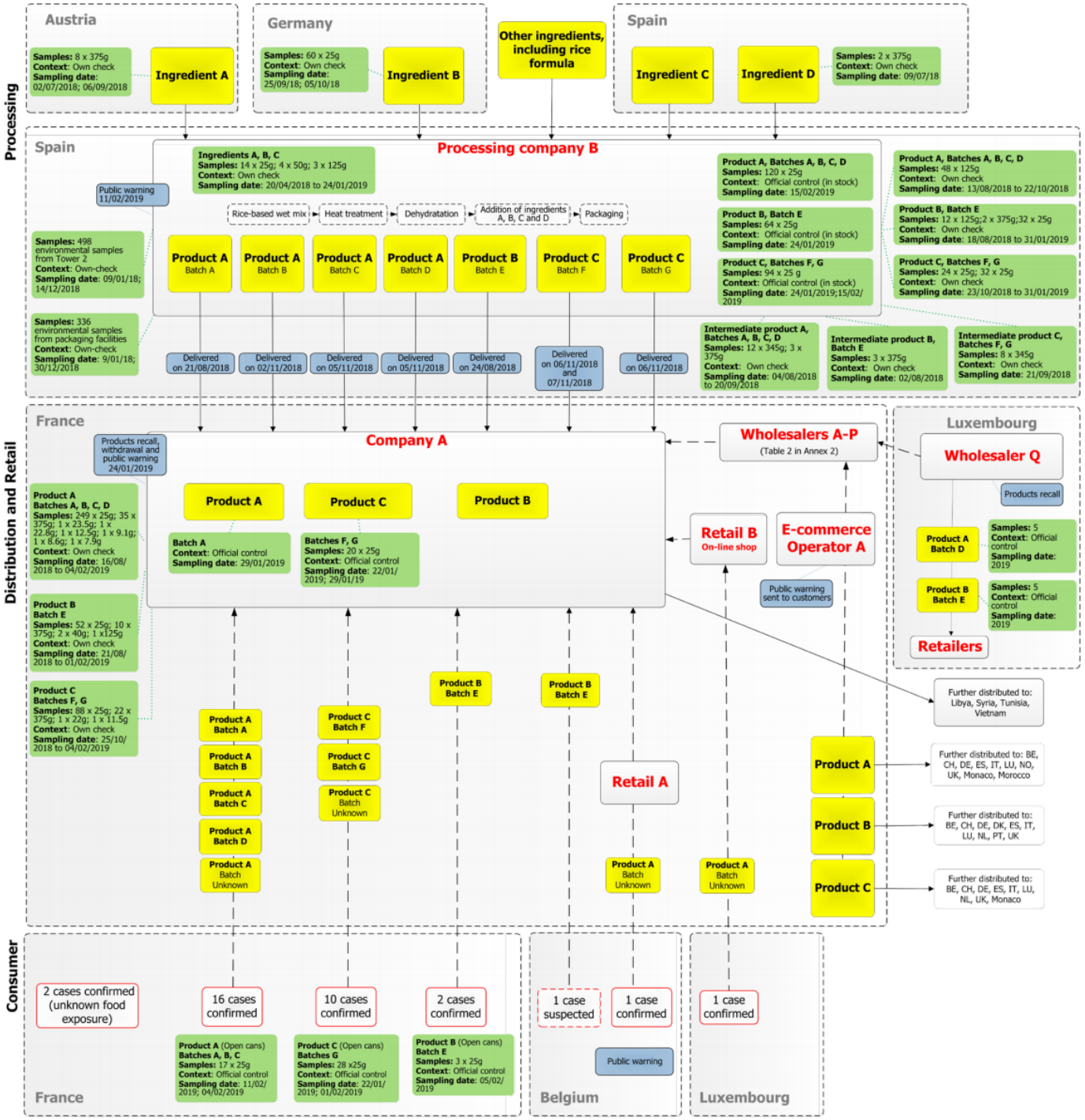
Update as of 5 March 2019

- *S.* Poona has not been detected in:
  - any sample of the implicated batches of infant formula tested either at the Spanish processing company or at the French company.
  - in the production environment of the Spanish processing company or in any other product dehydrated in the same drying tower since 2017.

Joint ROAs and risk management actions

On 22 January 2019, the Spanish processing company ceased operations in the drying tower where all the suspected products had been dehydrated.

Recalls, withdrawals and public warnings of infant formula products have been initiated in the countries involved and in countries where the products had been distributed.



EFSA activities on WGS

ENGAGE
(Thematic grant)
Salmonella
E. coli
AMR

LISEQ
Procurement
Listeria

INNUENDO
(Thematic grant)
Salmonella
E. coli
Campylobacter
Yersinia

Joint ECDC-EFSA ROAs
Salmonella, Listeria

Generated Sequences, information, analyses, tools, pipelines

Procurement NGS in Norovirus

EUSR-AMR Ref. testing
(EURL-AR, EC)
Salmonella, E. coli

GENCAMP
EFSA-MSs agreement
Campylobacter

WGS Training EFSA staff

Thanks for your attention!

Acknowledgements:
BIOCONTAM Unit
DATA Unit
ECDC
EC – SANTE G4

EFSA is committed to:

Excellence, Independency, Responsiveness and Transparency

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