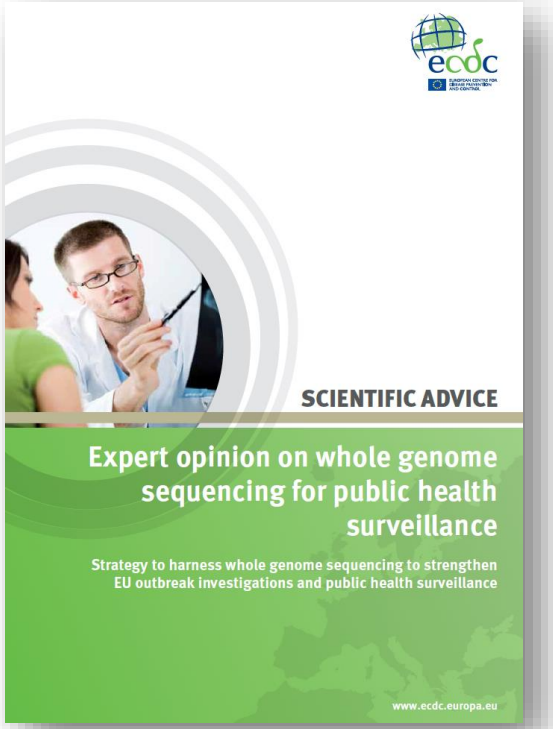
ECDC State of play on NGS and future perspectives in public health area

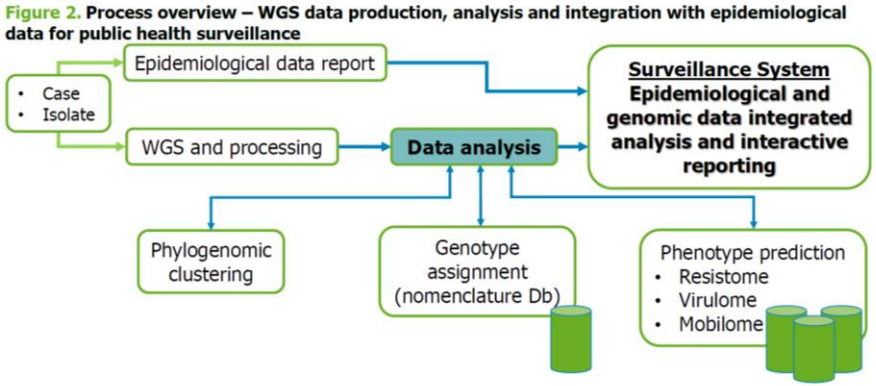
Saara Kotila, ECDC

"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

Whole Genome Sequencing: ECDC Vision 2020

- To establish standards and manage systems
- EU wide use of whole genome sequencing as the method of choice for typing microbial pathogens
- Accurate and effective risk assessment, outbreak investigation, disease surveillance and evaluation of prevention policies

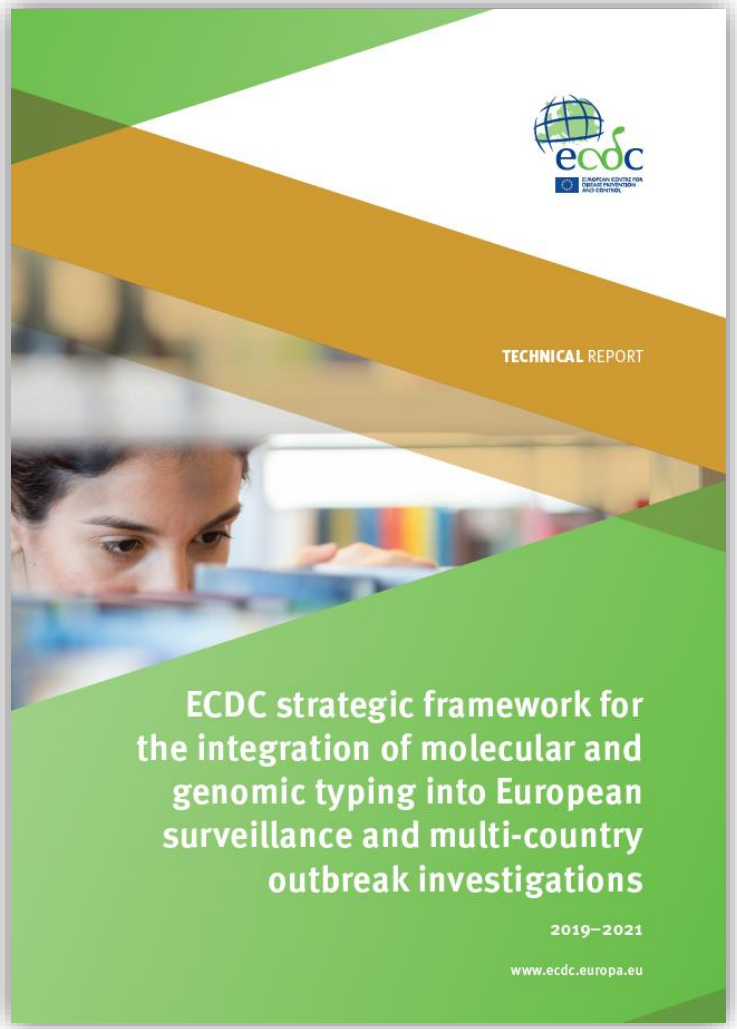




Expert Opinion on whole genome sequencing for public health surveillance. Stockholm: ECDC; 2016

Whole Genome Sequencing: Strategic framework 2021

- **Priorities for integration into EU surveillance and response support systems, 2019-2021**



ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations 2019–2021. ECDC; 2019

Public health applications of integrated epidemiological and WGS data collection and analysis

1. **Outbreak investigations**: real-time information sharing and analysis for *rapid risk assessment*, targeted public health response and transmission control
2. **Control-oriented surveillance**: real-time, continuous surveillance with maximal disease sampling frame for *early outbreak detection*
3. **Strategy-oriented surveillance**: either by *sentinel continuous surveillance* or *periodic surveys*, with representative sampling frame for programme evaluation and trend monitoring

ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations –2019–2021. Stockholm: ECDC; 2019

Priority criteria for integrating genomic typing data into EU epidemiological investigations

- Disease **public health priority** and added-value of WGS data for infection control
- **Feasibility** of standardised typing schemes and data sharing
- **Capacity** for WGS typing at Member State and ECDC level
- **Interoperability** with information systems of public health partners at EU and international levels

ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations –2019–2021. Stockholm: ECDC; 2019

WGS typing: EU Strategic priorities 2021*, by objective

Outbreak investigation
Any epidemic pathogen/MDR outbreak
Continuous real-time surveillance
• *Listeria monocytogenes* • *Neisseria meningitidis* • MDR tuberculosis • *Salmonella enterica* • Shiga toxin-producing *E.coli* • influenza virus
Sentinel surveys
• Carbapenem/ colistin-resistant *Enterobacteriaceae* • Antibiotic-resistant *Neisseria gonorrhoeae* • Carbapenem-resistant *Acinetobacter baumannii* • *Bordetella pertussis* •HIV-transmitted drug resistance • *Streptococcus pneumoniae*

Some postponements due to COVID-19 pandemic

ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations –2019–2021. 2019

EU Multi-country Foodborne outbreaks

Home News Multi-country Salmonella outbreak

27 October 2016

Multi-country Salmonella outbreak

Print

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Seven countries have reported human cases of *Salmonella* Ent
and 12 October 2016 (112 confirmed and 148 probable).

Cases have been reported by Belgium, Denmark, Luxembourg

E. coli cucumber scare: Spain angry at German claims

31 May 2011

EHEC O104:H4 Outbreak in Germany, 2011

EFSA and ECDC rep
egg, sesame seed S

By Joe Whitworth on September 26, 2018

More detail has emerged about two pa
in Europe.

One was caused by Salmonella Enteriti
Poland and the other by a previously u
imported sesame seeds.

France

Lactalis to withdraw 12m boxes of baby milk in salmonella scandal

Kim Willsher *in Paris*

Sun 14 Jan 2018 16.03 GMT

1,184

This article is over 9 months old

Emmanuel Besnier, chief executive of French dairy g
products from contaminated factory will be recalled

A French government official checks baby milk products in a pharmacy in Orl
Souvant/AFP/Getty Images

The head of a French dairy giant at the centre of an in
scandal has promised to withdraw 12m boxes of powe
the supermarket shelves of 83 countries.

'Most outbreaks remain undetected': How the EU is strengthening listeriosis surveillance

By Katy Askew

22-Aug-2018 - Last updated on 22-Aug-2018 at 14:16 GMT

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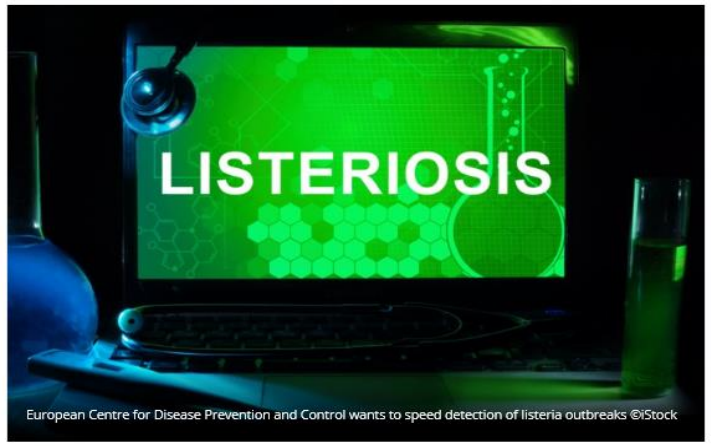


European Centre for Disease Prevention and Control wants to speed detection of listeria outbreaks ©iStock

Swedes get hepatitis A from eating infected frozen strawberries

File photo of frozen strawberries. Photo: Bertil Enevåg Ericson/TT

Swedes have been reminded not to eat frozen strawberries without properly heating them up first, after 13 people contracted hepatitis A from imported fruit.

Joint Molecular Typing for Enhanced Surveillance

STEC O104:H4 outbreak

EC vision on molecular typing support for outbreak preparedness

EC request to ECDC and EFSA on establishment of molecular typing databases

Joint ECDC-EFSA Steering Committee for a joint molecular typing database

EC request to ECDC and EFSA to upgrade joint molecular typing database with WGS

Start of WGS-enhanced surveillance of listeriosis in EU/EEA

2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020

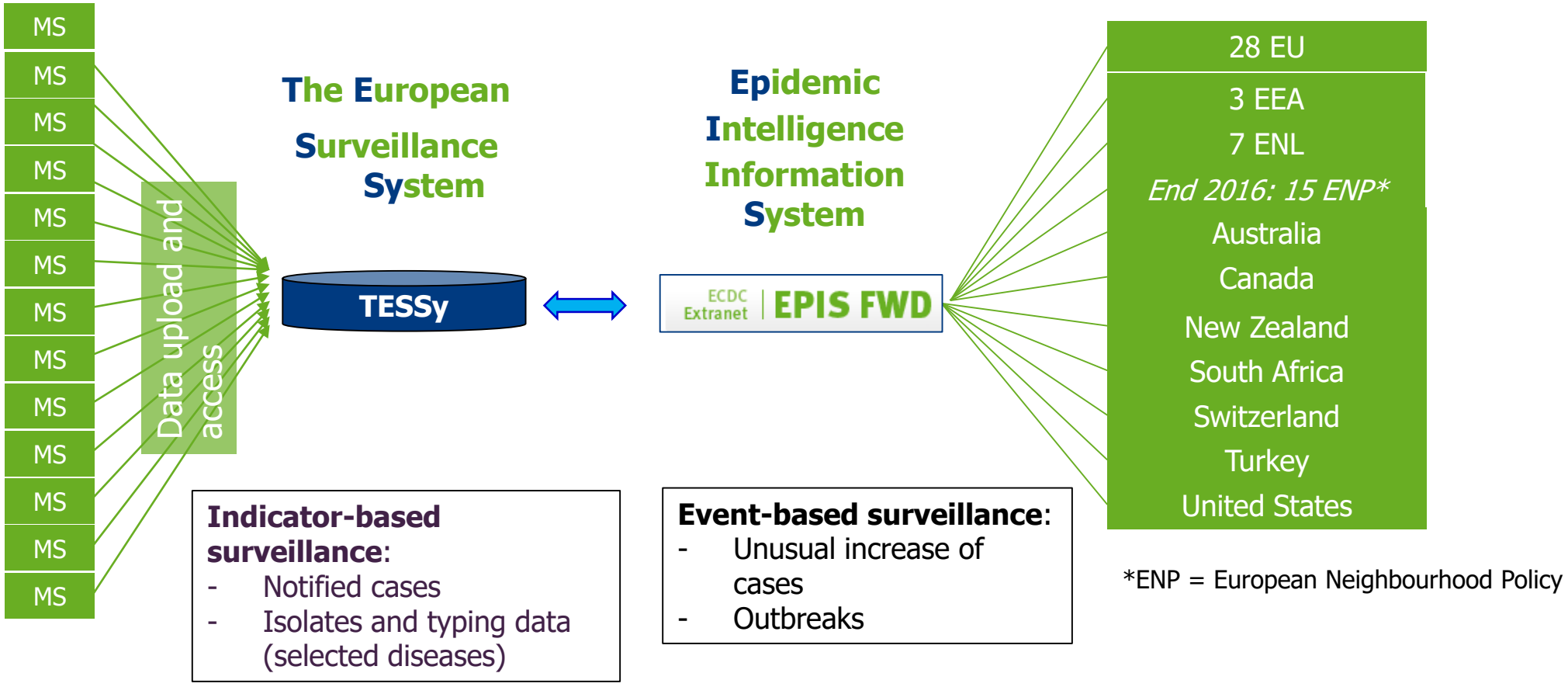
ECDC pilot molecular typing data collection PFGE and MLVA

Pilot study WGS *Listeria*

1st WGS support to multi-country outbreak investigation

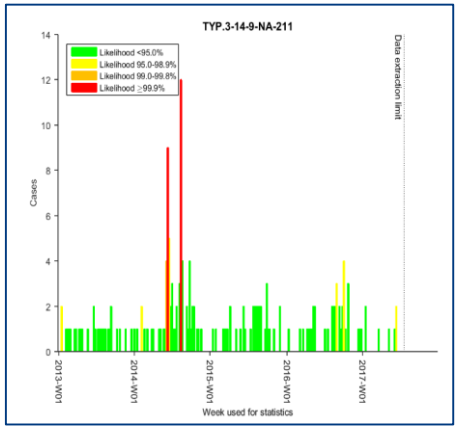
EU-wide validation study *Listeria* WGS

EU surveillance of foodborne diseases

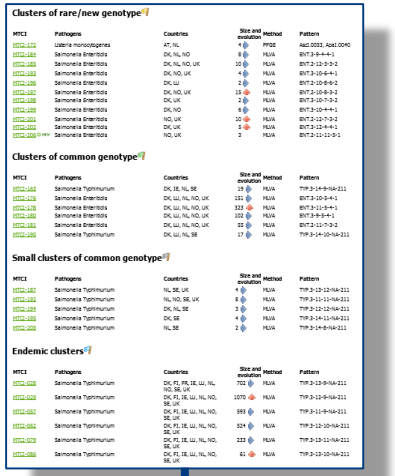


WGS Improved Signal Detection and Response to Multi-Country Foodborne Outbreaks

MLVA[1] + PFGE[2] +cgMLST[3]



Weekly cluster reports



ECDC Extranet | EPIS FWD

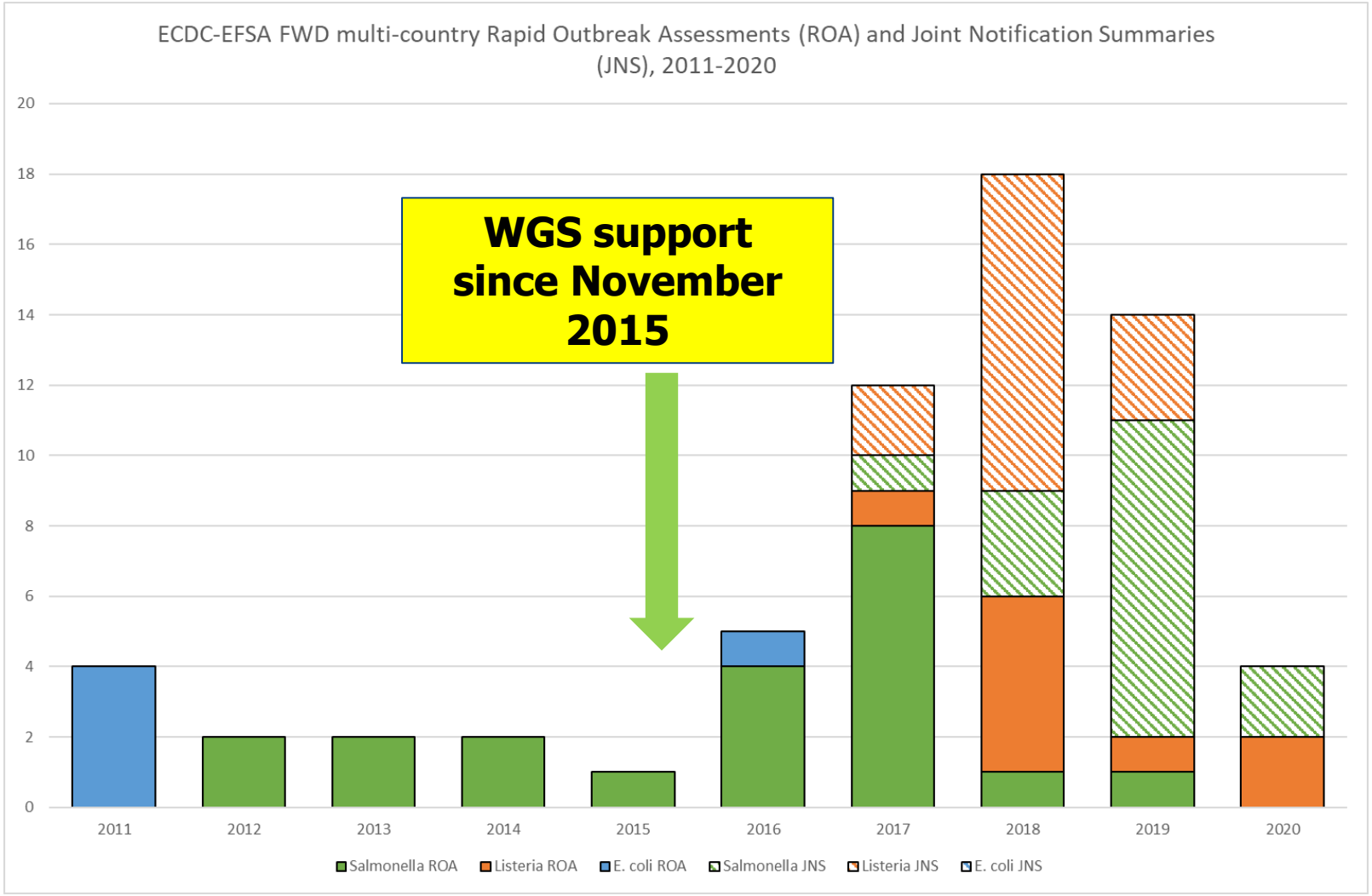
Urgent Inquiry: unusual increase of cases at national level

Whole genome sequencing support since 2015

Joint ECDC-EFSA Rapid Outbreak Assessments

[1]MLVA=Multi-Locus Variable number tandem repeat Analysis
[2]PFGE=Pulsed-field gel electrophoresis[2]PFGE=Pulsed-field gel electrophoresis
[3]cgMLST=core genome Multi-Locus Sequence Typing

ECDC-EFSA multi-country outbreak assessments and notifications for foodborne diseases, 2011 – 2020



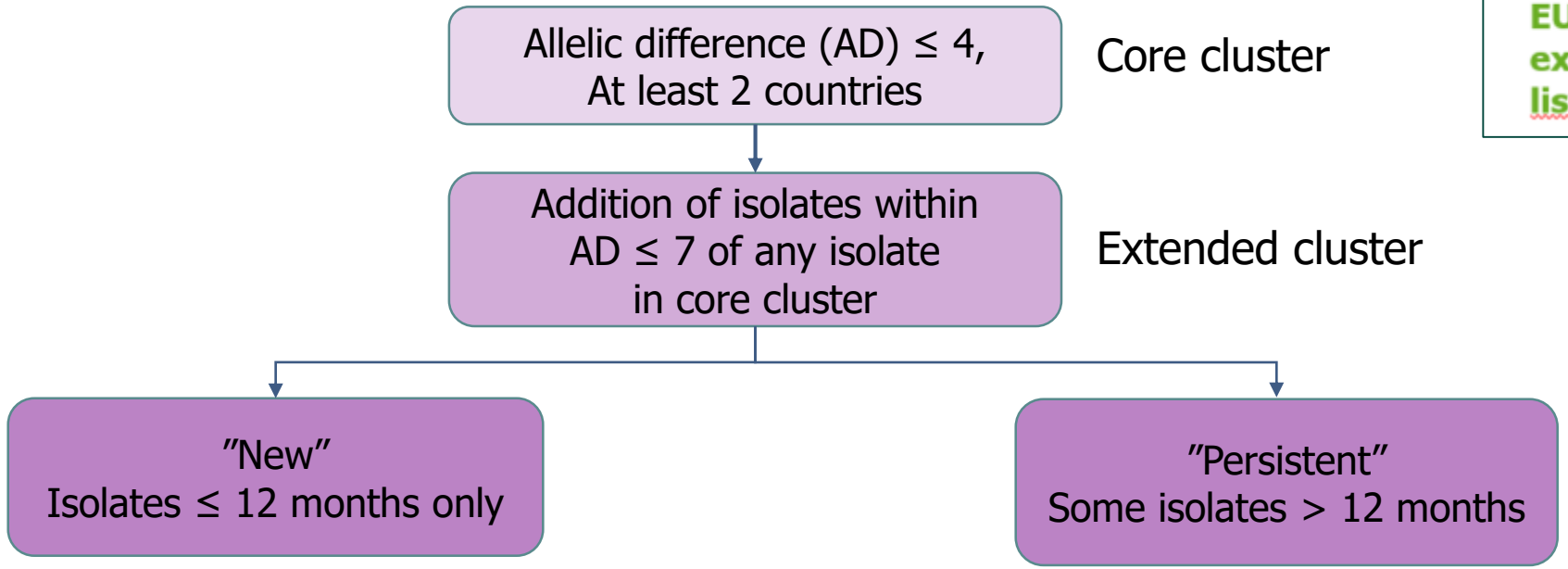
*As of September 2020

Implementing WGS for surveillance of listeriosis

Objective:

Early detection and **delineation** of multi-country listeriosis outbreaks and/or **dispersed clusters** to trigger **outbreak investigations** and contribute to **trace back and forward** investigations so that appropriate **control measures** can be implemented in the food chain

- Real-time reporting of human *Listeria monocytogenes* (*Lm*) sequences to ECDC
- Analytical pipeline: core genome MLST (cgMLST)
- Weekly analysis for signals of a multi-country event:



ECDC TECHNICAL DOCUMENT (DRAFT for MSs consultation)

EU protocol for the use of WGS and exposure data for the surveillance of listeriosis in EU/EEA

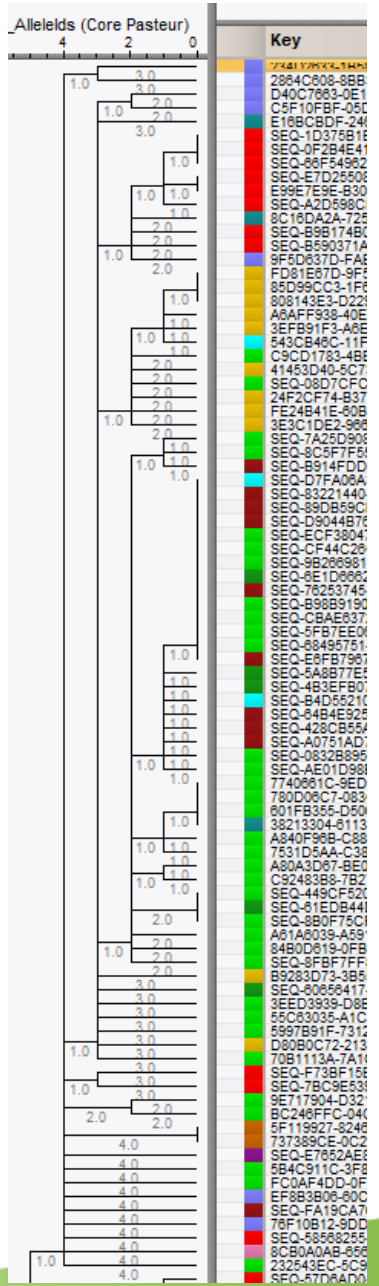
Standard questionnaire to be developed with MSs

Key statistics from listeriosis cluster detection, March 2019 – August 2020

Number of countries submitting sequences	16
Number of prospective* isolates submitted (range per country)	888 (1-452)
Number of multi-country clusters detected	30

	Core cluster (within 4 cg-AD)	Extended cluster (within 7 cg-AD)
Number of countries involved in clusters	2 (2-10)	3 (2-14)
Median number of isolates (range)	4 (2-48)	4.5 (2-149)
Median duration in years (range)	4.4 (0-15.6)	
Clusters escalated to urgent inquiry	2	

*date used for statistics in March 2019 onwards



Lessons learnt from start of listeriosis WGS-enhanced surveillance

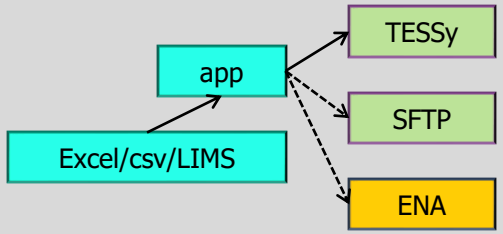
- Only few countries submitting data "in real-time" so far
  - Incentive with better visualisation tools and facilitated submissions?
  - Concerns with data sharing?
- Several WGS-confirmed genetically close strains persisting in the EU for years, even decades
  - Likely multi-source
  - Need to investigate by sub-cluster with more non-human isolate sequence data
- WGS technology has enabled seeing "the bigger picture", not only single source outbreaks
- More epidemiological data needed
- Good collaboration and timely sharing of data between public health and food safety authorities is crucial

Options for WGS data upload

ECDC WGS upload application

Features

- Can be configured to import data from databases or local files (MySQL, SQL Server, SQLite, Excel, csv)
- Configure only once, single click upload
- Can upload assemblies to TESSy and SFTP, raw reads to SFTP and ENA (configurable)
- Data sharing through SFTP and ENA

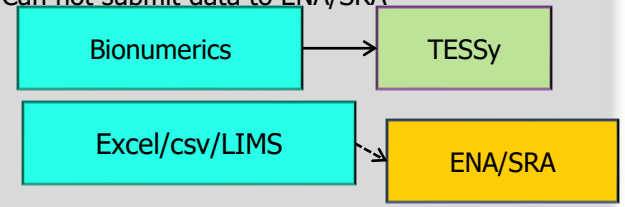


ECDC Bionumerics client plugin

Features

- Requires Bionumerics and that either ENA/SRA run accession or assemblies are stored in the Bionumerics database
- Simple upload process
- Can upload assemblies and ENA/SRA identifiers to TESSy

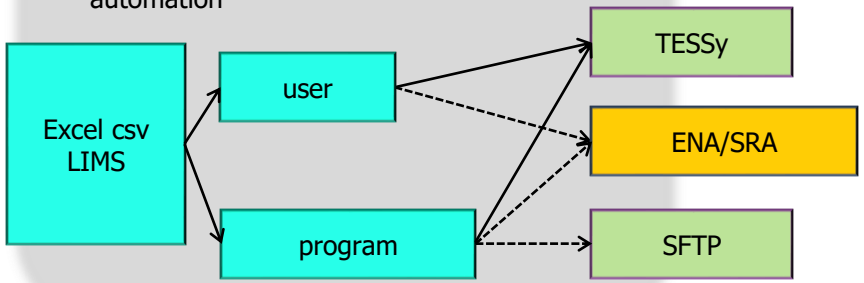
- Can not share raw reads through SFTP
- Can not submit data to ENA/SRA



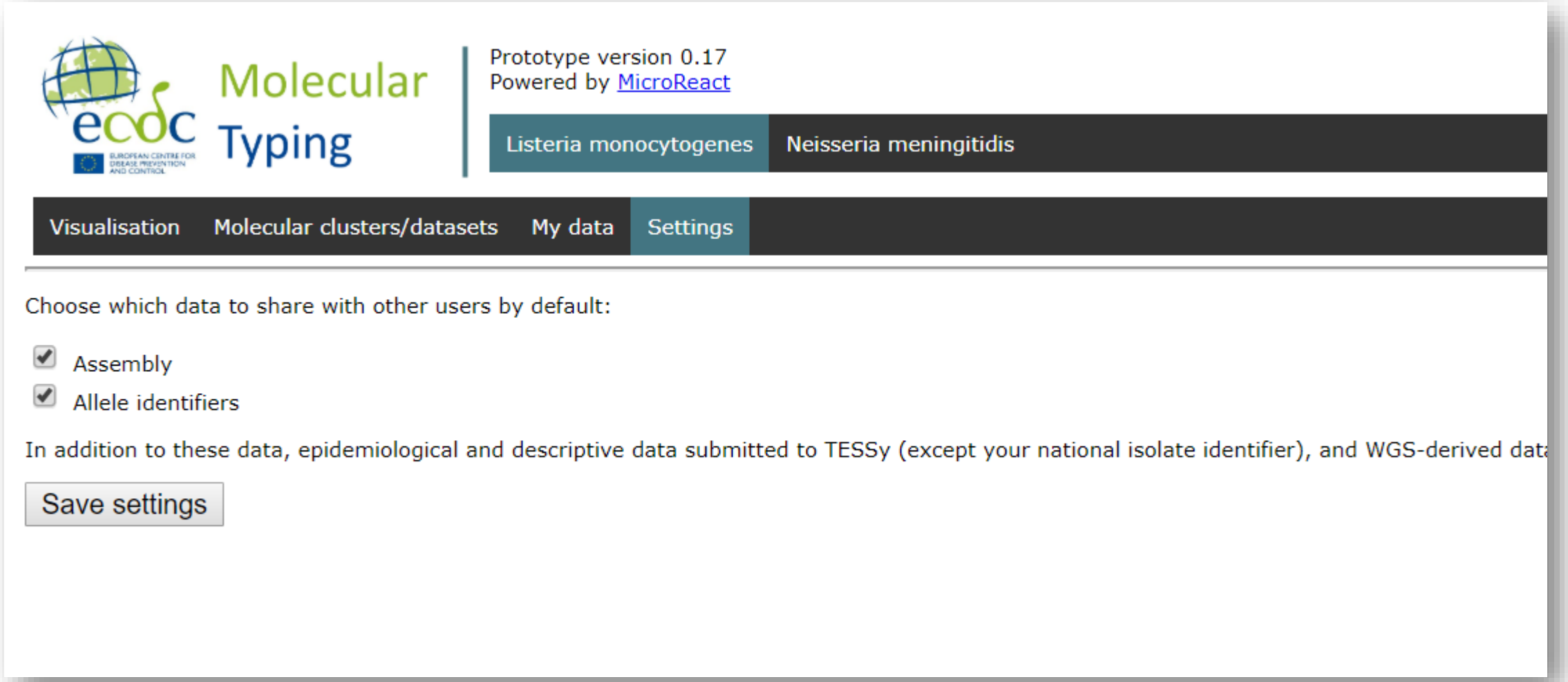
Direct TESSy submission – manual or machine-to-machine

Features

- Can upload assemblies and ENA/SRA identifiers to TESSy
- Manual upload is easy to set up but involves recurring manual work
- Machine-to-machine upload requires development but enables high levels of automation



User-defined sharing principles



Way forward

- Currently main focus on COVID-19 pandemic/SARS-CoV-2 sequencing
- Continue implementation of WGS for diseases previously postponed by pandemic
- Interoperable WGS analyses with EFSA for joint FWD investigations
- Listeriosis data collection and cross-sectoral collaboration

Thank you