

Integrating genomic data into surveillance and multi-country outbreak investigations: EU strategy implementation

Marc Struelens, Vicky Lefevre, ECDC 9th Seminar of National Reference Centres, Paris, 15 November 2019

MEETING REPORTS

Molecular epidemiology of human pathogens: how to translate breakthroughs into public health practice, Stockholm, November 2011

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MEETING REPORT

ECDC technical consultation on harnessing genomics for epidemiological surveillance

Paris, 1-2 October 2013

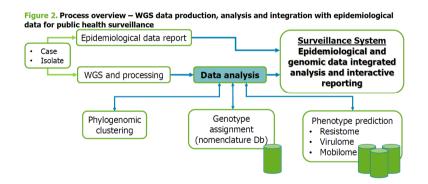


Whole Genome Sequencing: ECDC Vision 2020



- 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

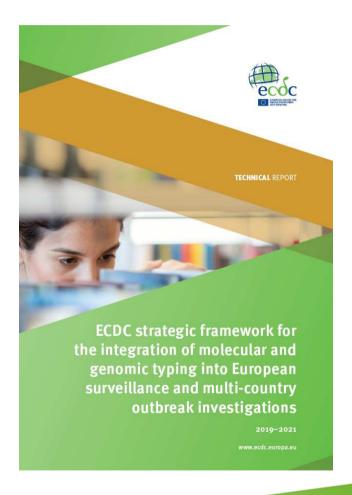




Whole Genome Sequencing: Strategic framework 2021



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



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



- 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

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

WGS capacity in public health reference laboratories **EU-EEA NMFP surveys**, 2015-2017



Objectives

- Monitor national arrangements and capacities for WGS use
- Inform the implementation of ECDC genomic surveillance roadmap
- Identify the areas where ECDC can foster capacity

Scope

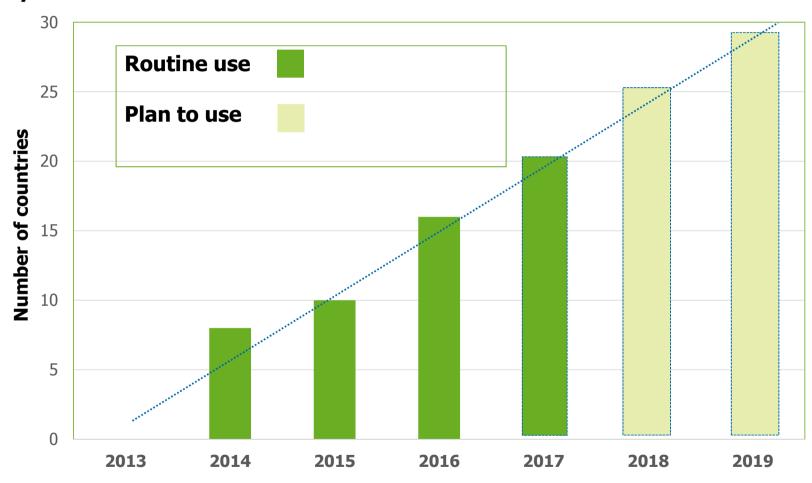
- Planned/actual use of WGS for national surveillance and outbreak investigations
- NGS platforms and bioinformatics pipelines

Methods

 Online surveys by the National Microbiology Focal Points on national reference laboratories routine use in 2015, 2016 and 2017

WGS-based typing used for national surveillance, EU/EEA, 2013-2019

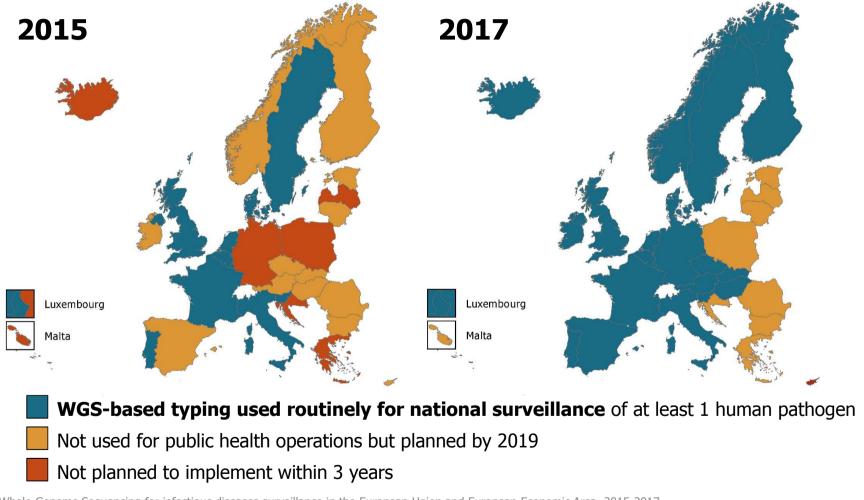




Source: ECDC NMFP surveys 2013-17 (n=30 EU/EEA countries).

Expansion of WGS-based typing use in national public health reference laboratories





Monitoring use of Whole-Genome Sequencing for infectious diseases surveillance in the European Union and European Economic Area, 2015-2017. Stockholm: ECDC; 2018

Public health genomics workshop, 23-24 October 2019



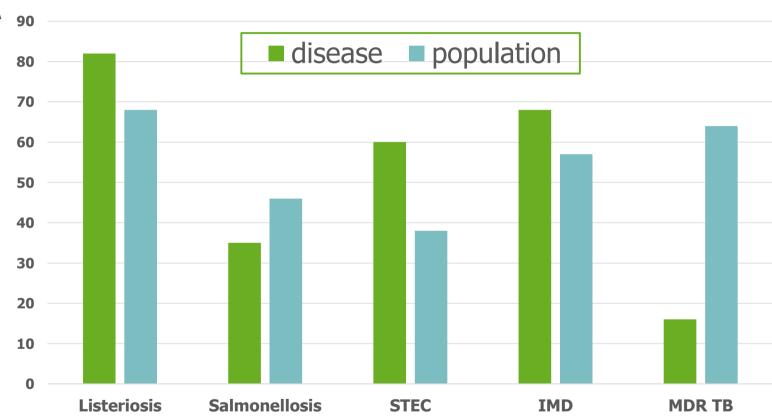
- Topics:
 - Basic concepts and methods of public health genomics
 - Integrated analysis and visualisation of WGS and epidemiological data
 - Multidisciplinary interpretation of results to inform disease control
- 20 participants from 12 countries: Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Germany, Greece, Latvia, Lithuania, Malta, Poland and Romania



EU coverage of genomic surveillance, 2017







WGS typing: EU Strategic priorities 2021, by objective



Outbreak investigation

Any epidemic pathogen/MDR outbreak

Continuous real-time surveillance

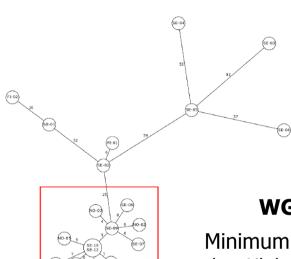
- · Listeria monocytogenes
- Neisseria meningitidis
- MDR tuberculosis
- · Salmonella enterica
- Shiga toxin E.coli
- influenza virus

Sentinel surveys

- Carbapenem/ colistin-resistant *Enterobacteriaceae*
- Antibiotic-resistant Neisseria gonorrhoeae
- Carbapenem-resistant Acinetobacter baumannii
- Bordetella pertussis
- · Streptococcus pneumoniae

Multi-country outbreaks of carbapenemase-producing Klebsiella pneumoniae: cooperative WGS investigations





WGS analysis

Minimum spanning tree showing the *Klebsiella pneumoniae* ST392 isolates from 2015-2018 analysed using SNPs (Public Health Agency of Sweden). The red box indicates the current outbreak cluster including 13 Swedish and Norwegian cases. Isolates (top right) are epidemiologically unrelated control isolates of *K. pneumoni*ae ST392.





RAPID RISK ASSESSMENT

Carbapenemase-producing (OXA-48)

Klebsiella pneumoniae ST392 in travellers
previously hospitalised in Gran Canaria, Spain

10 July 2018





RAPID RISK ASSESSMENT

Outbreak of carbapenemase-producing (NDM-1 and OXA-48) and colistin-resistant *Klebsiella pneumoniae* ST307, north-east Germany, 2019

28 October 2019

European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net)



Networks and partnerships



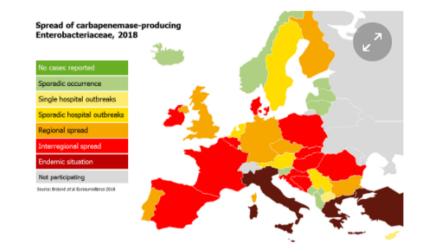






The European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) is a network for genomic-based surveillance of multidrug-resistant bacteria of public health importance, coordinated by the European Centre for Disease Prevention and Control (ECDC). National reference laboratories or equivalent laboratories of 37 European countries currently participate in EURGen-Net.

The public health objectives of this European whole genome sequencing (WGS)-based surveillance are to



determine the geographic distribution and population dynamics of multidrug-resistant clones and transmissible resistance elements to inform risk assessment, prevention and control polices and to support countries in developing technical capability and proficiency for genomic-based surveillance of multidrug-resistant bacteria with epidemic potential.



27 October

Print



Multi-country Salmonella outbreak



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

EU Multi-country Foodborne outbreaks

f 12 😏 in 🖂

E. coli cucumber scare: Spain angry at German claims



① 31 May 2011 P

EHEC 0104:H4 Outbreak in Germany, 2011



Swedes get hepatitis A from eating infected frozen strawberries

Lactalis to withdraw 12m boxes of baby France

EFSA and ECDC rep egg, sesame seed \$

More detail has emerged about two pas in Europe.

Poland and the other by a previously un imported sesame seeds.

milk in salmonella scandal 'Most outbreaks remain undetected': How Emmanuel Besnier, chief executive of French dairy { the EU is strengthening listeriosis products from contaminated factory will be recalled surveillance

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



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

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

By Joe Whitworth on September 26, 2018

The head of a French dairy giant at the centre of an ir One was caused by Salmonella Enteritiscandal has promised to withdraw 12m boxes of power the supermarket shelves of 83 countries.



efsam Joint Molecular Typing for Enhanced Surveillance



STEC 0104:H4 outbreak

EC vision on molecular typing support for outbreak preparedness Collaboration agreement: ECDC-EFSA- EURLs for Listeria monocytogenes, Salmonella and VTEC => PFGE and MLVA

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

First non-human isolate submitted to the joint database (PFGE)

2018

First joint cluster detections PFGE and MLVA

2019

2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017

ECDC pilot molecular typing data collection PFGE and MLVA

Pilot study WGS Listeria

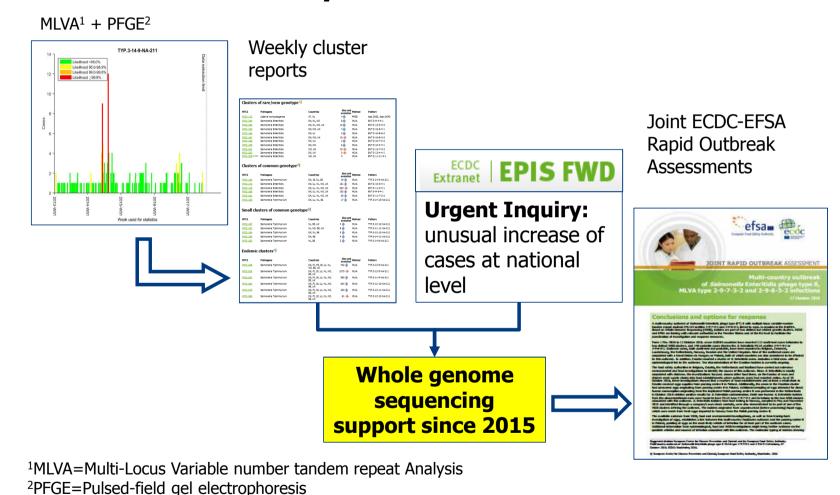
1st WGS support to multi-country outbreak investigation

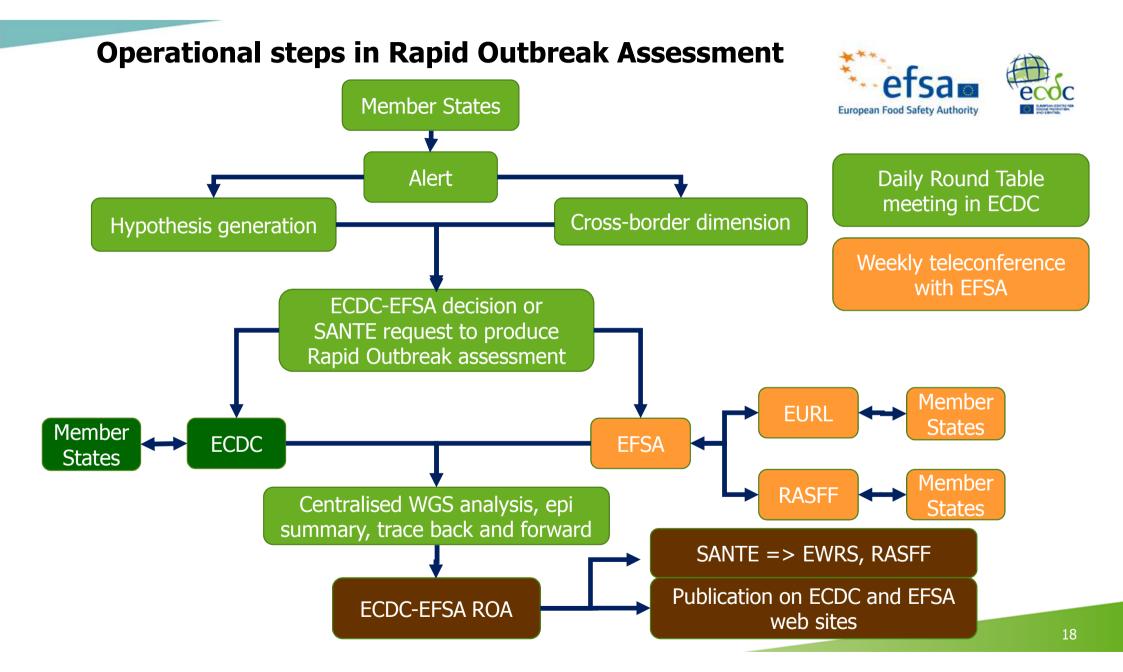
EU-wide validation study Listeria WGS Upgrade Tessy database WGS



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





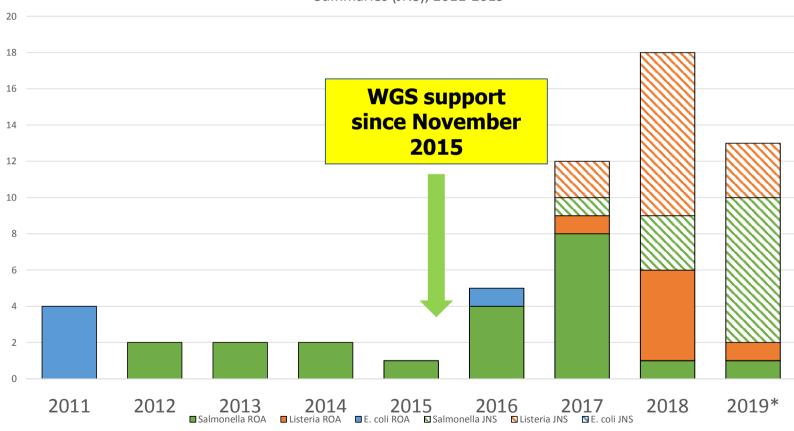




ECDC-EFSA multi-country outbreak assessments and notifications for foodborne diseases, 2011 – 2019



ECDC-EFSA FWD multi-country Rapid Outbreak Assessments (ROA) and Joint Notification Summaries (JNS), 2011-2019









RAPID RISK ASSESSMENT

Multi-country outbreak of *Listeria monocytogenes* PCR serogroup IVb, MLST ST6

6 December 201





JOINT ECDC-EFSA RAPID OUTBREAK ASSESSMENT

Multi-country outbreak of *Listeria monocytogenes* serogroup IVb, multi-locus sequence type 6, infections probably linked to frozen corn 22 March 2018







JOINT ECDC-EFSA RAPID OUTBREAK ASSESSMENT

Multi-country outbreak of *Listeria monocytogenes* serogroup IVb, multi-locus sequence type 6, infections linked to frozen corn and possibly to other frozen vegetables – first update

3 July 2018

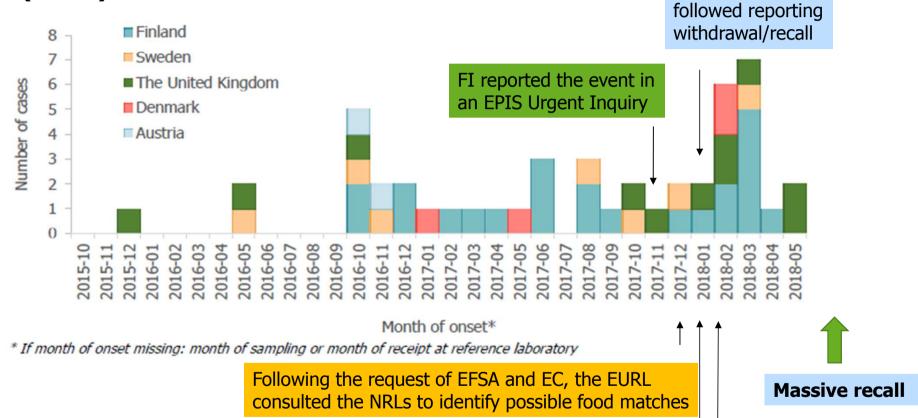


Listeria monocytogenes IVb, ST 6 confirmed outbreak cases by month of symptom onset*, EU 2015–2018 (N=47)



RASFF alert FI,

other countries



Some countries reported food matches related to frozen vegetable mix and frozen corn

Interviews of patients confirmed exposure to frozen corn.

Press Release



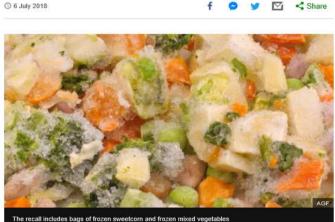
pased plant, produced between 13 August

Greenyard takes recall initiative for frozen vegetables from Hungary

Sint-Katelijne-Waver, Belgium, 4 July 2018 - Greenyard (Euronext Brussels: GREEN) takes recall initiative for frozen vegetables from Hungary due to potential listeria contamination

In line with a decision passed by the Hungarian Food Safety Agency dated 29 June 2018,

Supermarkets recall frozen vegetables over listeria fears



Supermarkets have recalled bags of frozen vegetables over fears they could contain a deadly bacteria.

The 43 sweetcorn-based products have been withdrawn by major supermarket supplier Greenyard Frozen UK.



Recall costs Greenyard 30 million

The recall of frozen veg by Greenyard is estimated to be costing 30 million euro. Greenyard is recalling its products ; headlines earlier in the year, while also revealing that it was ready to they might be infected with listeria.

Greenyard stock plummets 30 % at market opening

Monday, 16 July 2018 16:23







The share price of Greenyard, the Belgian vegetable supplier, fell by as much as 30 percent when the stock market opened today.



Thursday 13th September 2018, 14:23 London











Greenyard finds Listeria 'root cause'

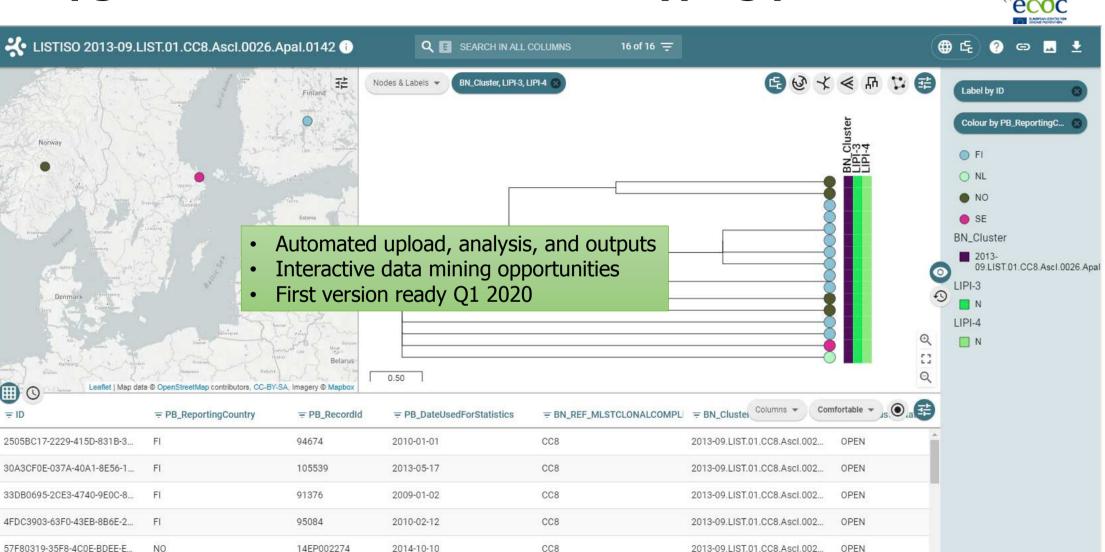
Following an extensive review of its Hungarian facility, Greenyard says it is ready to restart production

lobal fruit and vegetable giant Greenyard has announced that it has found the root cause of the Listeria outbreak that hit the restart production at the affected facility in Baja, Hungary.

In July, Greenyard reported on the recall of frozen products that were produced by its Hungarian production facility in Baja between 13 August 2016 and 20 June 2018, and on the ongoing investigations into an outbreak of Listeria monocytogenes between 2015 and 2018.



Upgrade of the ECDC molecular typing platform



User defined sharing principles





Choose which data to share with other users by default:

Assembly

Allele identifiers

In addition to these data, epidemiological and descriptive data submitted to TESSy (except your national isolate identifier), and WGS-derived data

Save settings

My data





Prototype version 0.17 Powered by <u>MicroReact</u>

Listeria monocytogenes

Neisseria meningitidis

Listeria monocytogenes isolates

Visualisation

Molecular clusters/datasets

My data

Settings

These table shows your uploaded data, you can choose to share or not share individual isolates with other users.

Save settings

Column visibility Copy CSV Show 100 ▼ entries

Country 🔷	BatchId 🔷	RecordI d, link to 7 AD ma tches	ECDC Id 🔻	Created date	Modified date	QC (PAS S/FAIL)	QC (Cont aminatio n)	QC (Core loci dete cted)
Search (Search I	Search I	Search I	Search (Search I	Search (Search (Search (
DE		LM18-04708	testUI607_2	2019-10-24 16:29:48	2019-10-25 09:29:46	Accepted	PASS	1747
DE		181109-18-7 861-LM18-0 4254	testUI607_1	2019-10-24 16:29:48	2019-10-25 09:29:42	Accepted	PASS	1747

Clusters



	Molecular					
BERGEFAN CENTRE FOR DEBARE PRESENTION AND CONTROL	Typing					

Prototype version 0.17 Powered by MicroReact

Listeria monocytogenes Neisseria meningitidis

Visualisation Molecular clusters/datasets My data Settings

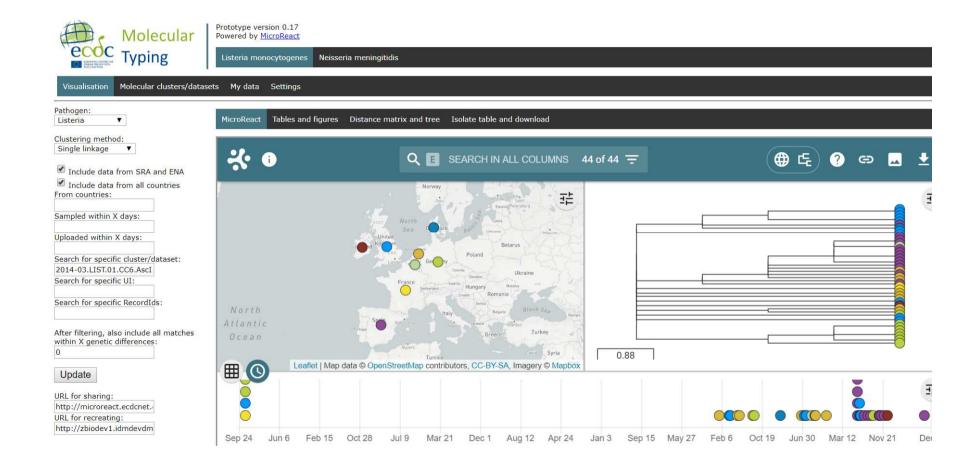
These tables shows molecular clusters detected by ECDC by applying automated algorithms, see respective surveillance protocols for details. Only multi-country clusters and clusters in your country are shown. Included are also generated datasets of particular interest.

csv Show 100 ▼ entries Search: Column visibility Listeria clusters

Cluster ID	Cluster info 🔷	Event ID 🔷	Cluster stat us	Number of isolates	Countries 🔷	Updated (7 d)	First date	Last date 🝦	Last update d	Extended cl uster	Genetic bac kground
Search Clu:	Search Clu:	Search Eve	Search Clu:	Search Nur	Search Cou	Search Upc	Search Firs	Search Las	Search Last	Search Ext	Search Ger
2014-03.LIST.0 1.CC6.AscI.000 2.ApaI.0064		<u>UI509 - cluster</u> 2	OPEN	37	ES(13), BE(1), NL(8), UK(4), I E(1), DK(1), DE (8), FR(1)	ES(13), BE(1), NL(8), UK(4), I E(1), DK(1), DE (8), FR(1)	2009-12-30	2018-08-26	2019-11-04	2014-03.LIST.0 1.CC6.AscI.000 2.ApaI.0064 +7 AD	2014-03.LIST.0 1.CC6.AscI.000 2.ApaI.0064 +5 0AD
2014-05.LIST.0 9.CC6.AscI.000 2.ApaI.0393			OPEN	2	FI(2)	FI(2)	2010-09-05	2011-06-23	2019-11-04	2014-05.LIST.0 9.CC6.AscI.000 2.ApaI.0393 +7 AD	2014-05.LIST.0 9.CC6.AscI.000 2.ApaI.0393 +5 0AD
2015-04.LIST.0 4.CC6.AscI.000 2.ApaI.0072		UI583 test	OPEN	43	NL(31), BE(3), DE(1), (5), FR (0), DK(2)	NL(31), BE(3), DE(1), FR(0), D K(2)	2003-04-09	2015-03-26	2019-11-04	2015-04.LIST.0 4.CC6.AscI.000 2.ApaI.0072 +7 AD	2015-04.LIST.0 4.CC6.AscI.000 2.ApaI.0072 +5 0AD
2016-11.LIST.0 1		<u>UI452</u>	OPEN	25	DK(9), SE(4), E E(9), FI(2), FR (1)		2014-07-23	2019-02-18	2019-10-23	2016-11.LIST.0 1 +7AD	2016-11.LIST.0 1 +50AD

Visualisation





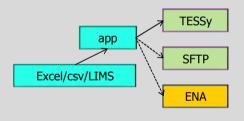
Options for WGS data upload



ECDC WGS upload application

Features

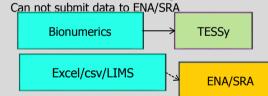
- Can be configured to import data from databases or local files (MySQL, SQL Server, SQLite, Excel, csv)
- Configure only once, single click upload
- Can upload assemblies to TESSy and SFTP, raw reads to SFTP and ENA (configurable)
- Data sharing through SFTP and ENA



ECDC Bionumerics client plugin

Features

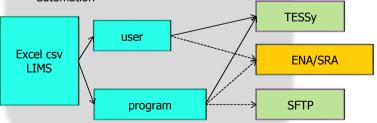
- Requires Bionumerics and that either ENA/SRA run accession or assemblies are stored in the Bionumerics database
- Simple upload process
- Can upload assemblies and ENA/SRA identifiers to TESSy
- Can not share raw reads through SFTP



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



Data sharing principles



- WGS data and minimal epidemiological data are shared with ECDC, either privately using SFTP or publically using ENA/SRA.
- Full epidemiological data together with a representative genome are shared between affected member states through the EPIS platform during outbreak investigations.
- Sequence data and epidemiological data are privately shared between ECDC, EFSA and EURLs for outbreaks that involve food or animal sources.
- The main ECDC outputs from outbreak investigations are Rapid Risk Assessments (public) and Joint Notification Summaries to the European Commission (non-public).
- ECDC encourages and can assist with release of at least one raw reads genome to be released in the public domain when a Rapid Risk Assessment is released.

ECDC WGS Strategic Framework: Acknowledgements



Draft: Eeva Broberg, Joana Revez, Erik Alm, Ivo Van Walle, Daniel Palm and Marc Struelens.

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THANK YOU