Data sharing, events, clusters and cut-offs

Cecilia Jernberg, FWD AMR RefLabCap 3rd multidisciplinary training workshop,
28 June 2024

- Briefly touch upon **data sharing** and **reporting** mechanisms to the ECDC and between member states.

- Explore the **functionalities of EpiPulse**, a platform for epidemiological and genomic data sharing and visualization, and its significance in EU-level surveillance efforts.
- Automatic cluster detection, cluster cut-offs in the MTT

- Dissect and discuss an event cluster of *Campylobacter* !

EU legal framework for molecular pathogen data sharing

ECDC is mandated to collect ‘pathogen data, including at molecular level, if required for epidemiological surveillance and for detecting or investigating serious cross-border threats to health.

Link: *EUR-Lex - 32022R2370 - EN - EUR-Lex (europa.eu)*

The National competent Authorities shall communicate, to the ECDC, the Commission and to participating authorities within the disease networks, molecular pathogen data based on agreed indicators and standards, if required for detecting or investigating serious cross-border threats to health.

Link: *Regulation (EU) 2022/2371 on serious cross-border threats to health*

Support to EU/EEA countries to capacity build for genomic surveillance to strengthen public health surveillance, nationally -> EU level

- EC HERA sequencing and bioinformatics capacity building grants
- GenEpiBioTrain (ECDC, FWD wave Institut Pastuer)
- Sequencing support projects – *Salmonella* and *Campylobacter* AMR sequencing capacity building project (ECDC)
- Sequencing support for events and outbreaks (ECDC)
- FWD AMR-RefLabCap (SSI, HaDEA)

- Development of EpiPulse Molecular Typing Tool – analysis and visualisation of your data

Objectives for the *Salmonella* and *Campylobacter* AMR sequencing support project – 10 countries participating

- Learn how to submit WGS data to TESSy using your own data, receive bioinformatics support and get acquainted with the EpiPulse Molecular Typing tool
- With the results from EpiPulse Molecular Typing tool, the country can
  - get an overview of the resistance situation in their country
  - matches with isolates from other countries
- Use the data for national genomic surveillance
- Still lacking data from some participants! Contact ECDC for support - upload on your behalf? The project need to be summarised.

ECDC's vision for EU-level FWD AMR surveillance

- WGS should be the method for EU level *Salmonella* and *Campylobacter* AMR surveillance
- All countries are reporting a representative subset of *Campylobacter* and *Salmonella* isolates with sequencing data each year

- Transition period, report both phenotypic and genotypic data for the same isolates for validation, when possible

EpiPulse

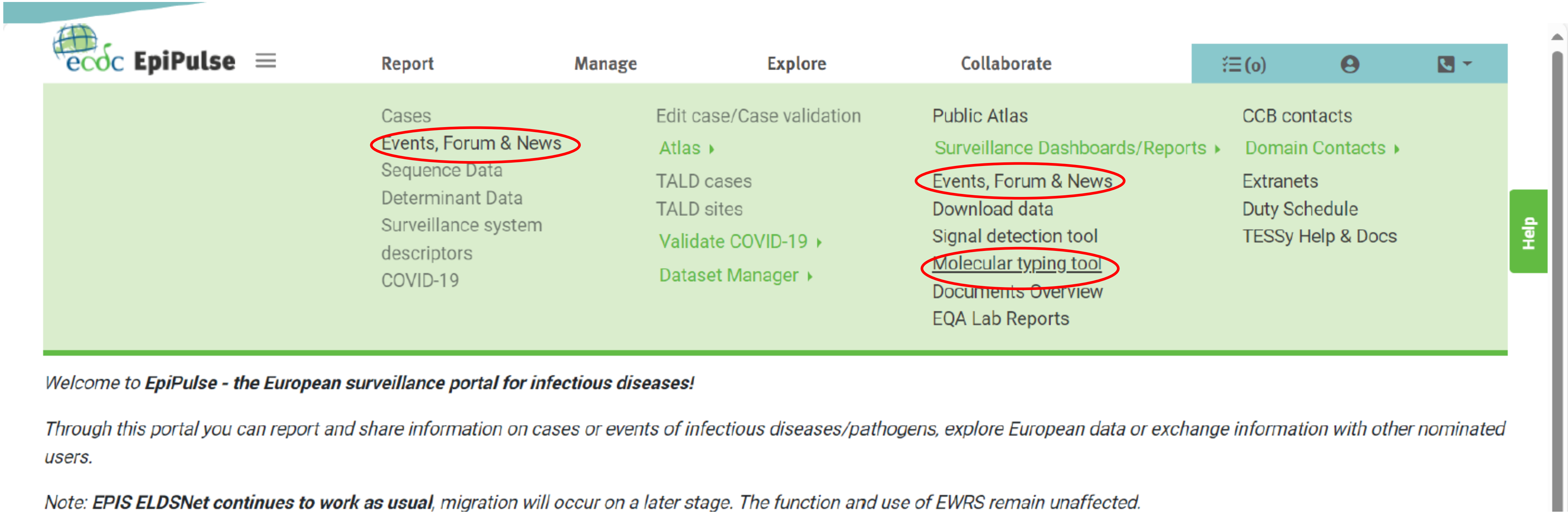
Epipulse - The ECDC platform for nominated users

Events, Forum & News

Notification and discussion platform

Molecular Typing Tool

A tool for visualising WGS based results integrated with epidemiological data



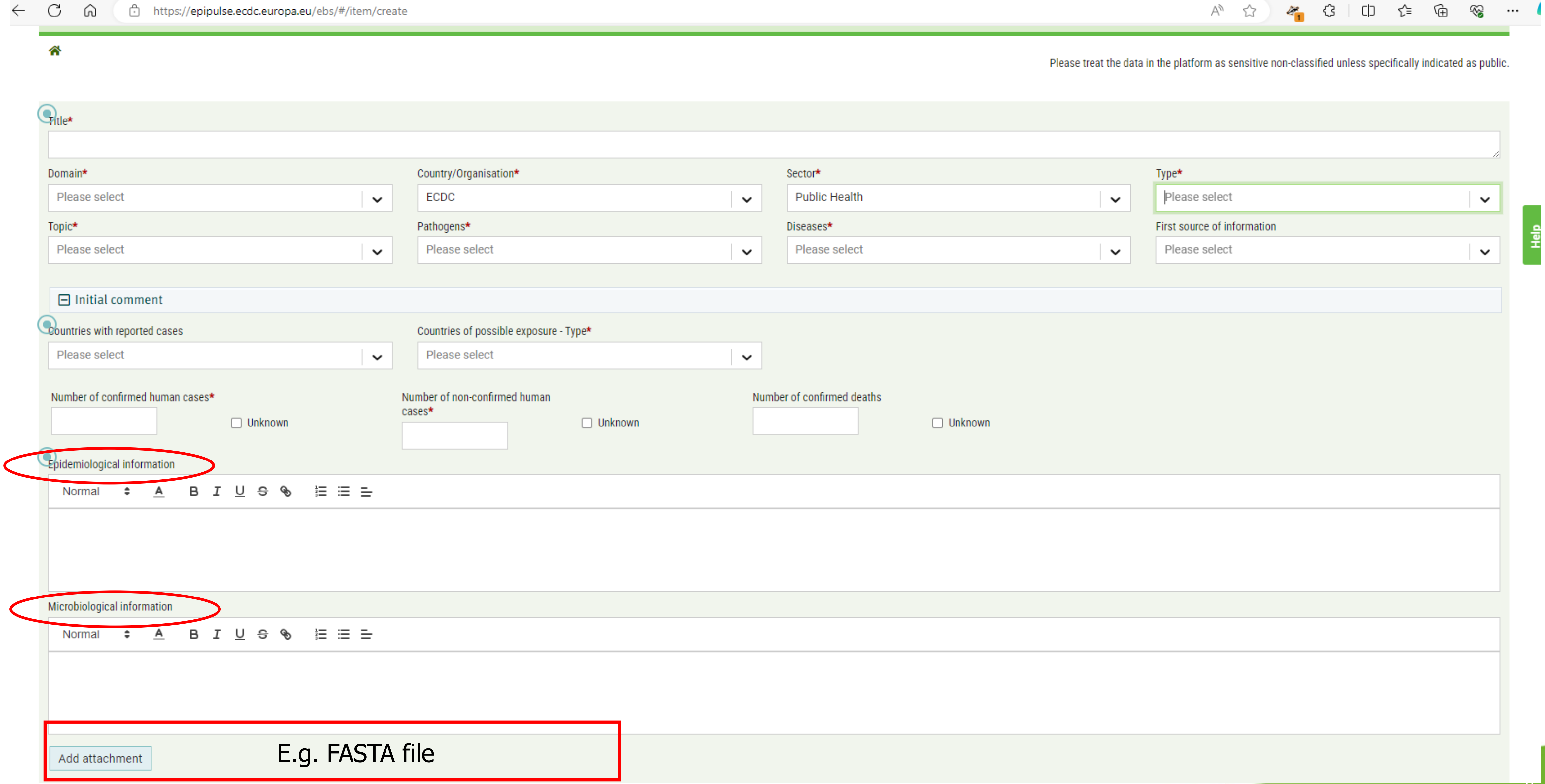
EpiPulse
Report
Manage
Explore
Collaborate
Cases
Events, Forum & News
Sequence Data
Determinant Data
Surveillance system descriptors
COVID-19
Edit case/Case validation
Atlas
TALD cases
TALD sites
Validate COVID-19
Dataset Manager
Public Atlas
Surveillance Dashboards/Reports
Events, Forum & News
Download data
Signal detection tool
Molecular typing tool
Documents Overview
EQA Lab Reports
CCB contacts
Domain Contacts
Extranets
Duty Schedule
TESSy Help & Docs
Help

*Welcome to **EpiPulse - the European surveillance portal for infectious diseases!***

Through this portal you can report and share information on cases or events of infectious diseases/pathogens, explore European data or exchange information with other nominated users.

*Note: **EPIS ELDSNet continues to work as usual**, migration will occur on a later stage. The function and use of EWRS remain unaffected.*

Report an event in EpiPulse



https://epipulse.ecdc.europa.eu/ebs/#/item/create

Please treat the data in the platform as sensitive non-classified unless specifically indicated as public.

Title*

Domain*: Please select

Country/Organisation*: ECDC

Sector*: Public Health

Type*: Please select

Topic*: Please select

Pathogens*: Please select

Diseases*: Please select

First source of information: Please select

Initial comment

Countries with reported cases: Please select

Countries of possible exposure - Type*: Please select

Number of confirmed human cases* ☐ Unknown

Number of non-confirmed human cases* ☐ Unknown

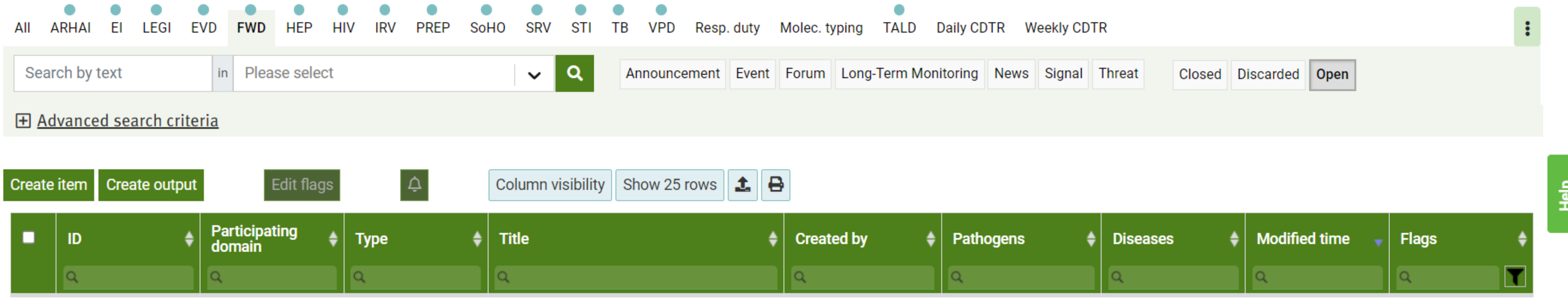
Number of confirmed deaths ☐ Unknown

Epidemiological information

Microbiological information

Add attachment

E.g. FASTA file


All
ARHAI
EI
LEGI
EVD
FWD
HEP
HIV
IRV
PREP
SoHO
SRV
STI
TB
VPD
Resp. duty
Molec. typing
TALD
Daily CDTR
Weekly CDTR
Search by text
in
Please select
Announcement
Event
Forum
Long-Term Monitoring
News
Signal
Threat
Closed
Discarded
Open
Advanced search criteria
Create item
Create output
Edit flags
Column visibility
Show 25 rows
ID
Participating domain
Type
Title
Created by
Pathogens
Diseases
Modified time
Flags
Help

List of events appear here

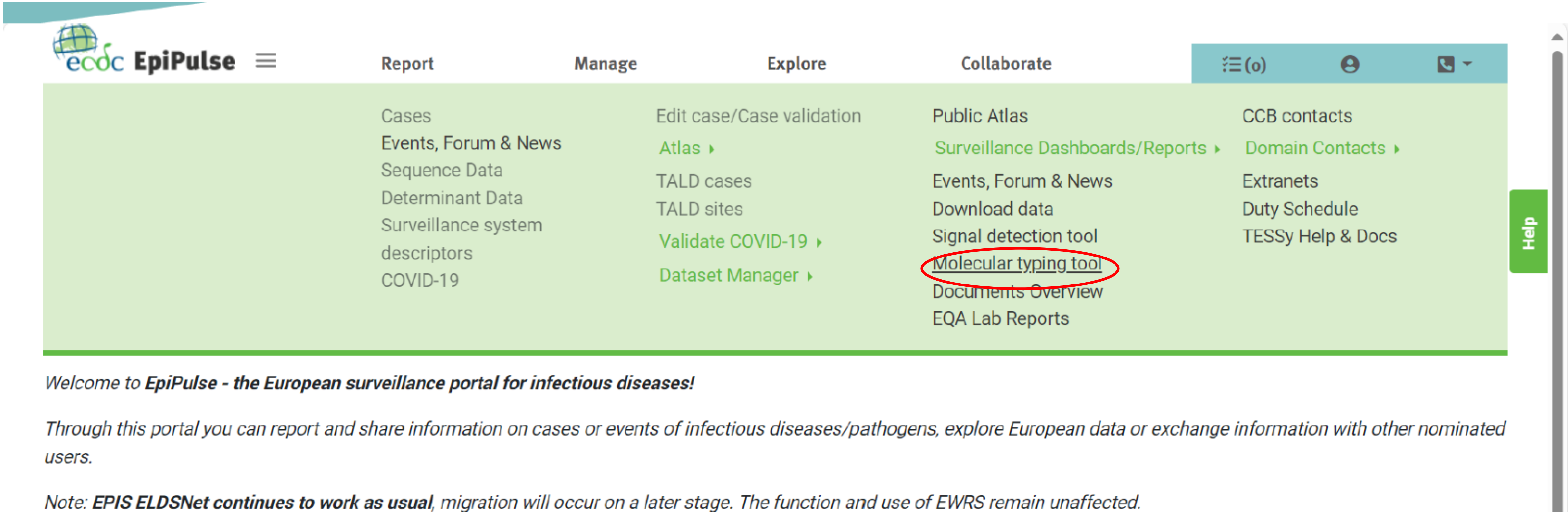
Epipulse - The ECDC platform for nominated users

Events, Forum & News

Notification and discussion platform

Molecular Typing Tool

A tool for visualising WGS based results integrated with epidemiological data


EpiPulse
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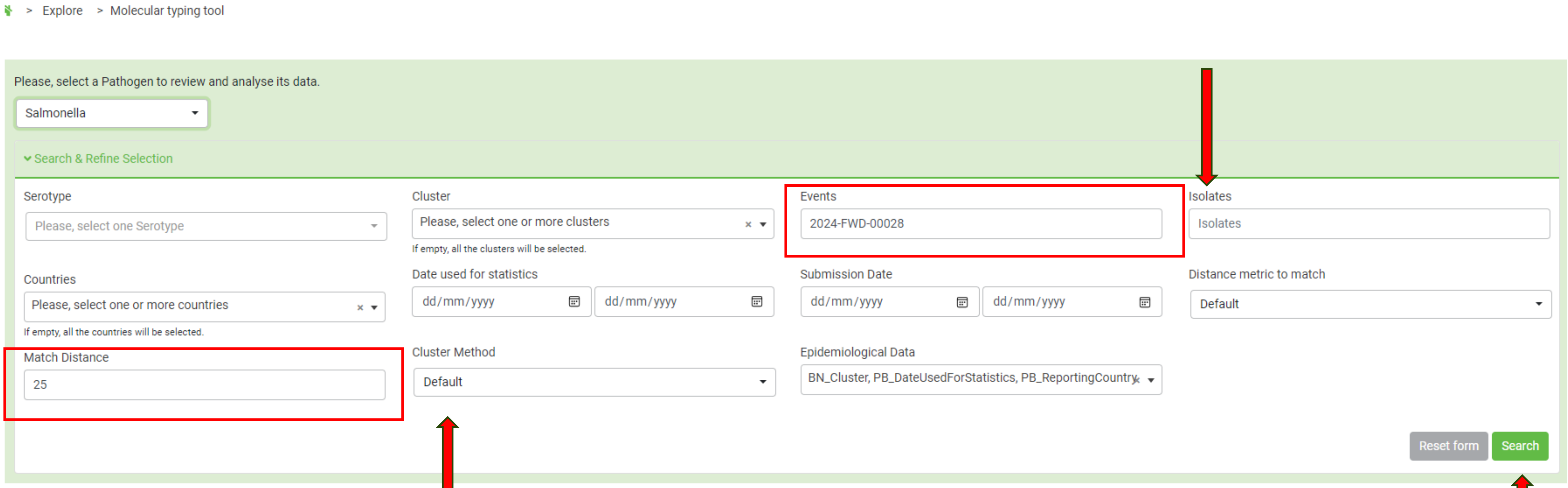
EpiPulse Molecular Typing Tool search function



> Explore > Molecular typing tool

Please, select a Pathogen to review and analyse its data.

Salmonella

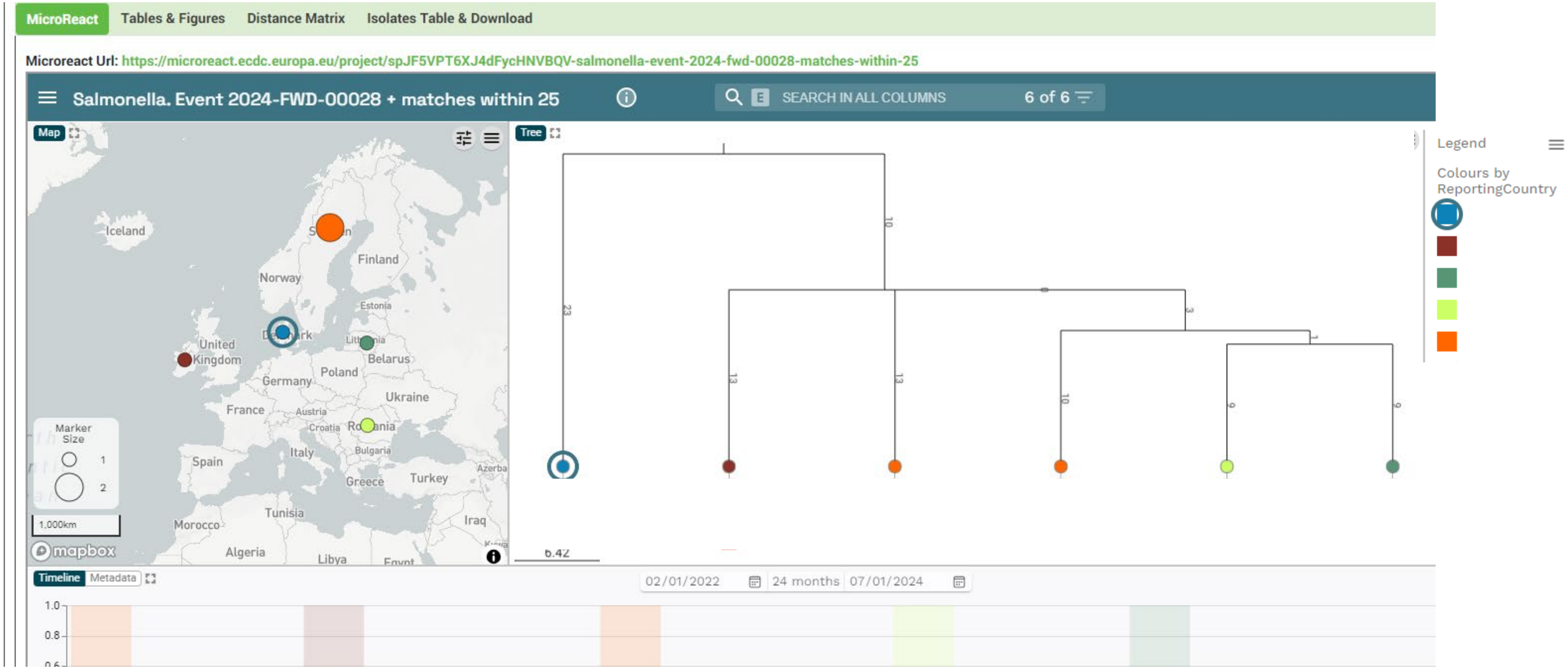
Search & Refine Selection

Serotype: Please, select one Serotype	Cluster: Please, select one or more clusters If empty, all the clusters will be selected.	Events: 2024-FWD-00028	Isolates: Isolates
Countries: Please, select one or more countries If empty, all the countries will be selected.	Date used for statistics: dd/mm/yyyy – dd/mm/yyyy	Submission Date: dd/mm/yyyy – dd/mm/yyyy	Distance metric to match: Default
Match Distance: 25	Cluster Method: Default	Epidemiological Data: BN_Cluster, PB_DateUsedForStatistics, PB_ReportingCountry	

Single linkage
Complete linkage
Neigbor joining

No matching isolates in the system.

Publicly available sequence data shared by the UK show many matching isolates



Microreact Url: https://microreact.ecdc.europa.eu/project/spJF5VPT6XJ4dFycHNVBQV-salmonella-event-2024-fwd-00028-matches-within-25

Salmonella. Event 2024-FWD-00028 + matches within 25

Legend

Colours by ReportingCountry

MicroReact
Tables & Figures
Distance Matrix
Isolates Table & Download
SEARCH IN ALL COLUMNS
6 of 6
Map
Iceland
Finland
Norway
Estonia
United Kingdom
Lithuania
Belarus
Poland
Germany
Ukraine
France
Austria
Croatia
Romania
Bulgaria
Spain
Italy
Greece
Turkey
Azerba
Tunisia
Iraq
Morocco
Algeria
Libya
Egypt
Marker Size
1
2
1,000km
mapbox
Tree
10
23
3
1
13
13
10
9
9
6.42
Timeline
Metadata
02/01/2022
24 months
07/01/2024
1.0
0.8
0.6

Access rights EpiPulse and the Molecular typing Tool

If you are working with, or soon will be working with, sharing data, information for surveillance and within events on EpiPulse you need the right access rights!

EpiPulse access rights for events forum and news etc

TESSy access rights for the EpiPulse Molecular Typing Tool

Note! Contact ECDC if you cannot access and/or do not have access rights and need support.

Relevant for epi, micro and bioinfo working hands-on with the data.

Let’s discuss cluster cut-offs

Regular automatic cluster detection of all sequences uploaded to the ECDC database

- Automatic cluster detection once a week for *Listeria* and *Salmonella*.
- Clusters including two or more human isolates are queried to EFSA database.
- Matching non-human isolates from EFSA db are integrated and visualised in the MTT

Species specific cluster criteria for automatic cluster detection on ECDC platform

- *Salmonella* spp.: core cluster within 5 AD, extended cluster 10 AD. For certain serotypes/subtypes, for example *S*. Enteritidis, a tighter core cluster could be needed for outbreak investigations. In addition, the single linkage clustering approach possibly needs to be replaced with a Neighbour joining clustering approach for endemic clones.
- *Campylobacter* spp.: core cluster within 5 AD, extended cluster 10 AD. Automatic cluster detection to come.

N.B Specific cluster cut-offs could be applied for multi country outbreak case definitions.

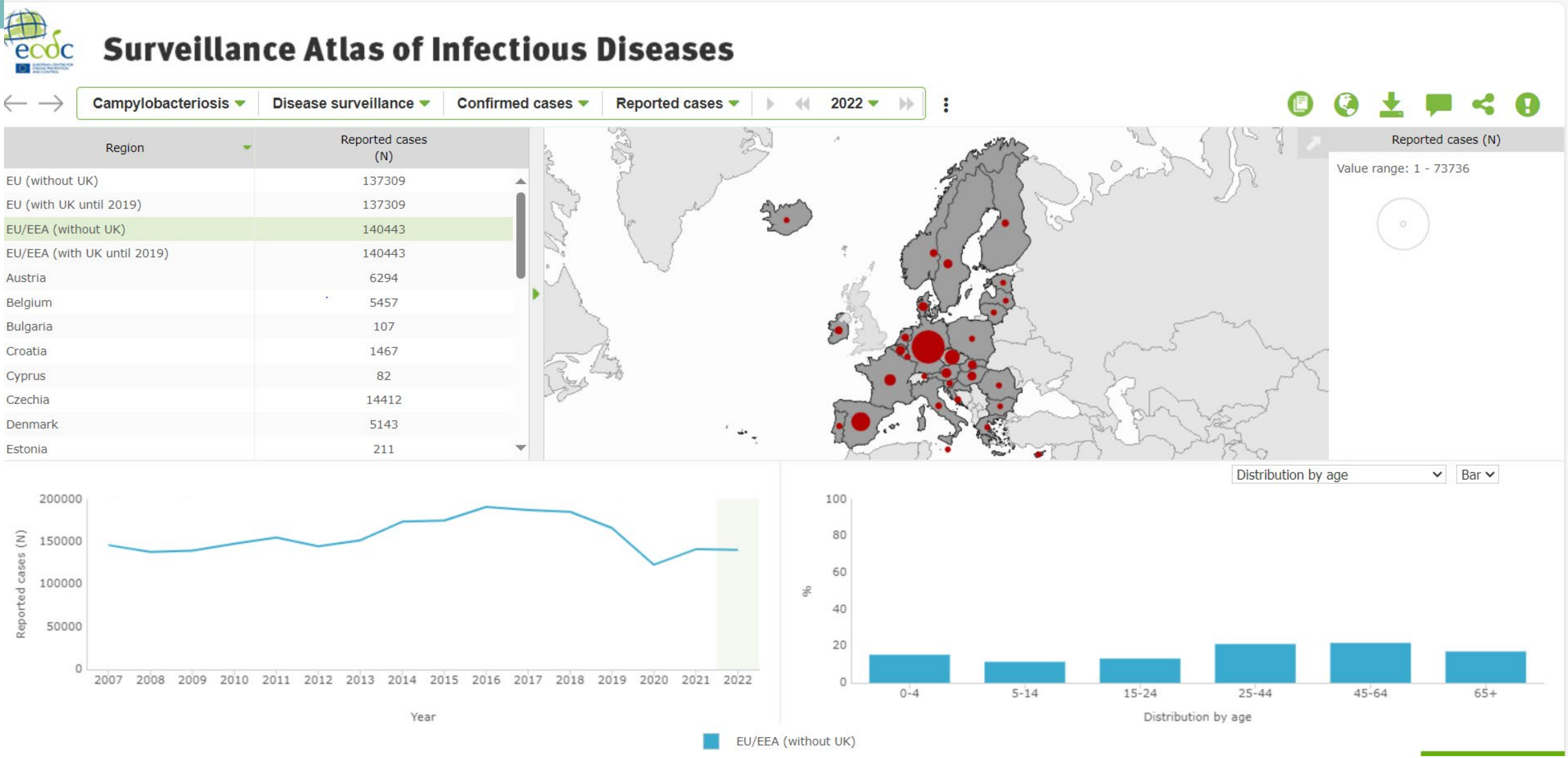
Note!

In the centralised WGS analysis (at ECDC) a wider cut-off (AD) for clusters than national criteria is expected.

WGS data from different platforms can generate some artefactual differences. EQAs have shown approximal 2 AD can be seen between the EQA participants.

Multi country Campylobacter event with a microbiological cluster in the Molecular Typing Tool

An illustration on how to interpret a cluster, questions to be asked and investigations to be made



Surveillance Atlas of Infectious Diseases

Campylobacteriosis | Disease surveillance | Confirmed cases | Reported cases | 2022

Region	Reported cases (N)
EU (without UK)	137309
EU (with UK until 2019)	137309
EU/EEA (without UK)	140443
EU/EEA (with UK until 2019)	140443
Austria	6294
Belgium	5457
Bulgaria	107
Croatia	1467
Cyprus	82
Czechia	14412
Denmark	5143
Estonia	211

Reported cases (N)

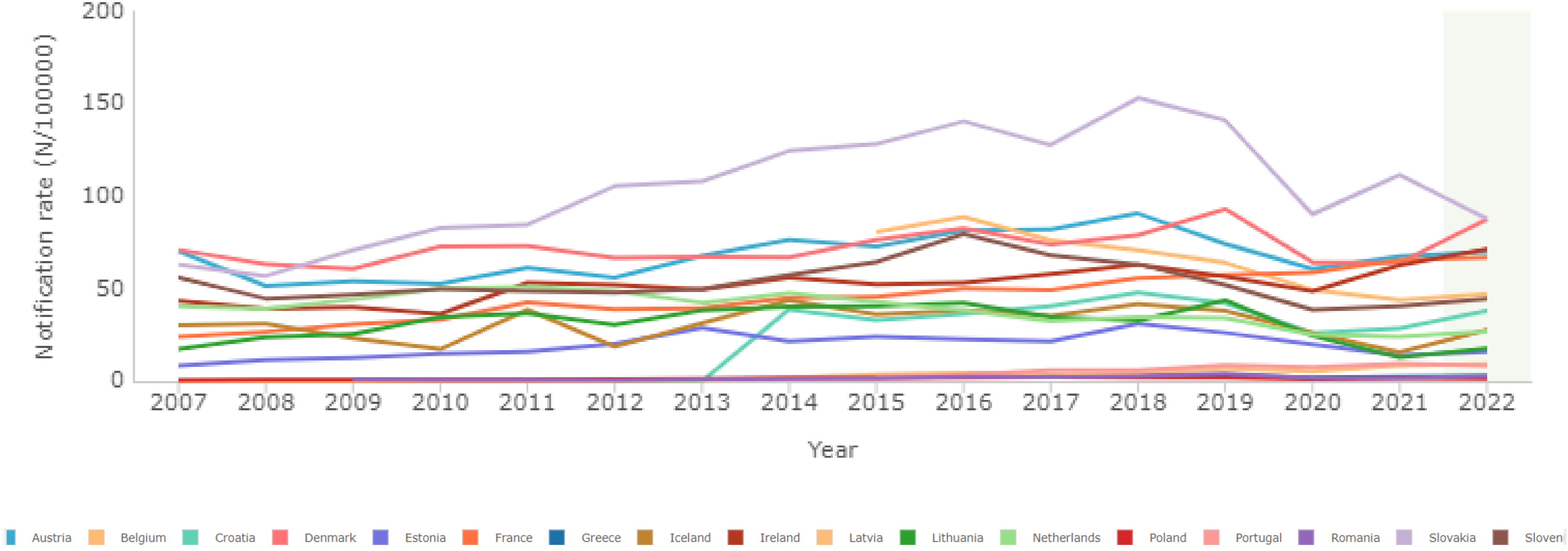
Value range: 1 - 73736

Distribution by age: Bar

200000
150000
100000
50000
0
Reported cases (N)
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
100
80
60
40
20
0
%
0-4
5-14
15-24
25-44
45-64
65+
Distribution by age
EU/EEA (without UK)

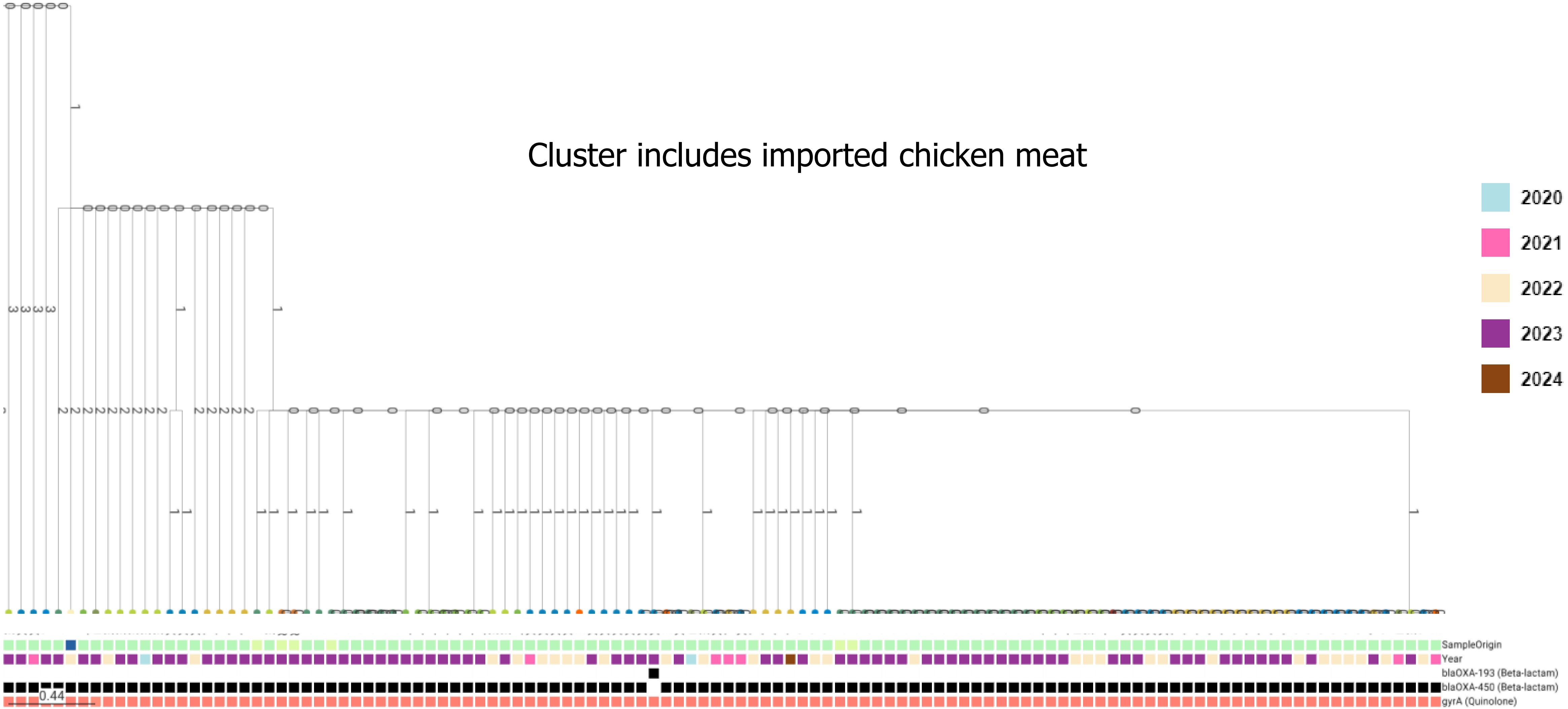
[Surveillance Atlas of Infectious Diseases (europa.eu)](https://atlas.ecdc.europa.eu)

Campylobacteriosis, 2022. Notification rate 46.93, 140 241 cases in EU/EEA notification rate (100 000 population)



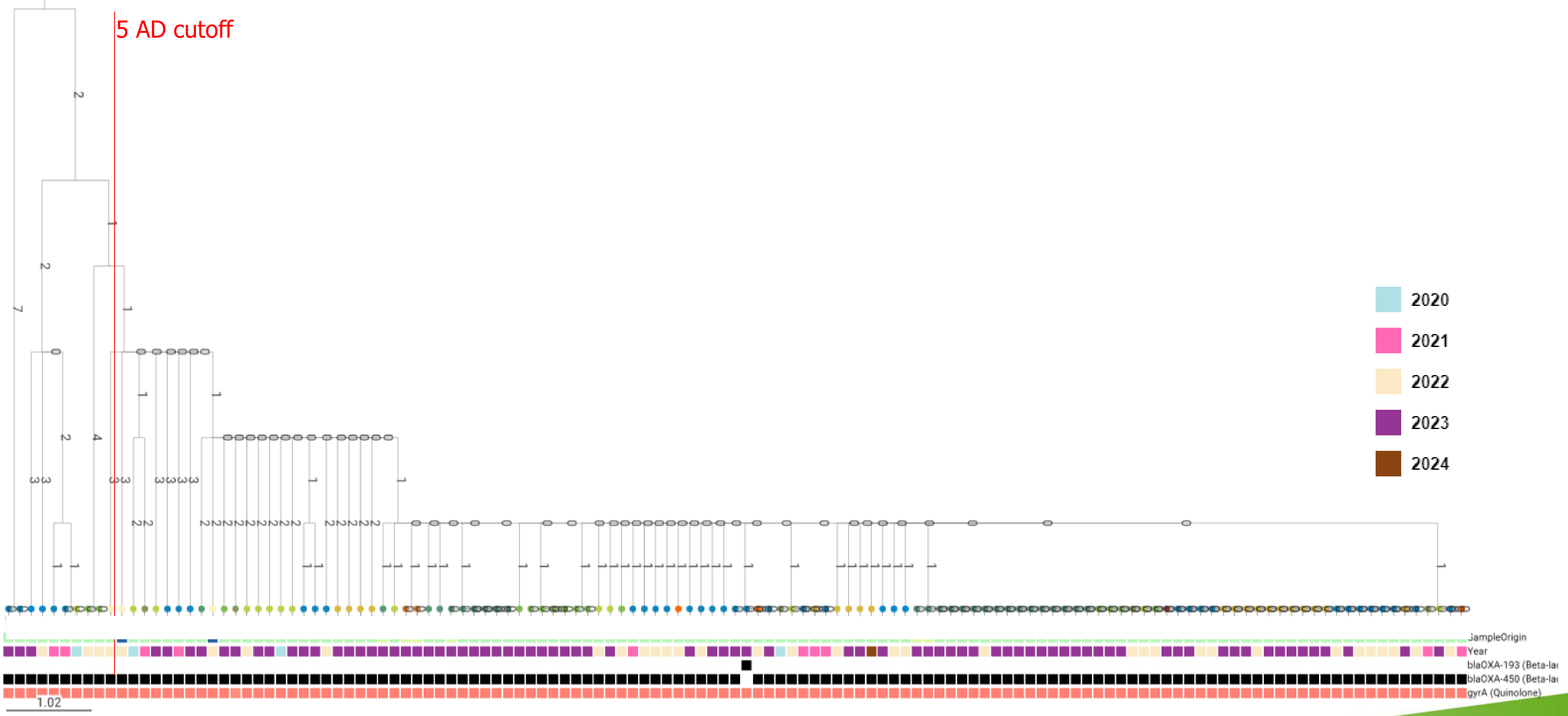
Example *Campylobacter* cluster connected to an EpiPulse event, ST-464.

5 AD, 11 countries, 120 isolates. Single linkage.



Cluster includes imported chicken meat

10 AD cut-off, 129 isolates, 11 countries

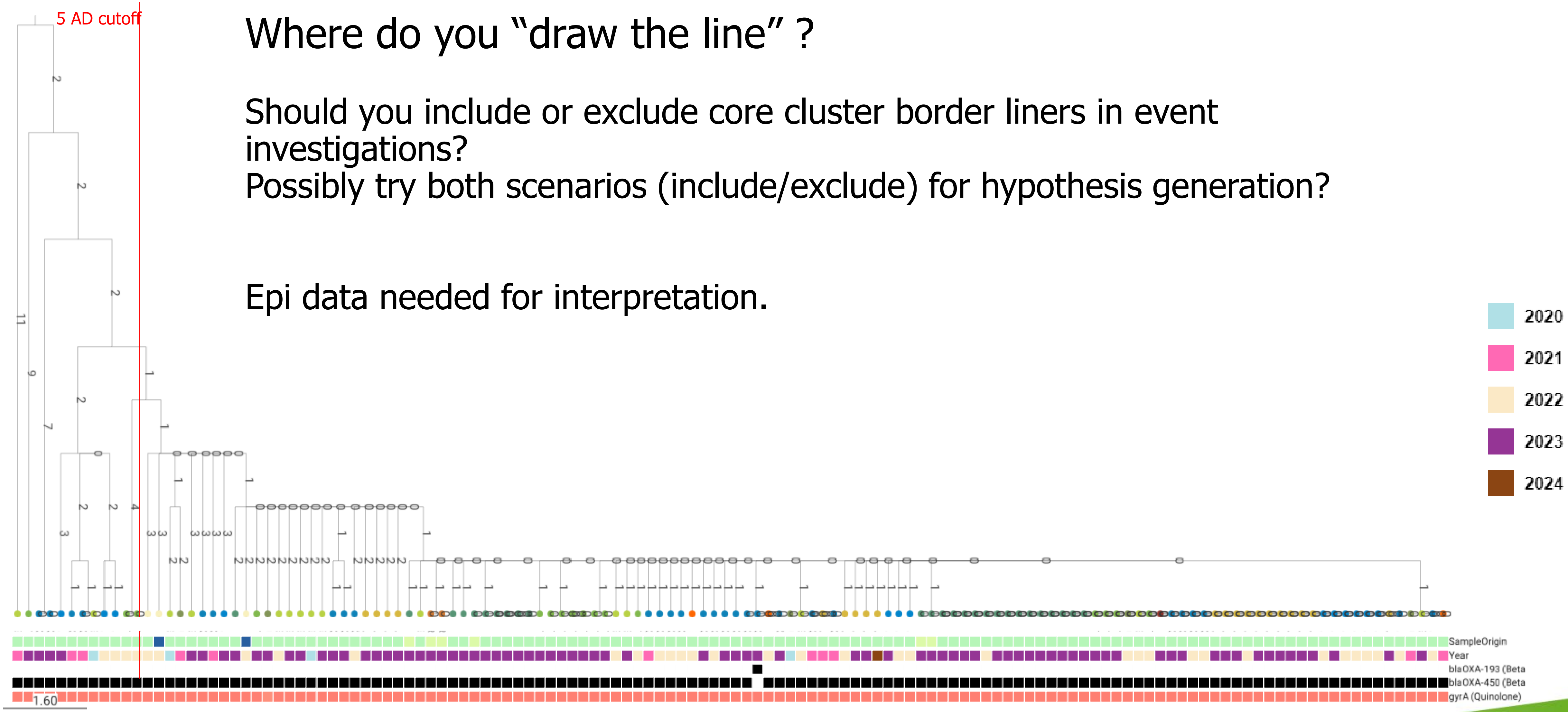


The clade has a maximum of 13 AD, 132 isolates, 11 countries

Where do you "draw the line" ?

Should you include or exclude core cluster border liners in event investigations?
Possibly try both scenarios (include/exclude) for hypothesis generation?

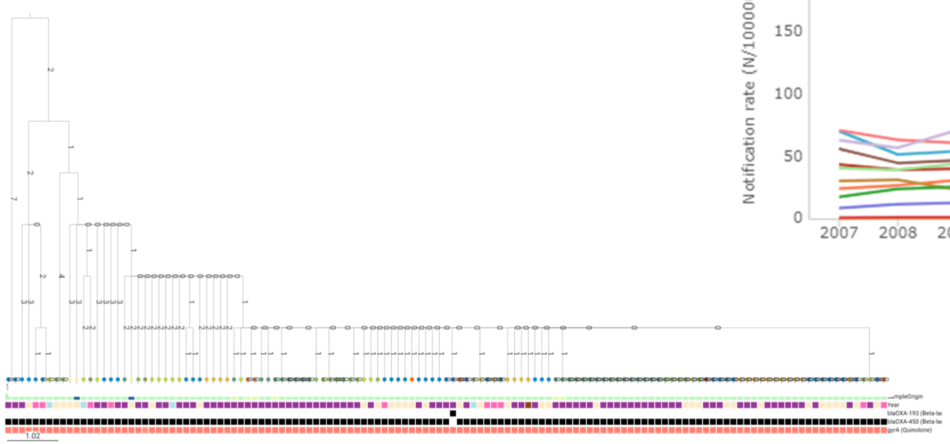
Epi data needed for interpretation.

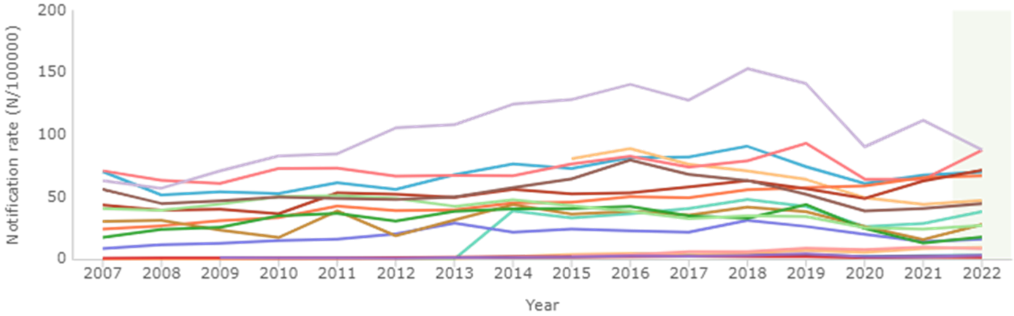


Context of the sequenced *Campylobacter* isolates identified in the EpiPulse Molecular Typing Tool

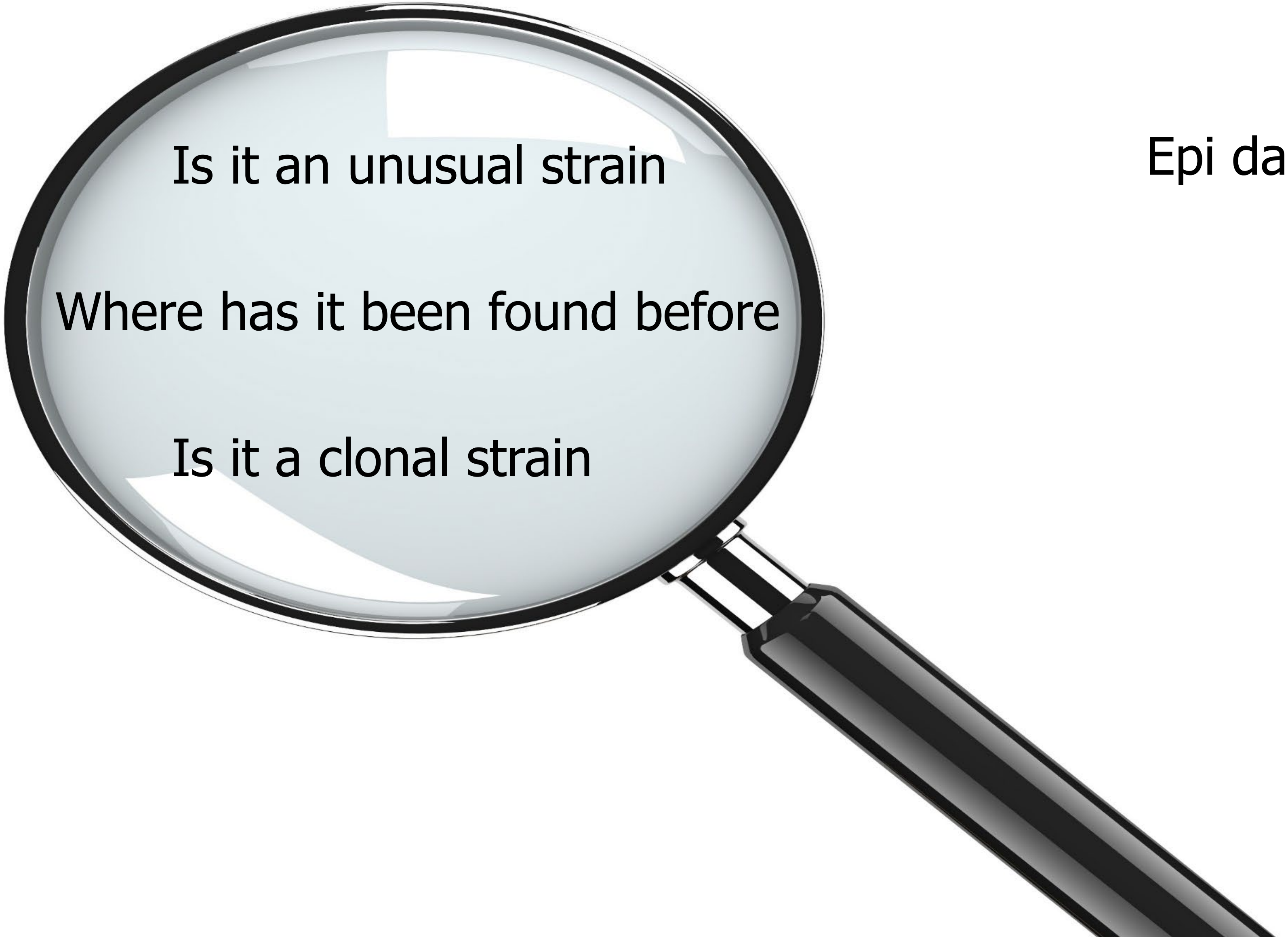
- Reported number of campylobacteriosis cases, tip of the iceberg
- Proportion of sequenced isolates of reported cases, the snow flake of the iceberg tip
    - Matching isolates from several countries participating in the ECDC seq support project

What does it mean that such a large cluster of this specific strain has isolates represented from so many countries?


SampleOrigin
Year
blaOXA-193 (Beta-la
blaOXA-450 (Beta-la
gyrA (Quinolone)
1.02



What does it mean that such a large cluster of this specific strain has been identified in so many countries?



Is it an unusual strain

Where has it been found before

Is it a clonal strain

Epi data always needed!

⌛

🏠

🚺

What does it mean that such a large cluster of this specific strain has been identified in so many countries? Cont.

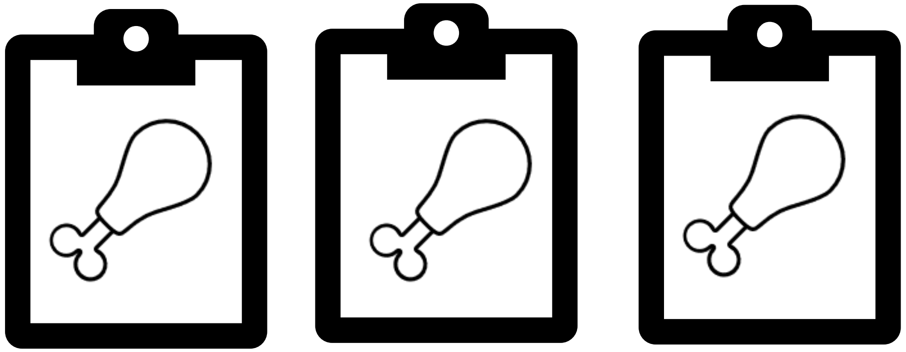
Suggested microbiological explanations:

- It is too clonal over time, genetically stable, to draw conclusions.
    - But Campy said to be genetically unstable, large clusters seldom identified, cross border outbreaks seldom identified.

- It is a strain persistant in the (production) of a large producer

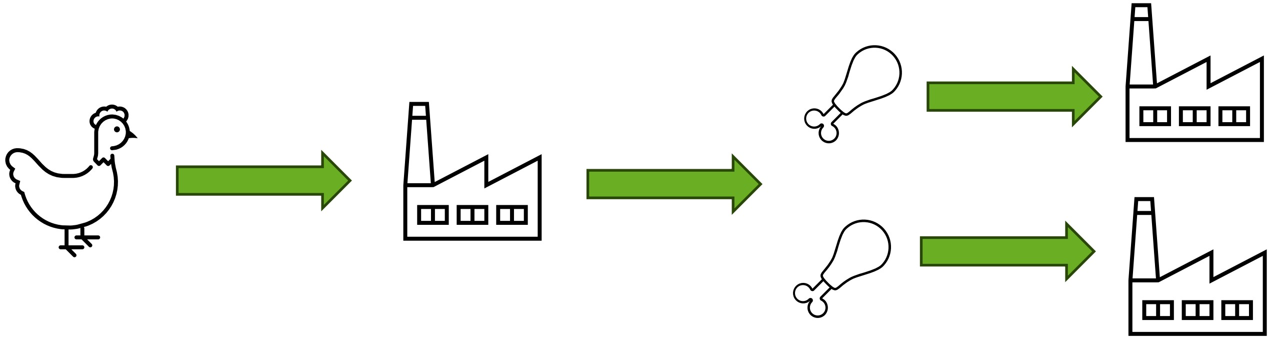
  e. g. improved survival capability due to oxygen tolerance

What does it mean that such a large cluster of this specific strain has been identified in so many countries? Cont.



- Questionnaire data challenging:
  ”everyone eats chicken”

- Information on the food side (cooperation with FS colleagues) when positive findings:
  Is it a food item exported at large to many countries.
  Is the raw material coming from one country, processed in another
  Is it a food item produced in one country and packed repacked in another



For the ST-464 this puzzle remains to be laid

Share data between countries, WGS and epi data

Share this data also between sectors

Please go to the MTT and access the cluster and support with your piece in the puzzle!

[Link to 2024-FWD-00011 event EpiPulse]()

ECDC tools for risk assessment outputs of an EU/EEA-wide foodborne events with or without EFSA

ECDC Rapid Risk Assessment

- **Aim**: to assess a cross-border health risk
- **Food information**: no
- **Main use** to inform public of risks (often travel-related) where specific foodborne risks are not specified
- **Published** on ECDC website

ECDC Notification Summary

- **Aim**: immediate notification of a cross-border foodborne risk
- **Food information**: only based on patient interviews or epidemiological studies (hypothesis on suspected vehicle)
- **Main use** to inform risk managers and to trigger food and epi investigations
- **Restricted** distribution to risk managers:
  ECDC => EC/EWRS, FWD-Net
  EFSA => EC/RASFF

ECDC-EFSA Joint Notification Summary

- **Aim**: immediate notification of a cross-border foodborne risk
- **Food information**: from EFSA database and public repository for sequences, RASFF information included if available
- **Main use** to inform risk managers and to trigger targeted food and epi investigations
- **Restricted** distribution to risk managers:
  ECDC => EC/EWRS, FWD-Net
  EFSA => EC/RASFF

ECDC-EFSA Joint Rapid Outbreak Assessment

- **Aim**: assess a cross-border foodborne public health threat
- **Food information:** from EFSA database and public repository for sequences, RASFF information for trace back and forward analysis
- **Main use** to inform public, public health professionals, and risk managers
- **Published** on ECDC and EFSA web sites

Thank you for your attention!

Please let us know how we can support you with data sharing, reporting, using EpiPulse tools etc!

ECDC.Microbiology@ecdc.europa.eu
cecilia.jernberg@ecdc.europa.eu