MINIMUM AND OPTIMAL REQUIREMENTS FOR NPHRL

SURVEY RESULTS ON CAPACITY FOR TESTING AND SURVEILLANCE OF AMR

Egle Kudirkiene

Network meeting

2021 November 30 – December 1

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- All Member States (MS) are obliged to **collect relevant and comparable data** on *Salmonella* and *Campylobacter:*

  - infections in humans,

  - food-related outbreaks, and

  - the occurrence of resistance to antimicrobials (AMR) relevant for the treatment of human infections with these bacteria

    Directive 2003/99/EC

- **The data must be reported to ECDC**, however the **it is not always comparable due to**:
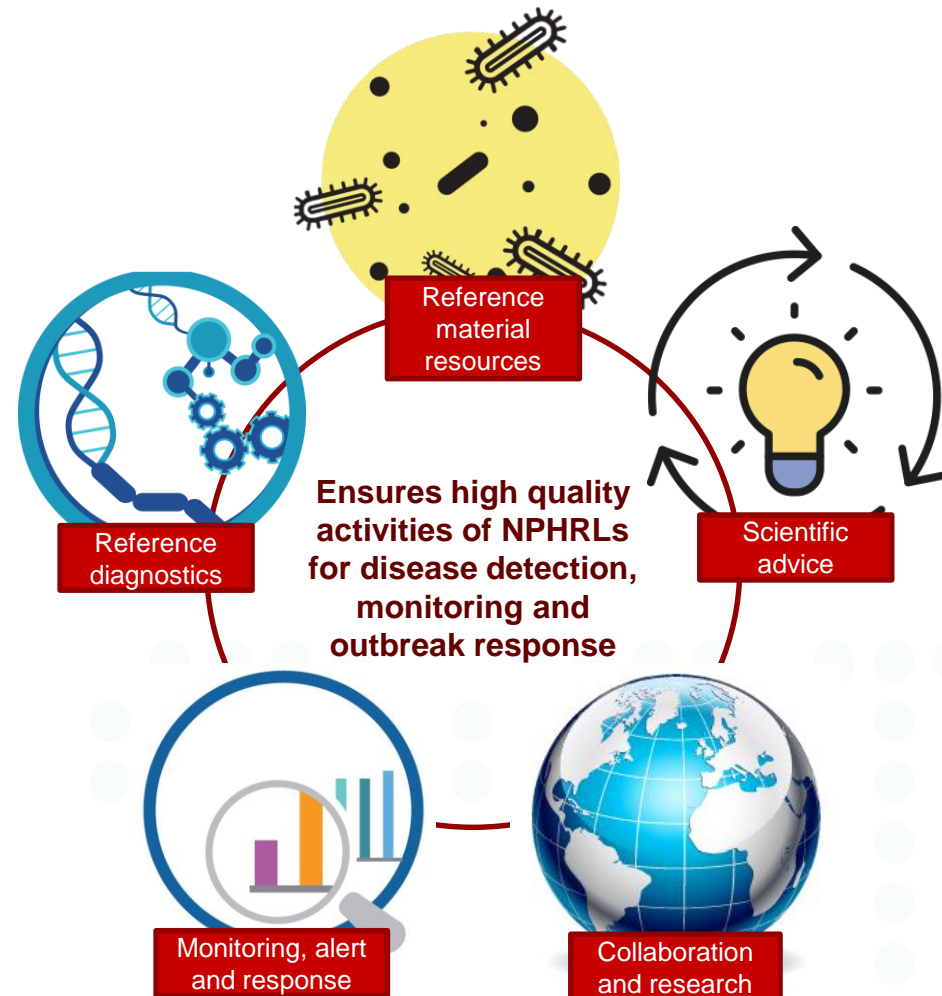
  - dissimilar **organisation and operation of the national public health reference laboratories (NPHRLs)** in different MSs

  - variation in **data quality level**

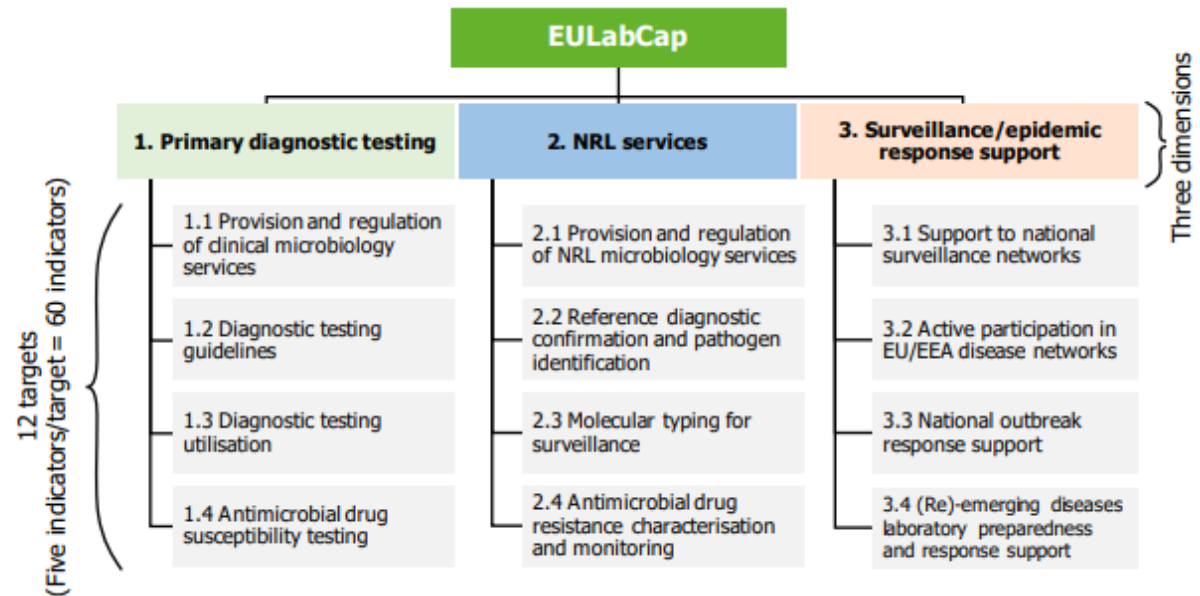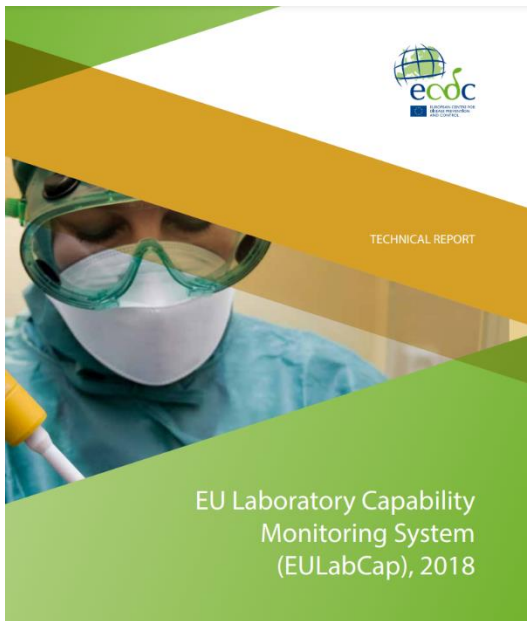 - differences in the **case definitions and methodologies used**

TECHNICAL REPORT

EU Laboratory Capability
Monitoring System
(EULabCap), 2018

EULabCap

1. Primary diagnostic testing	2. NRL services	3. Surveillance/epidemic response support
1.1 Provision and regulation of clinical microbiology services	2.1 Provision and regulation of NRL microbiology services	3.1 Support to national surveillance networks
1.2 Diagnostic testing guidelines	2.2 Reference diagnostic confirmation and pathogen identification	3.2 Active participation in EU/EEA disease networks
1.3 Diagnostic testing utilisation	2.3 Molecular typing for surveillance	3.3 National outbreak response support
1.4 Antimicrobial drug susceptibility testing	2.4 Antimicrobial drug resistance characterisation and monitoring	3.4 (Re)-emerging diseases laboratory preparedness and response support

Three dimensions

12 targets
(Five indicators/target = 60 indicators)

Substantial variation in capacities and capabilities between the laboratories

Some laboratories:

- Had an insufficient level of laboratory capacity and capability to conduct effective public health surveillance

- Were unable to provide an adequate level of disease threat response

RECOMMENDATIONS OF MINIMUM AND OPTIMAL REQUIREMENTS OF THE REFERENCE LEVEL FUNCTIONS FOR THE NATIONAL SURVEILLANCE SYSTEMS FOR AMR IN *SALMONELLA* AND *CAMPYLOBACTER* IN HUMANS

1. Support to primary diagnostic testing

2. Laboratory-based surveillance of AMR, alert and response
- Support to national surveillance networks
- National outbreak response support
- Participation in EU disease networks and research
- The design of AMR surveillance system, sampling and testing frequency
- Referral, timing and storage of *Salmonella* and *Campylobacter* isolates

3. National Public Health Reference Laboratory Services
- Internal and external quality control
- Reference diagnostics and characterisation of *Salmonella*
- Reference diagnostics and characterisation of *Campylobacter*

- In the same laboratory, **both minimum and optimal requirements may be applied**, e.g.

  - minimum requirements - for the majority of clinical samples/isolates

  - optimal requirements - on a subset of samples/isolates

- If, **NPHRLs do not have the capacity and capability to operate according to at least minimum requirements**

  - service level agreement(s) with other expert or reference level laboratories should be in place

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Salmonella

Requirements	Serotyping	Antimicrobial resistance	Cluster detection
Minimum	Phenotypic or genotypic: common serovars	Phenotypic AST or genotypic AMR prediction	High resolution molecular typing (e.g. MLVA)
Optimal	Phenotypic or genotypic: all serovars	Phenotypic AST and WGS-based AMR prediction*	WGS-based (e.g. cgMLST, wgMLST, SNP)

Campylobacter

Requirements	Species	Antimicrobial resistance	Cluster detection
Minimum	Phenotypic or genotypic: *C. jejuni, C. coli*	Phenotypic AST or genotypic AMR prediction	Not applicable**
Optimal	Phenotypic or genotypic: all species	Phenotypic AST and WGS-based AMR prediction*	WGS-based (e.g., cgMLST, wgMLST, SNP)

* a defined proportion of isolates or selected isolates are periodically tested phenotypically to ensure detection of novel resistance mechanisms

** Some laboratories may use Pulsed-field gel electrophoresis (PFGE) for cluster detection but this is not considered as a minimum requirement

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- to **identify capacity and capability gaps in technical and analytical skills of AMR testing and strain subtyping** at national level in all countries

- **identify countries with the greatest needs for capacity building in phenotypic and genomic testing of AMR ('priority countries')**
  - provide tailored **technical and operational support** for implementation of phenotypic and genomic testing of AMR in human *Salmonella* and *Campylobacter*
  - provide direct advice and **support for each country to create an action plan** to strengthen its national reference laboratory capacities in line with standards set out in EULabCap documentation

- **identify 'additional countries' facing challenges to identify and manage outbreaks** of *Salmonella* spp. and *Campylobacter* spp.

- Sent to 37 countries (32 EU/EEA/EU Health programme countries and 5 EU-candidate countries)

- **Responses received from 31 EU/EEA/EU Health programme countries and all 5 EU-candidate countries** (n=36)
  - In 29/36 countries responses from the same laboratory covering both *Salmonella* and *Campylobacter* were received
  - In 6/36 countries responses from two laboratories covering either *Salmonella* or *Campylobacter* were received
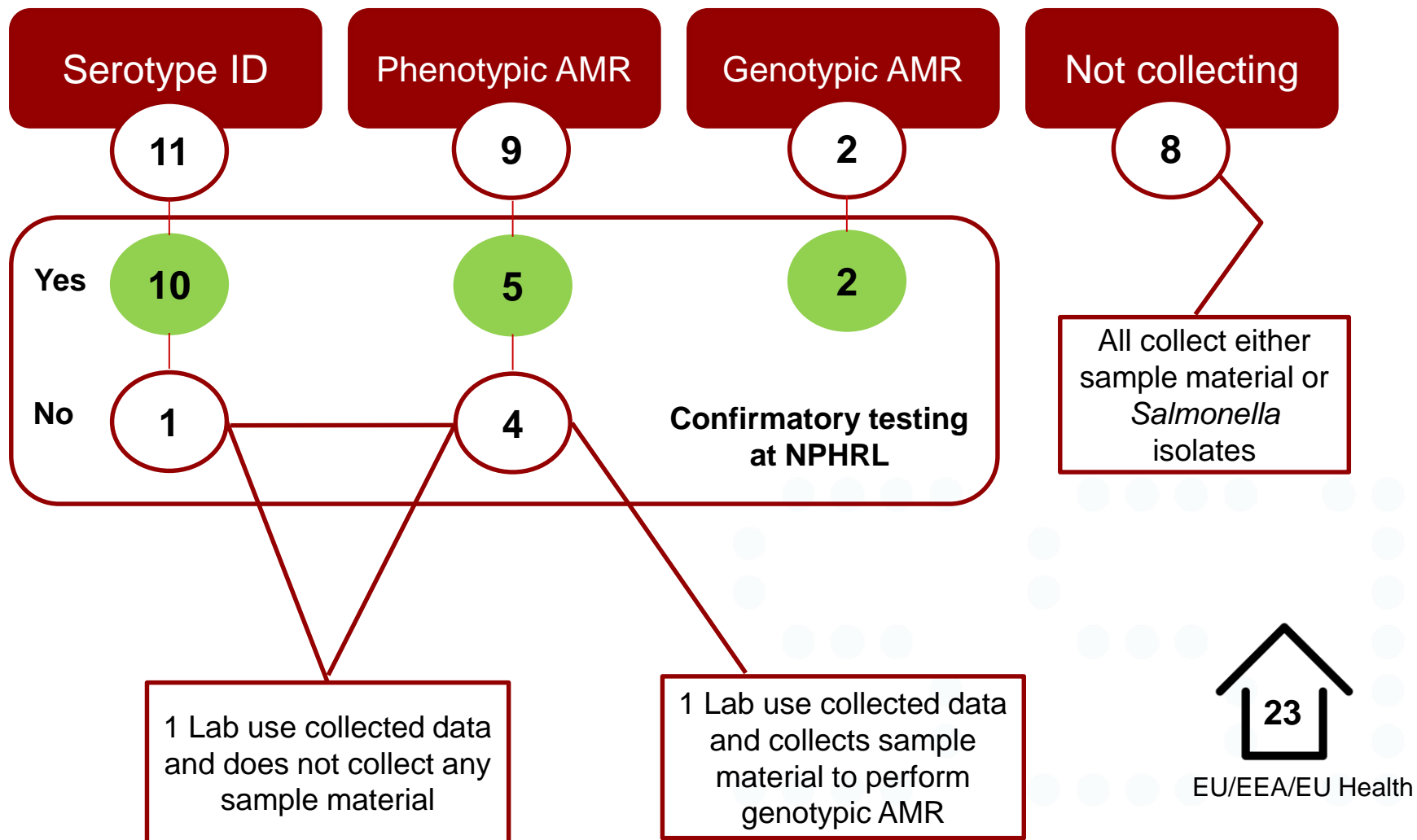 - One country responded for *Salmonella* spp. only

SALMONELLA

- AMR testing overview
- Data and sample collection for surveillance of AMR
- National AMR surveillance system coverage
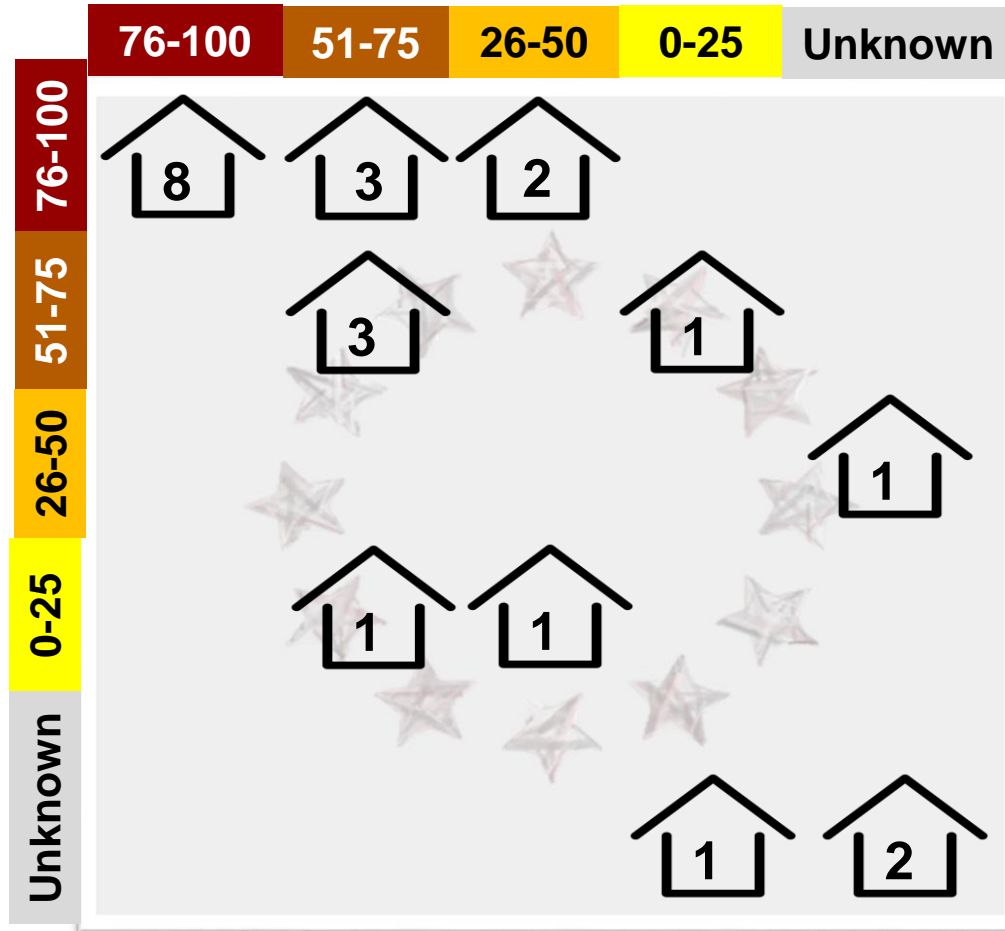- Molecular subtyping of *Salmonella* isolates

The purpose and the number of antimicrobials tested (phenotypic and genotypic)

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:• Collection of laboratory data

Serotype ID	Phenotypic AMR	Genotypic AMR	Not collecting
11	9	2	8

Yes 10 5 2

No 1 4 **Confirmatory testing at NPHRL**

All collect either sample material or *Salmonella* isolates

1 Lab use collected data and does not collect any sample material

1 Lab use collected data and collects sample material to perform genotypic AMR

23
EU/EEA/EU Health

COVERAGE OF NATIONAL AMR SURVEILLANCE SYSTEM

% of the total number of *Salmonella* enteritis cases tested for AMR annually

% of the local/regional clinical laboratories submitting laboratory data and/or sample material for national surveillance of AMR
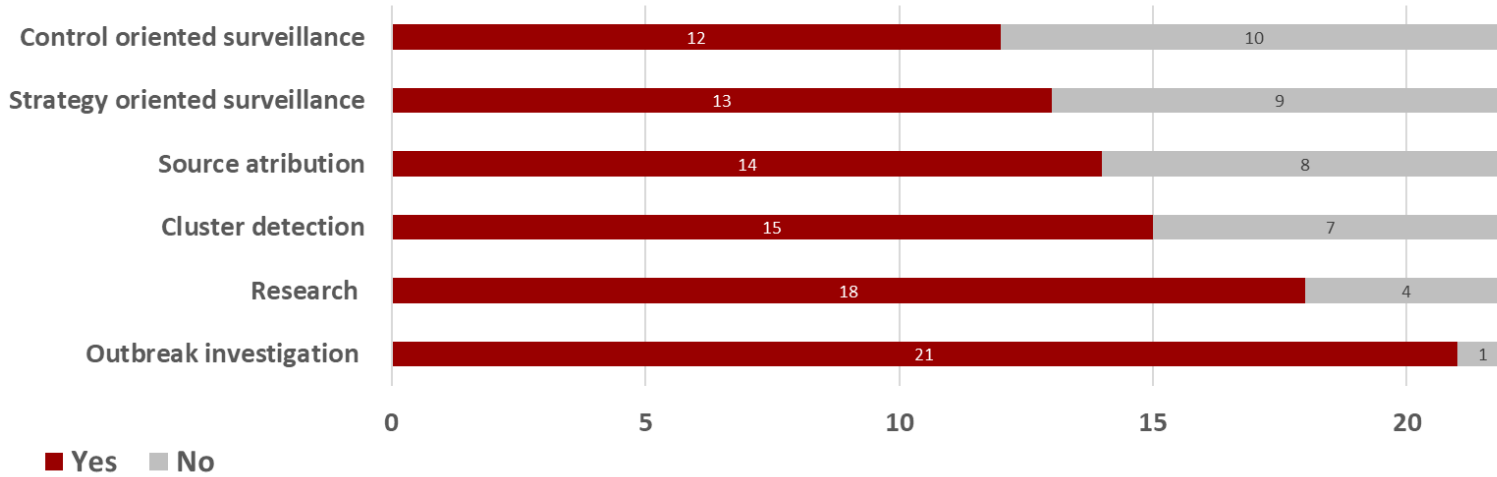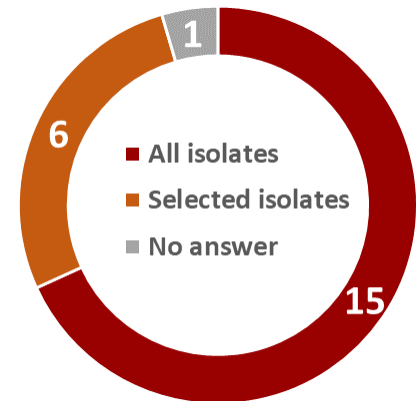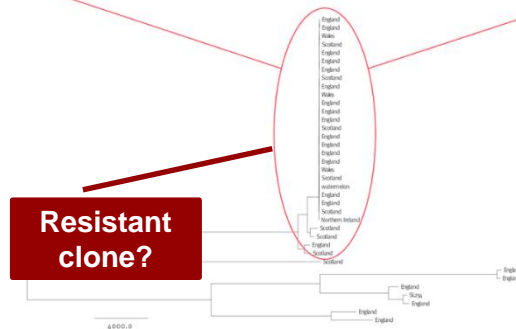
76-100	51-75	26-50	0-25	Unknown

23
EU/EEA/EU Health

MOLECULAR SUBTYPING OF SALMONELLA ISOLATES

Objectives of molecular subtyping

	Yes	No
Control oriented surveillance	12	10
Strategy oriented surveillance	13	9
Source atribution	14	8
Cluster detection	15	7
Research	18	4
Outbreak investigation	21	1

■ Yes   ■ No

22

EU/EEA/EU Health

AMR testing on outbreak isolates

Resistant clone?

- All isolates — 15
- Selected isolates — 6
- No answer — 1

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- 7 - 13 antimicrobials tested in all countries
- 5 - phenotypic, 1 - genotypic methods
- 2 - all serovars, 2 - most common in the country, 1 - random testing
- 4 - follow harmonised EU protocol

- 5 - DD, 4 – GS, 3 – AS, 2 - CBD
- 4 - EUCAST CBP, 3 - EUCAST EBP, 1 - CLSI CBP
- 2 - perceive high level of performance, 3 - need improvements

AMR testing N=5

AST N=5

Surveillance N=3

Strain subtyping N=1

5

EU candidate countries

- 3 countries for 7-10 antimicrobials
- 2 - with 0-25% cov. of local/regional laboratories and 76-100% cov. of cases
- 1 - with 76-100% cov. of local/regional laboratories and with unknown coverage of cases

- 1 - uses PFGE for outbreak investigations, source attribution and research
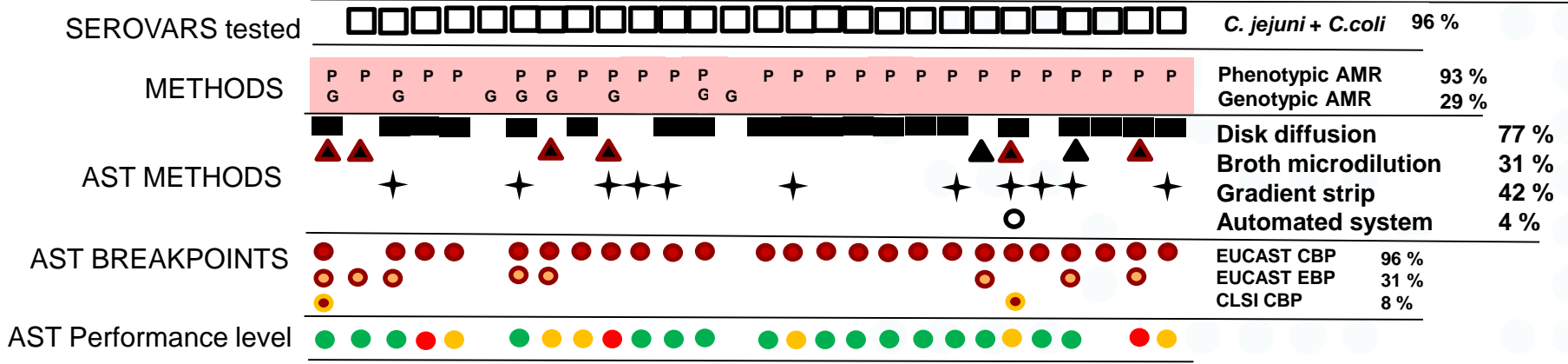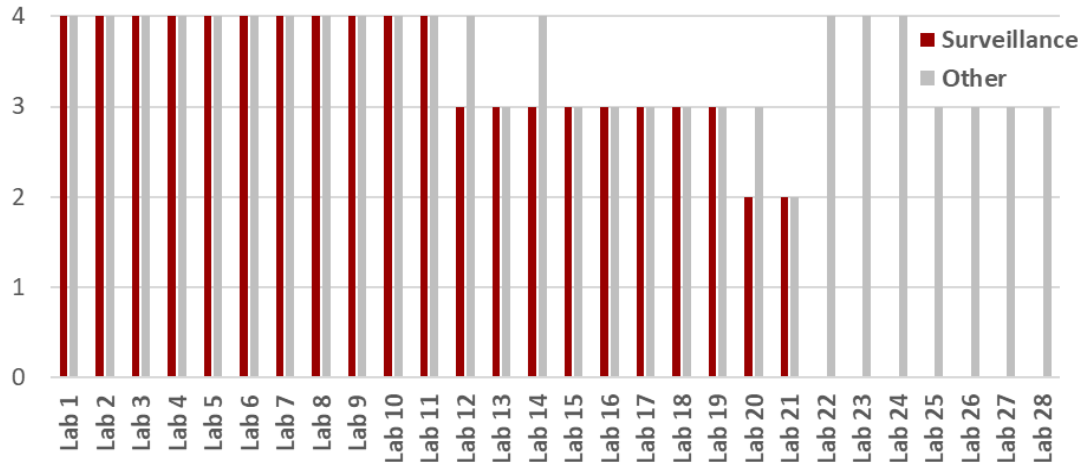
CAMPYLOBACTER

- AMR testing overview
- Data and sample collection for surveillance of AMR
- National AMR surveillance system coverage
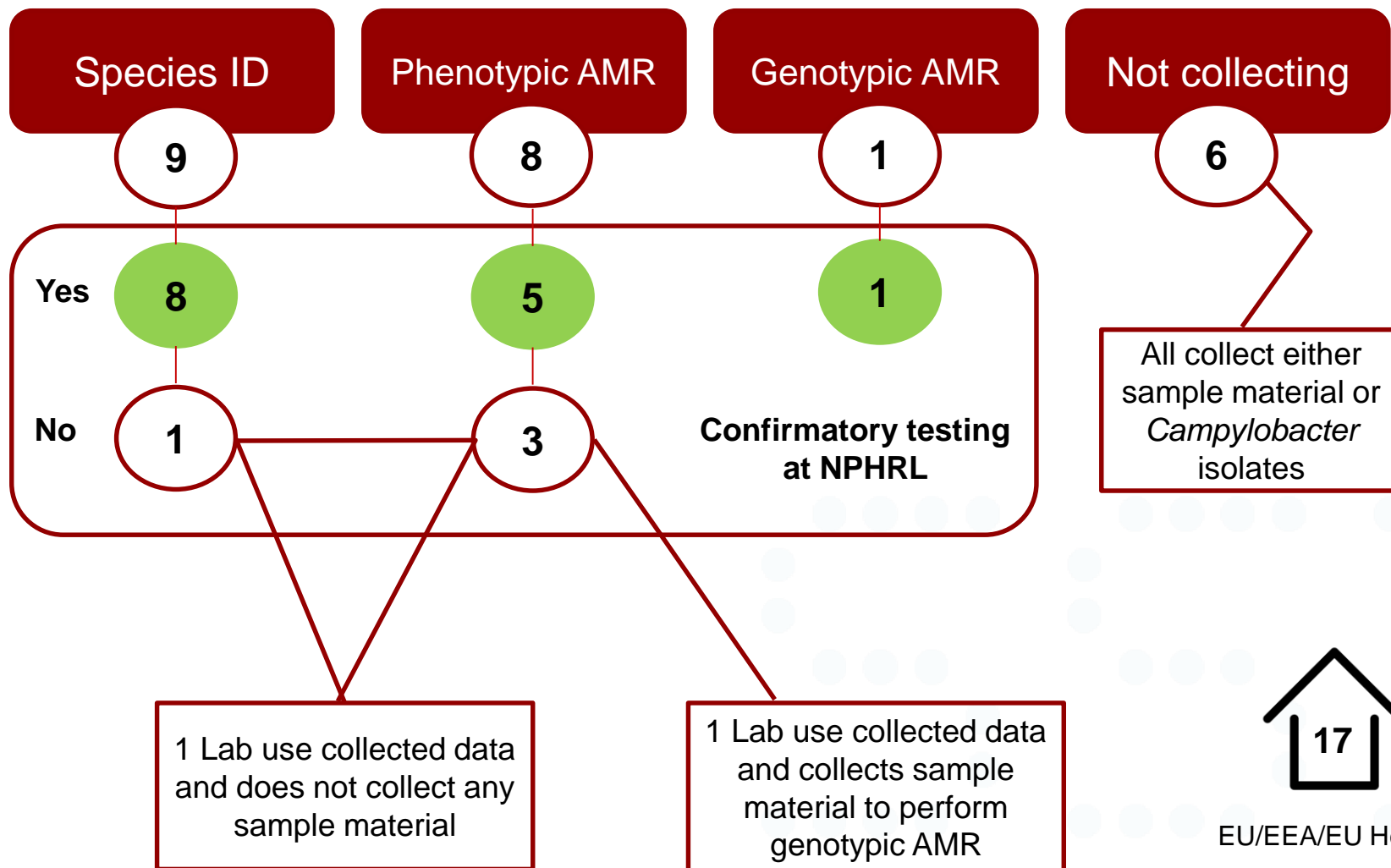- Molecular subtyping of *Campylobacter* isolates

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Collection of laboratory data

	Species ID	Phenotypic AMR	Genotypic AMR	Not collecting
	9	8	1	6
Yes	8	5	1	
No	1	3		

Confirmatory testing at NPHRL

All collect either sample material or *Campylobacter* isolates

1 Lab use collected data and does not collect any sample material

1 Lab use collected data and collects sample material to perform genotypic AMR

17

EU/EEA/EU Health

COVERAGE OF NATIONAL AMR SURVEILLANCE SYSTEM

Objectives of molecular subtyping

Objectives of molecular subtyping chart (Yes/No):

Objective	Yes	No
Control oriented surveillance	4	12
Source atribution	6	10
Cluster detection	10	6
Strategy oriented surveillance	10	6
Outbreak investigation	11	5
Research	14	2

■ Yes ■ No

16

EU/EEA/EU Health

AMR testing on outbreak isolates

- ■ All isolates: 7
- ■ Selected isolates: 3
- ■ No answer: 6
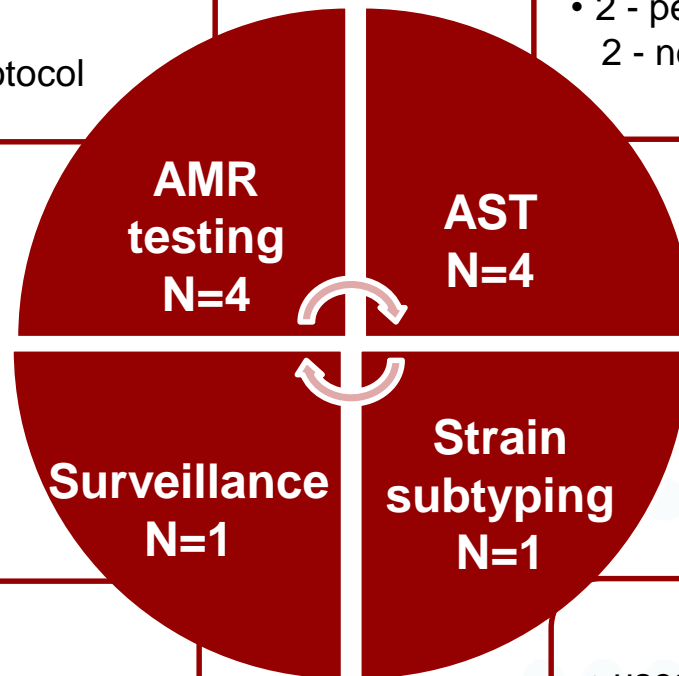
CAMPYLOBACTER AMR SURVEILLANCE IN NON-EU COUNTRIES

- 3 - 4 antimicrobials tested in all countries
- All use phenotypic methods
- All - *C. jejuni*, 1 - *C. coli*
- 4 - follow harmonised EU protocol

- 4 - DD, 3 - GS
- 4 - EUCAST CBP, 1 - EUCAST EBP
- 2 - perceive high level of performance, 2 - need improvements

AMR testing N=4

AST N=4

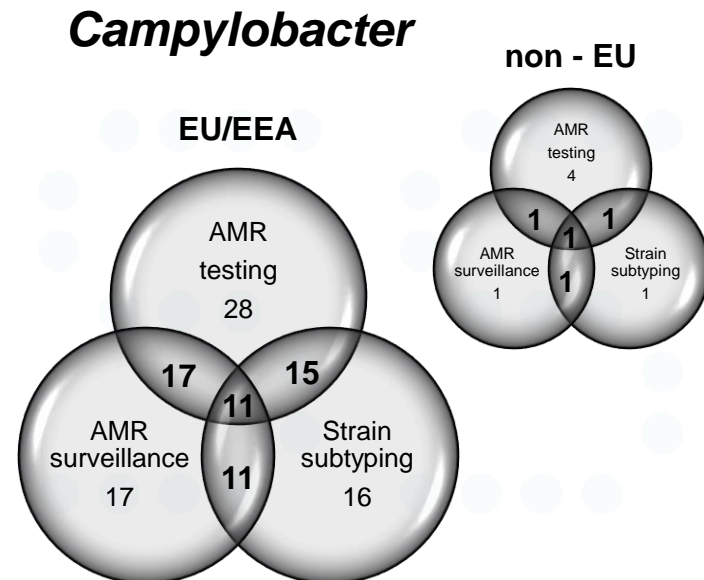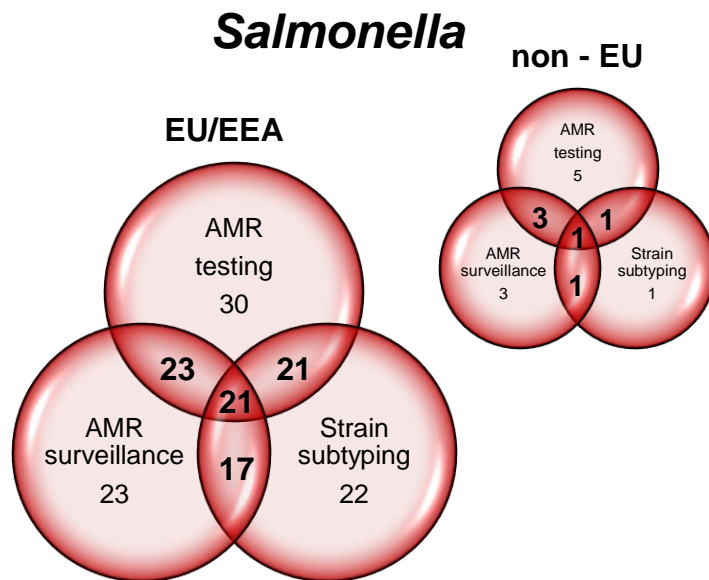**Surveillance N=1**

Strain subtyping N=1

4

EU candidate countries

- For 4 antimicrobials
- with 0-25% cov. of local/regional laboratories and 51 - 75% cov. of cases

- uses PFGE for outbreak investigations, source attribution and research

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- Nearly all NPHRLs have a capacity to perform testing of AMR in *Salmonella* and *Campylobacter* isolates from humans using either phenotypic of genotypic methods, however:

  - Approx. 2/3 of NPHRLs perform AMR surveillance and strain subtyping of *Salmonella* isolates

  - Approx. 1/3 of NPHRLs perform AMR surveillance and strain subtyping of *Campylobacter* isolates

Salmonella

non - EU

EU/EEA

AMR testing 30 / AMR surveillance 23 / Strain subtyping 22 — 23, 21, 21, 17

non-EU: AMR testing 5 / AMR surveillance 3 / Strain subtyping 1 — 3, 1, 1, 1

Campylobacter

non - EU

EU/EEA

AMR testing 28 / AMR surveillance 17 / Strain subtyping 16 — 17, 15, 11, 11

non-EU: AMR testing 4 / AMR surveillance 1 / Strain subtyping 1 — 1, 1, 1, 1

Team members at SSI

- Eva Møller Nielsen
- Susanne Schjørring
- Malgorzata Ligowska-Marzeta
- Jeppe Boel
- etc.

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EURGen-RefLabCap team at SSI:

- Valeria Bortolaia
- Camilla Wiuff Coia

Everyone who responded to the survey!