



# Integration of enhanced molecular typing into surveillance at EU level

## TESSY 3.0 molecular typing pilot

Angela Lahuerta

Food and water-borne diseases and zoonoses programme (FWD)

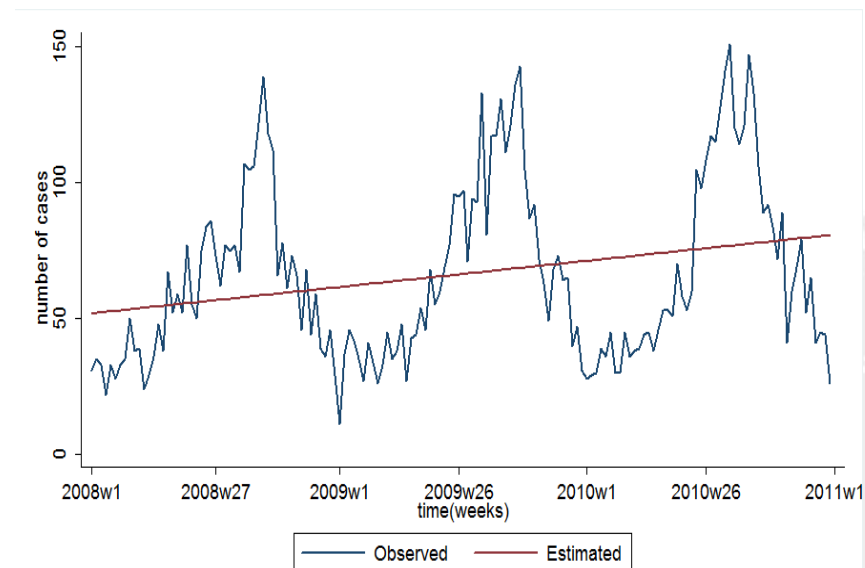
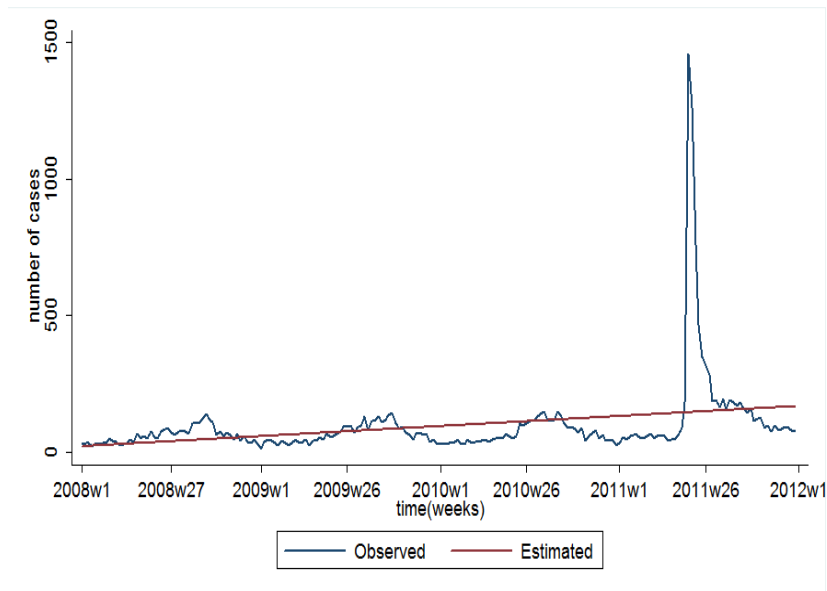
European Centre for Disease Prevention and Control (ECDC)

EUROL *E. coli* annual workshop, Rome 8<sup>th</sup> and 9<sup>th</sup> November 2012

*Slides kindly provided by Ivo Van Walle and Jaime Martinez-Urtaza*

# Human VTEC infections in the EU

- There were 9,478 confirmed VTEC human cases reported in 2011, 1.97 cases per 100,000 pop.;
- EHEC/EAEC O104:H4 outbreak occurred in Germany in 2011, 3813 human cases and 54 deaths;
- Significant increasing trend of VTEC infections in the EU 2008-2011, regardless of the EHEC/EAEC O104 outbreak (below);



# ECDC's Molecular Surveillance Roadmap



Objectives are to improve:

- Rapid detection of dispersed international outbreaks.
- Trace-back of the source of an outbreak and identify risk factors.
- Investigation of transmission chains across EU and globally.
- Detection of emergence of new virulent type or drug resistant strain.
- Monitoring of the emergence of vaccine escape variants.

Five year implementation plan (2012-2016):

- List of priority disease/pathogen and typing method.
- Expected public health use.
- Technical support activities.
- Estimated resource needs.



# TESSy 3.0 molecular typing pilot



Generic platform for handling molecular typing data:

- Any selected pathogen can be added,  
FWD: Salmonella, VTEC and Listeria
- Any selected typing method can be added

Curation and cluster management

Supports linking laboratory and clinical/epidemiological data

System security

- Established system with well-defined nomination procedures
- Follows general TESSy data access policy which has been approved by MS
- No publications by ECDC on this data during pilot phase
- Isolate identifiers are not shared across MS

# FWD Pilot in 2012

## Extended user acceptance testing

Member States

AF, NMFP and NSFP  
Consultation on Pilot project  
protocol

Outsourced

Coordination of laboratory support; EQA, data validation, expert advice, regular cluster reports

FWD Network:  
voluntary labs

Test data upload, validation, cluster search, feedback on metadataset

ECDC

Validation of historical PFGE data

Invitation of min. 3-5  
voluntary labs (14 NRLs  
agreed)

Validation of Listeria PFGE data as part of joint ECDC-EFSA  
Listeria typing study

Feb

Mar

Apr

May

Jun

Jul

Aug

Sep

Oct

Nov

Dec



AF29



Update on pilot  
phase to AF,  
NMFP, NSFP



Workshop



Review of  
metadataset by  
NSFP

# FWD Pilot in 2013

## Voluntary data collection, analysis and evaluation

Member States

Coordination of laboratory support; EQA, data validation, expert advice, regular cluster reports (outsourced)

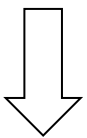
Data upload, validation, cluster search by laboratories (FWD Network)

ECDC

14 voluntary labs  
+ other nominated users

User satisfaction  
survey

Pilot evaluation



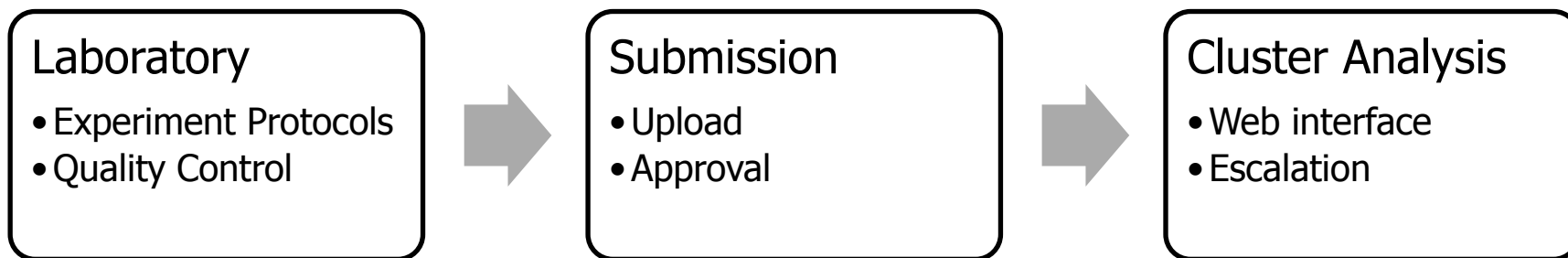
Follow-up of identified clusters (EPIS FWD); Listeria prospective cluster monitoring



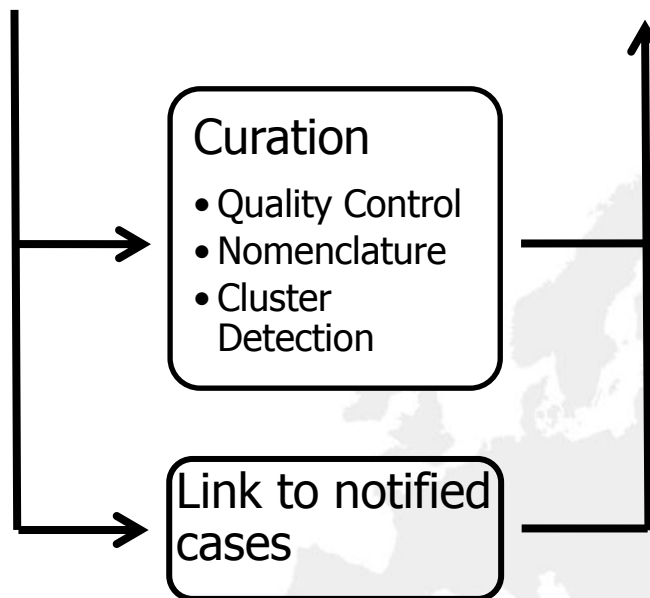
Update on pilot progress to AF, NMFP, NSFP

Presentation of pilot evaluation to AF, NMFP, NSFP  
Review of metadataset by NSFP

# Main work flow



- Processes described fully by Standard Operating Procedures, now v0.2.
- Constant drive to improve efficiency and achieve/maintain acceptable quality.



# Data curation

Contracts for VTEC, Salmonella and Listeria in place (SSI, DK)

## Initial curator tasks:

- Review data quality
- Provide individual advice to users on improving data quality
- Nomenclature assignment
- Cluster detection
- Advice ECDC on potential outbreaks

## Start work on historical data

- 21,000 lanes for *Salmonella* and 1,500 for *Listeria* from PulseNet Europe
- Other historical data submitted by users



# Cluster Analysis in TESSy

## Cluster Search

### Query database

Genetic distance:  PFGE XbaI bands difference

Time distance:  days (optional)

Query

### Results

Tree algorithm:

UPGMA

Experiments:

1 of 8 selected

Nomenclature:

select nomenclature

Isolate data:

3 of 23 selected

Linked case data:

2 of 46 selected

Dendrogram (percent similarity)	<input checked="" type="checkbox"/>	PFGE_XbaI	<input type="checkbox"/>	Isolate	<input type="checkbox"/>	Isolate	<input type="checkbox"/>	Isolate	<input type="checkbox"/>	Linked case	<input type="checkbox"/>	Linked case	<input type="checkbox"/>
				DateOfSampling		ReportingCountry		Serotype		DateOfOnset		Imported	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-20		AA		STANLEY		2012-06-18		N	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-25		BB		STANLEY		2012-06-23		Y	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-26		BB		STANLEY		2012-06-24		N	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-21		AA		STANLEY		2012-06-19		Y	
96.3	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-07-18		CC		STANLEY		2012-07-16		N	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-07-19		CC		STANLEY		2012-07-17		Y	
95.5	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-07-20		CC		STANLEY		2012-07-18		N	
96.3	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-05-15		DD		STANLEY		2012-05-13		Y	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-27		BB		STANLEY		2012-06-25		N	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-28		BB		STANLEY		2012-06-26		Y	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-29		BB		STANLEY		2012-06-27		N	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-05-16		DD		STANLEY		2012-05-14		Y	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-06-30		BB		STANLEY		2012-06-28		N	
95.5	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-05-17		DD		STANLEY		2012-05-15		Y	
	<input checked="" type="checkbox"/>		<input type="checkbox"/>	2012-05-18		DD		STANLEY		2012-05-16		N	

Copy Selected

Export

# Cluster Analysis Interface in TESSy



## Cluster Search

### Query database

Genetic distance:  PFGE XbaI bands difference

Time distance:  days (optional)

### Results

Tree algorithm:

Experiments:

Nomenclature:

Isolate data:

Linked case data:

UPGMA

1 of 8 selected

select nomenclature

3 of 23 selected

2 of 46 selected

Dendrogram (percent similarity)	<input checked="" type="checkbox"/>	PFGE_XbaI	<input checked="" type="checkbox"/>	Isolate	<input checked="" type="checkbox"/>	Isolate	<input checked="" type="checkbox"/>	Isolate	<input checked="" type="checkbox"/>	Isolate	<input checked="" type="checkbox"/>	Case	<input checked="" type="checkbox"/>
				DateOfSampling		ReportingCountry		Serotype		SampleOrigin		DateOfOnset	
	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-06-20		AA		STANLEY		HUMAN		2012-06-18	
	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-06-25		BB		STANLEY		HUMAN		2012-06-23	
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	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-07-18		CC		STANLEY		HUMAN		2012-07-16	
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	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-05-16		DD		STANLEY		ENVIRONMENT*			
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	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-05-17		DD		STANLEY		FOOD*			
	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-05-18		DD		STANLEY		HUMAN		2012-05-16	
	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	2012-05-19		DD		STANLEY		HUMAN		2012-05-17	

\*Technically possible, but requires broad agreement. No other than human data is expected to be collected.

# Current situation

TESSy MSS system will be launched for actual use mid November.

National experts have nearly all been nominated.

## Training

- Nearly all participating labs have attended the workshop.
- On site visits for further training are ongoing.

Historical data, to be selected and uploaded first thing after launch.

# Thank you!

## On behalf of ECDC FWD team

Johanna Takkinen  
Jaime Martinez-Urtaza  
Milka Docheva  
Celine Gossner  
Taina Niskanen  
Thomas Van Cangh  
Therese Westrell  
Irene Zanetti  
Birgitta de Jong  
Carmen Varela Santos  
Angela Lahuerta-Marin



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### Food- and Water-borne Diseases and Zoonoses Programme

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The Programme Food- and Waterborne Diseases and Zoonoses (FWD) was set up in 2006, and at present covers the following diseases: anthrax, botulism, brucellosis, campylobacteriosis, cholera, cryptosporidiosis, echinococcosis, giardiasis, hepatitis A, legionellosis, leptospirosis, listeriosis, salmonellosis, shigellosis, toxoplasmosis, trichinellosis, tularaemia, typhoid/paratyphoid fever, variant Creutzfeldt-Jakob disease (vCJD), VTEC/STEC (verotoxin/shigatoxin producing E. coli) infection, and yersiniosis.

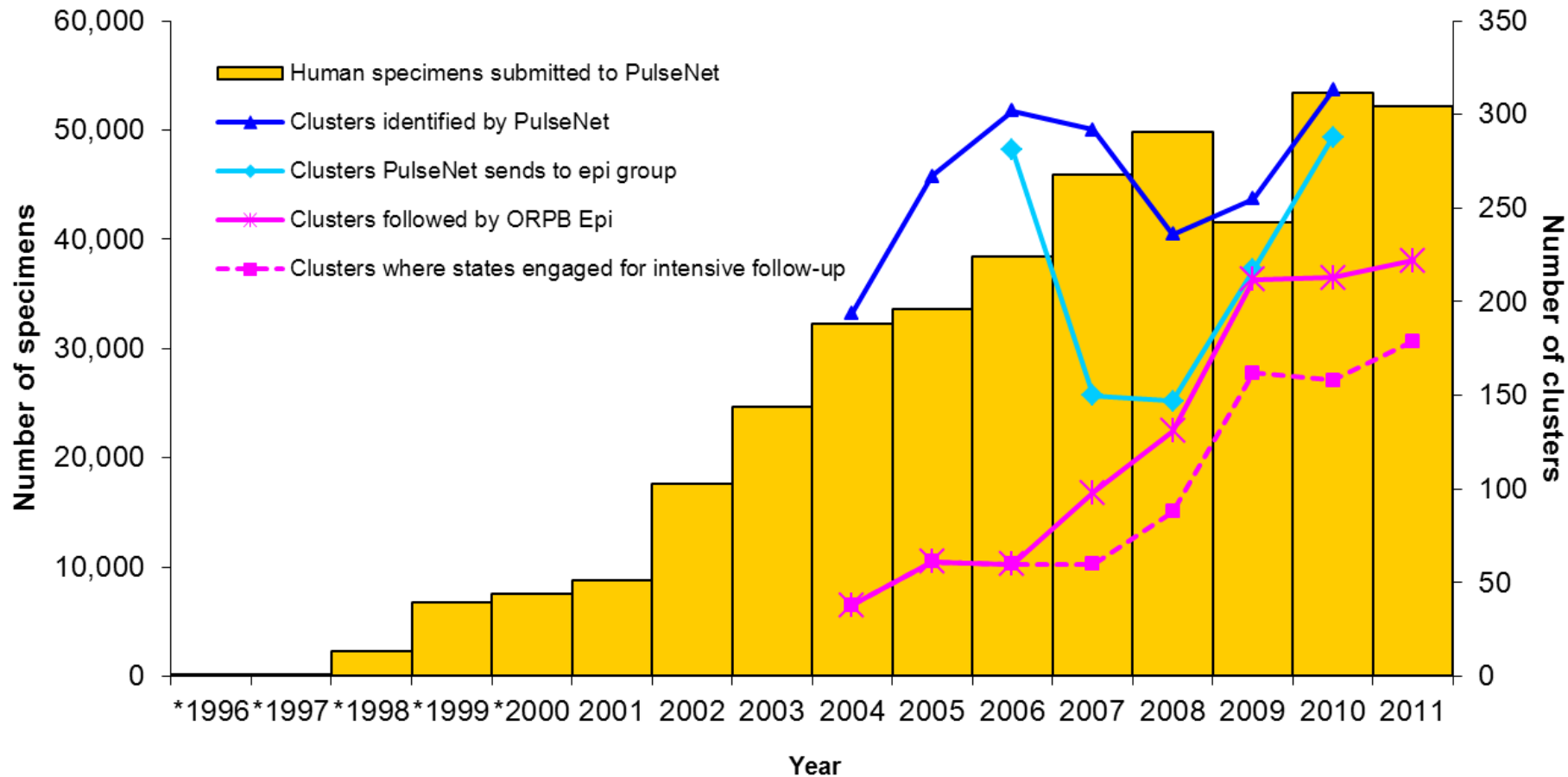
[Read more about the programme](#)





# Extra slides

# Potential long term situation: the example of PulseNet USA



# Submission

Open format to submit data: XML, CSV or manual on website.

ECDC plugin for BioNumerics allows to submit data over web service (i.e. machine to machine communication) directly from BioNumerics:

- 1) Select isolates or PFGE images.
- 2) Upload data.
- 3) Review validation results and adjust data if necessary.
- 4) Approve uploaded data.

Nominated users only.

Weekly submission of data expected.

# Laboratory

## Current typing methods supported

### VTEC

- Regular 'text' values like AntigenO.
- PFGE.
- Antimicrobial Susceptibility Testing, including 'raw' values.

### Salmonella

- Regular 'text' values like serotype.
- PFGE.
- MLVA (Typhimurium only).
- Antimicrobial Susceptibility Testing, including 'raw' values.

### Listeria

- Regular 'text' values like serotype.
- PFGE.

