The presence and future in antimicrobial resistance surveillance

Rene S. Hendriksen,
Research Group of Genomic Epidemiology
WHO CC AMR & Genomics / EU Ref. Lab. AMR
National Food Institute, Technical University of Denmark (DTU Food)

Global situation of antimicrobial resistance

"**Antimicrobial resistance is a crisis** that must be managed with the **outmost urgency**…..

….**Antimicrobial resistance threatens the very core of modern medicine** and the sustainability of an effective, global public health response to the enduring threat from infectious diseases…

…**Without harmonized and immediate action on a global scale, the world is heading towards a post-antibiotic era in which common infections could once again kill**"

Dr Margaret Chan

Director-General (former)

World Health Organization

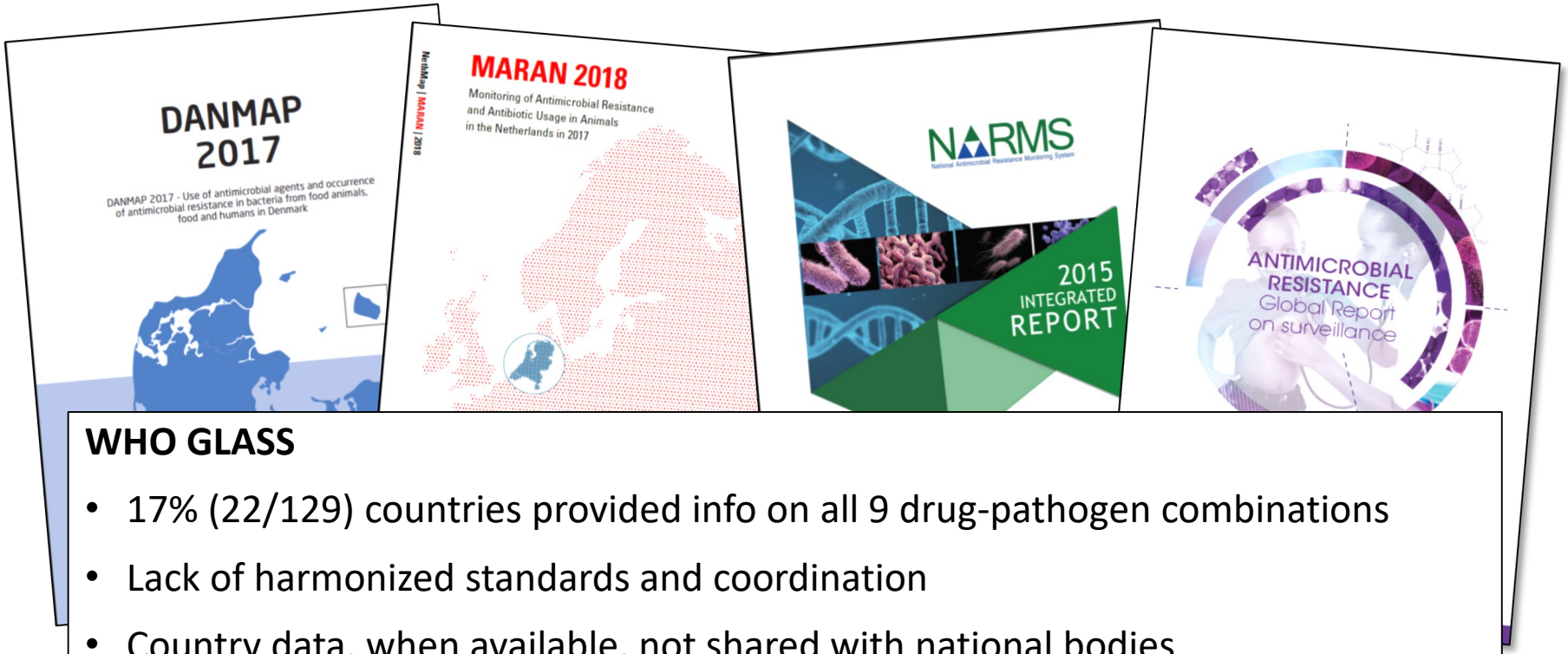
Purpose of Surveillance

- Estimate burden of disease
  - How big is the problem?
  - Relative importance of pathogens and reservoirs
- Monitor trends
  - Is it getting better or worse?
  - Measure effect of interventions
- Detect outbreaks
  - Is urgent action needed?
- Assess control programs
  - How are we doing?
  - Launch target interventions

The main purpose of Surveillance

- Knowledge of the distribution of health events
- Rapid detection of outbreak
- Public health planning and evaluation

Surveillance systems in place



WHO GLASS

- 17% (22/129) countries provided info on all 9 drug-pathogen combinations
- Lack of harmonized standards and coordination
- Country data, when available, not shared with national bodies
- Limited information on impact of antibacterial resistance on humans
- As of today, 22 March 2019, 75 countries participate in GLASS

EU AMR surveillance system in food and animals in place - 2014 - 2020

SCIENTIFIC REPORT

APPROVED: 31 January 2019

doi: 10.2903/j.efsa.2019.5598

The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2017

European Food Safety Authority and
European Centre for Disease Prevention and Control

Abstract

The data on antimicrobial resistance in zoonotic and indicator bacteria in 2017, submitted by 28 EU Member States (MSs), were jointly analysed by EFSA and ECDC. Resistance in zoonotic *Salmonella* and *Campylobacter* from humans, animals and food, and resistance in indicator *Escherichia coli* as well as meticillin-resistant *Staphylococcus aureus* in animals and food were addressed, and temporal trends assessed. 'Microbiological' resistance was assessed using epidemiological cut-off (ECOFF) values; for some countries, qualitative data on human isolates were interpreted in a way which corresponds closely to the ECOFF-defined 'microbiological' resistance. In *Salmonella* from humans, as well as in *Salmonella* and *E. coli* isolates from fattening pigs and calves of less than 1 year of age, high proportions of isolates were resistant to ampicillin, sulfonamides and tetracyclines, whereas resistance to third-generation cephalosporins was uncommon. Varying occurrences/prevalence rates of presumptive extended-spectrum beta-lactamase (ESBL)/AmpC producers in *Salmonella* and *E. coli* monitored in meat (pork and beef), fattening pigs and calves, and *Salmonella* monitored in humans, were observed between countries. Carbapenemase-producing *E. coli* were detected in one single sample from fattening pigs in one MS. Resistance to colistin was observed at low levels in *Salmonella* and *E. coli* from fattening pigs and calves and meat thereof and in *Salmonella* from humans. In *Campylobacter* from humans, high to extremely high proportions of isolates were resistant to ciprofloxacin and tetracyclines, particularly in *Campylobacter coli*. In five countries, high to very high proportions of *C. coli* from humans were resistant also to erythromycin, leaving few options for treatment of severe *Campylobacter* infections. High resistance to ciprofloxacin and tetracyclines was observed in *C. coli* isolates from fattening pigs, whereas much lower levels were recorded for erythromycin. Combined resistance to critically important antimicrobials in both human and animal isolates was generally uncommon but very high to extremely high multidrug resistance levels were observed in *S.* Typhimurium and its monophasic variant in both humans and animals. *S.* Kentucky from humans exhibited high-level resistance to ciprofloxacin, in addition to a high prevalence of ESBL.

Keywords: antimicrobial resistance, zoonotic bacteria, indicator bacteria, ESBL

Requestor: European Commission

Question number: EFSA-Q-2017-00752

Correspondence: zoonoses@efsa.europa.eu (EFSA); FWD@ecdc.europa.eu (ECDC)

L 303/26 EN Official Journal of the European Union 14.11.2013

DECISIONS

COMMISSION IMPLEMENTING DECISION

of 12 November 2013

on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria

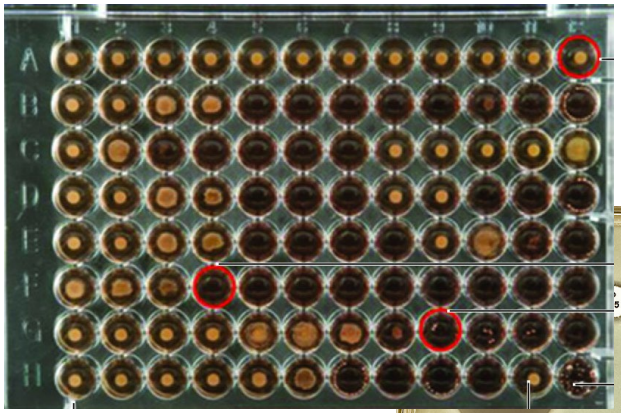
(notified under document C(2013) 7145)

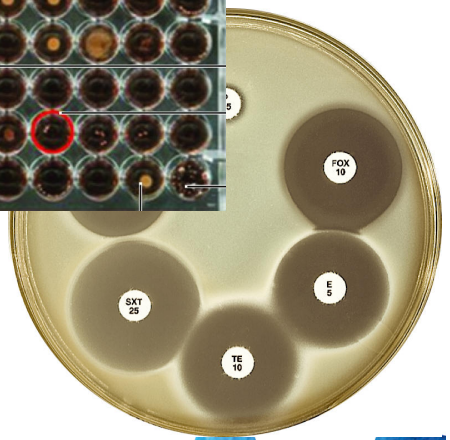
(Text with EEA relevance)

(2013/652/EU)

Phenotypic antimicrobial susceptibility testing - Methodology

- Well-tested standardized approach based on ISO
- Most variable harmonized e.g. drug panels, MIC, ECOFFs etc.
- Used to infer resistance (S/I/R)





Criteria for interpretation of *Escherichia coli*, panel 2 results

1. ESBL-Phenotype
- FOT or TAZ > 1 mg/L AND
- MERO ≤ 0.12 mg/L AND
- FOX ≤ 8 mg/L AND
- SYN FOT/CLV and/or TAZ/CLV

2. AmpC-Phenotype
- FOT or TAZ > 1 mg/L AND
- MERO ≤ 0.12 mg/L AND
- FOX > 8 mg/L AND
- No SYN FOT/CLV nor TAZ/CLV
- (Not excluded presence of ESBLs)

3. ESBL + AmpC-Phenotype
- FOT or TAZ > 1 mg/L AND
- MERO ≤ 0.12 mg/L AND
- FOX >8 mg/L AND
- SYN FOT/CLV and/or TAZ/CLV

4. Carbapenemase-Phenotype
- MERO > 0.12 mg/L
- Needs confirmation
- (Not excluded presence of ESBLs or AmpC)

Susceptible

FOT-TAZ-FOX-MEM ≤ ECOFF

5. Other phenotypes

1) If FOT or TAZ > 1 mg/ml AND
- MEM ≤ 0.12 mg/L AND
- FOX ≤ 8 mg/L AND
- NO SYN FOT/CLV nor TAZ/CLV
- Not excluded CPs (consult EURL)

2) If FOT and/or TAZ ≤ 1 mg/L AND > ECOFF AND
- MERO ≤ 0.12 mg/L
- FOX ≤ 8 mg/L

3) If FOT and TAZ ≤ 1 mg/L
- MERO ≤ 0.12 mg/L
- FOX > 8 mg/L

*cAmpCs could be included here

4) If MERO ≤ 0.12 mg/L BUT
- ETP > ECOFF AND/OR
- IMI > ECOFF
- Not excluded CPs, needs confirmation (consult EURL)

5) Any other combinations not described in previous boxes (consult EURL)

Phenotypic antimicrobial susceptibility testing - Deviation level based on PTs

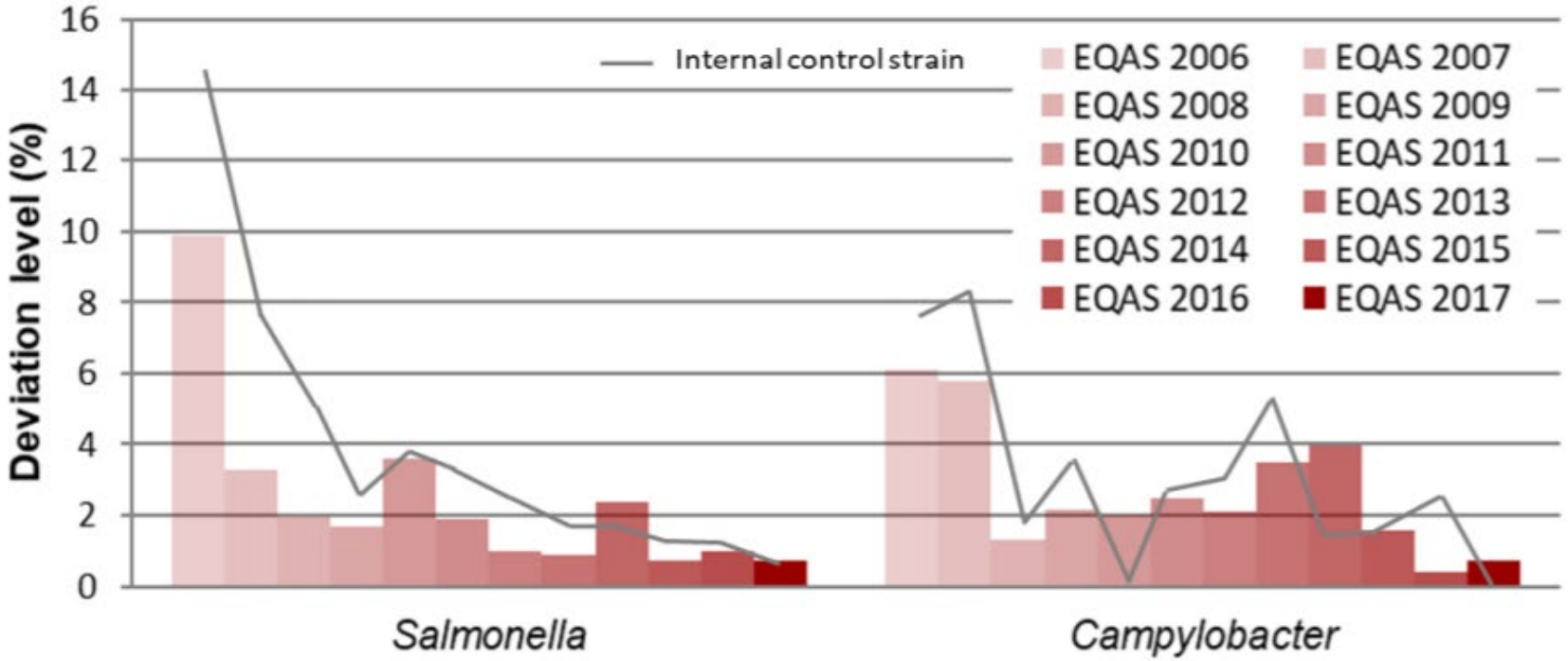
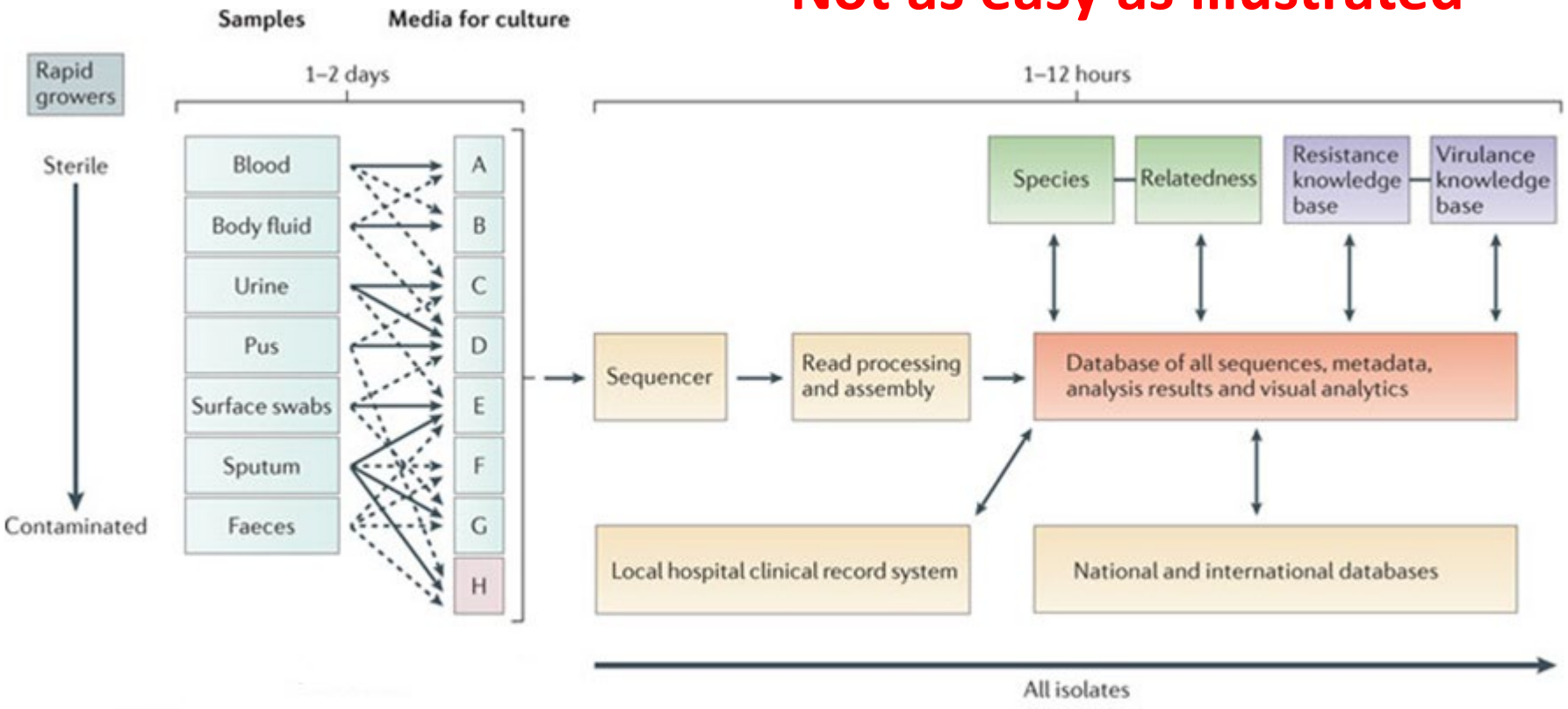


Figure 2: A comparison between the EURL-AR EQAS's since 2006, showing the total percentage of deviations for antimicrobial susceptibility testing performed by participating laboratories.

Paradigm shift in surveillance – "going genomics"

Not as easy as illustrated



Paradigm shift in surveillance – "Biggest revolution since Pasteur"

"It is likely that in 5 to 10 years, all clinical microbiological laboratories will have a DNA sequencer in use - the costs for a complete bacterial genome sequence might be less than 50 EURO (or US$).

The capacity to exchange – and manage - large data quantities over web-based systems has likewise increased dramatically over recent years

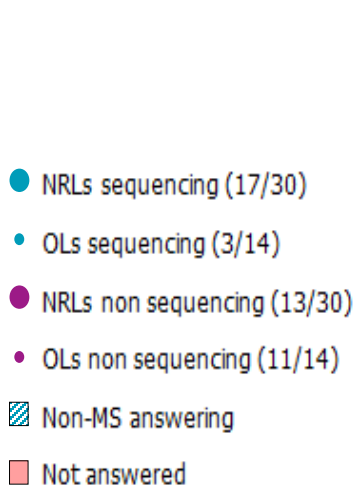
Enabling the potential creation of global databases consisting of DNA-codes of all relevant microbiological strains"

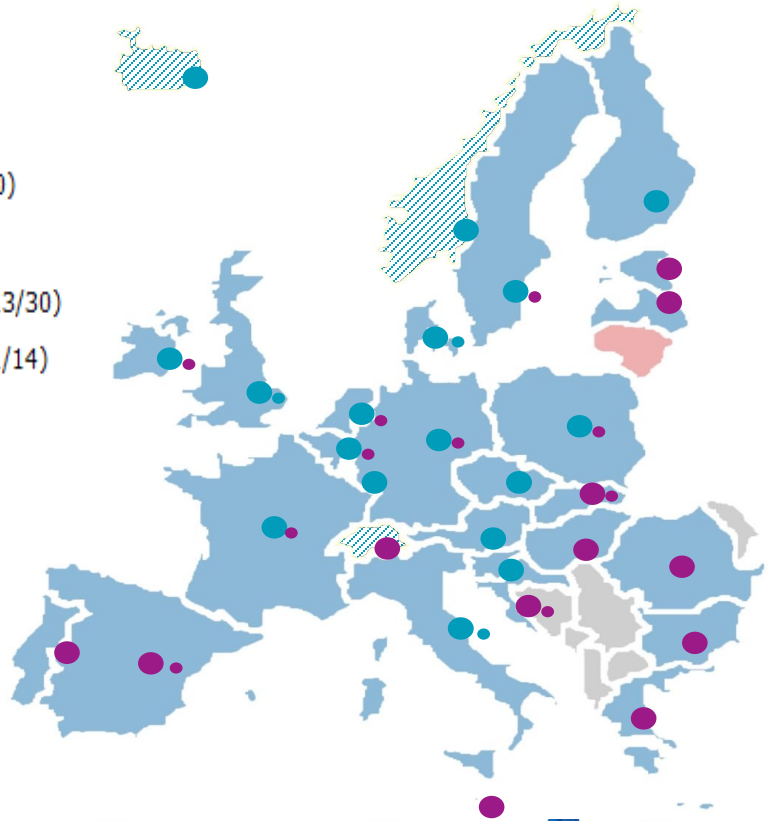
What do we have in place?

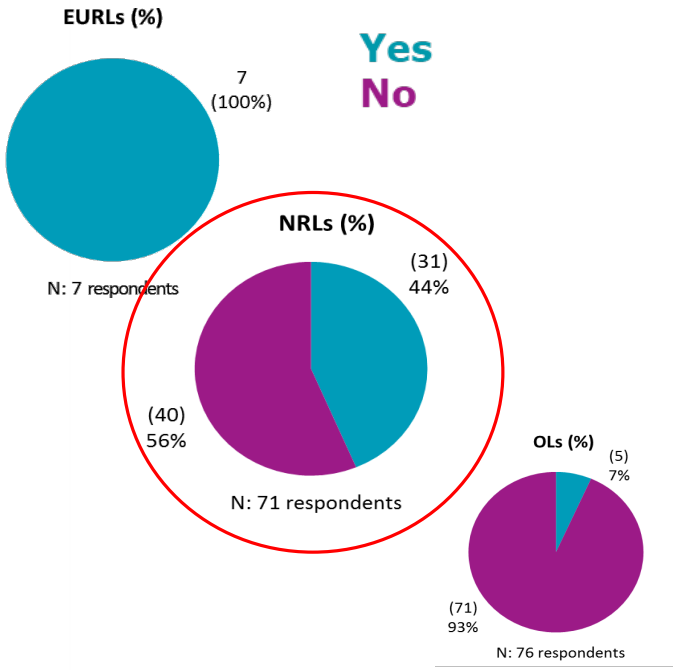
Source: Statement from the international expert meeting on GMI 1-2 September 2011 in Brussels, Belgium.

Sequencing capacity in EU (EFSA survey – 2016)

Q1. DO YOU CARRY OUT WGS ACTIVITIES? 28% YES (N=154 respondents)



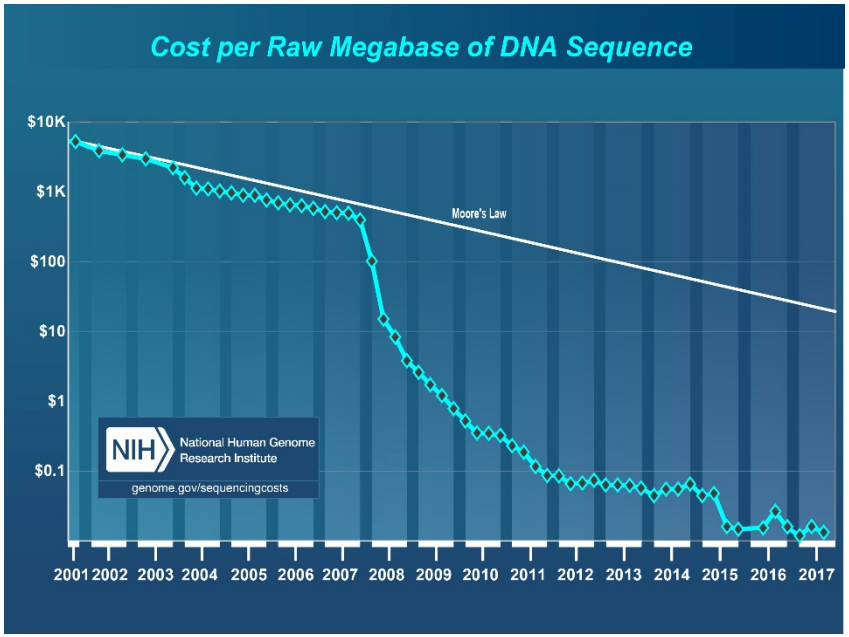


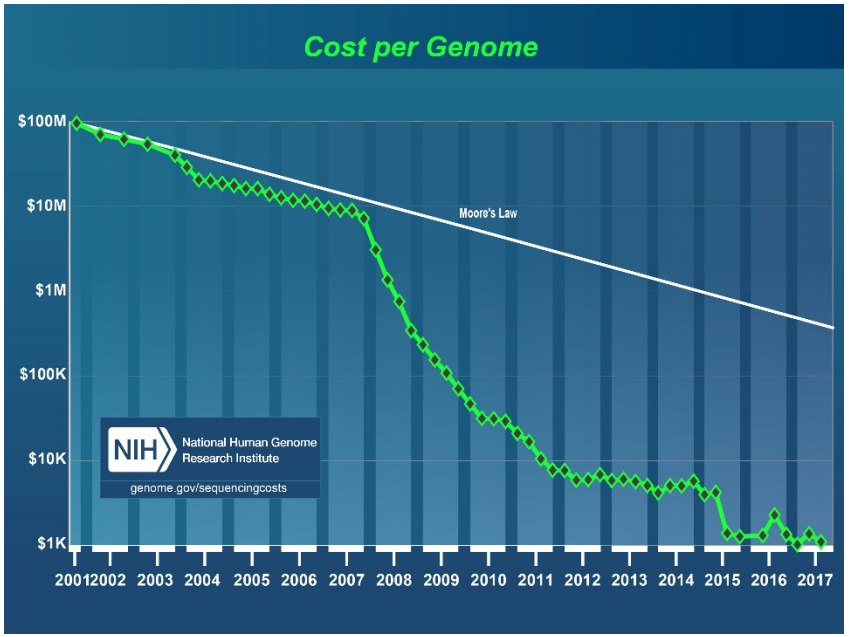


Status December 2016

Courtesy of Beatriz Guerra

Sequencing costs

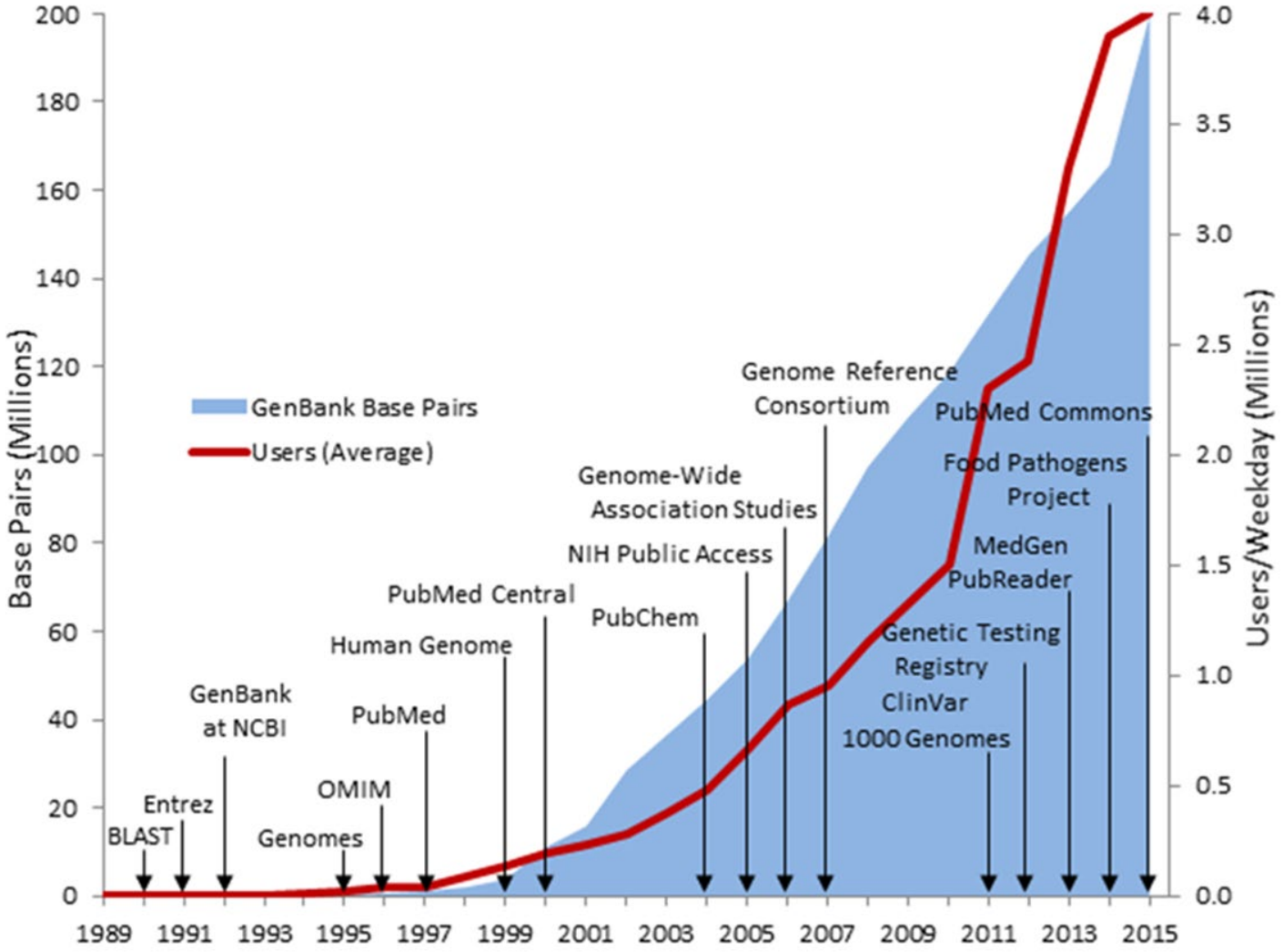




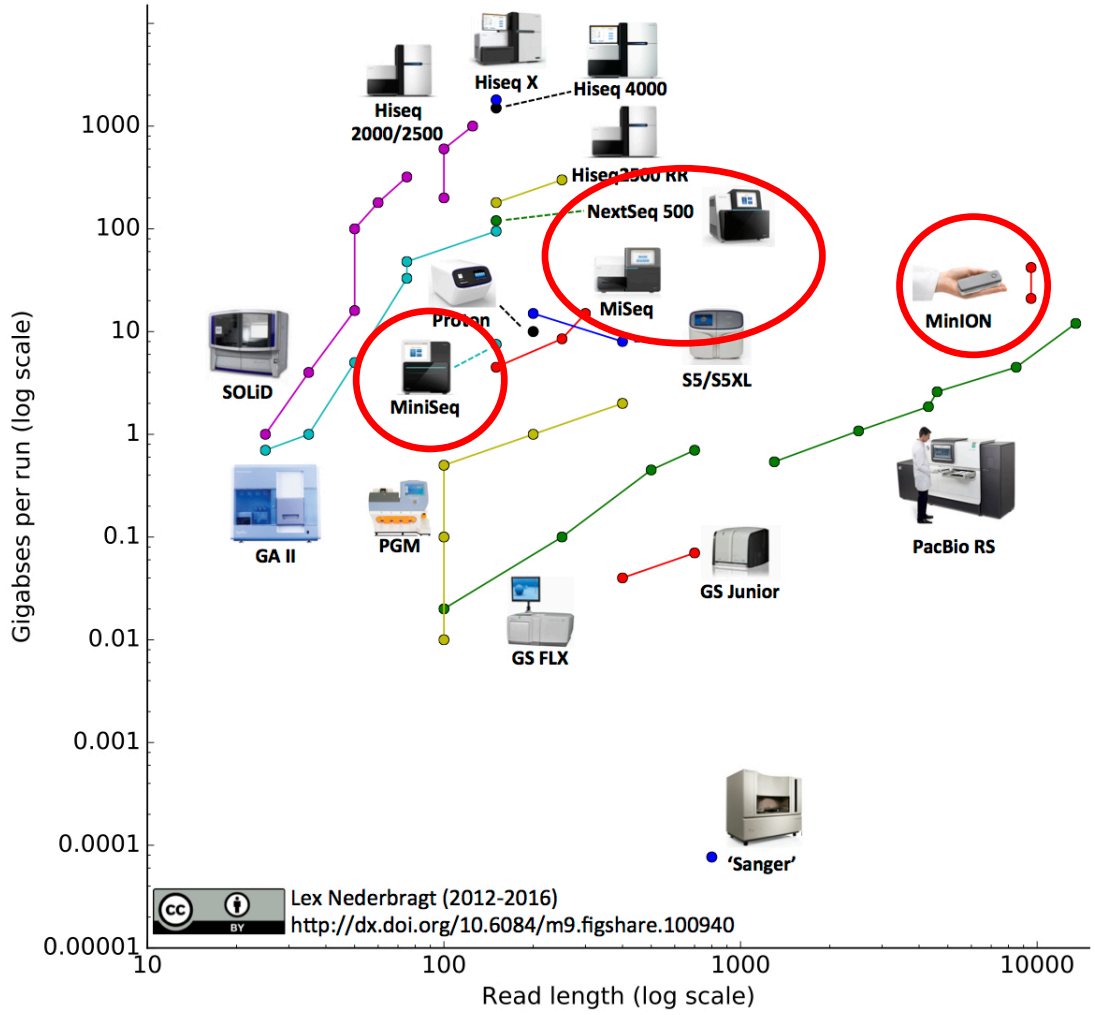
Cost of determining 1 Mb

Cost of sequencing a human-sized genome – $1K/3000Mb

Sequencing Bp production

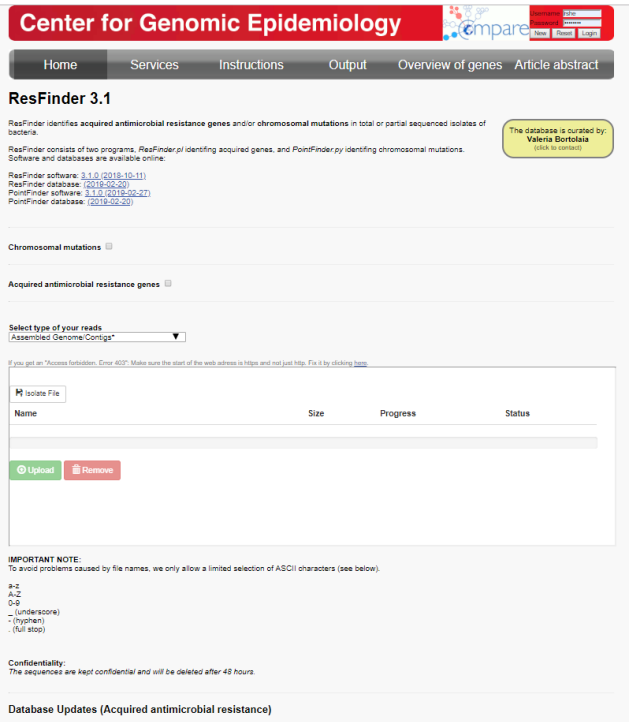


Sequencing platform development



Tools to predict antimicrobial resistance genes

- App. 40 resources for *in silico* prediction of AMR exists
- System features differ widely as to in- and out-put format
- Web-based vs commandline (GitHub) – shield end-user from complexities
- Open access vs commercial available
- Computing time
  - ARG-ANNOT
  - CARD
  - SRST2
  - MEGARes
  - GeneFinder
  - ARIBA
  - KmerFinder
  - AMRFinder (NARMS)
  - ResFinder (DANMAP)
  - etc….



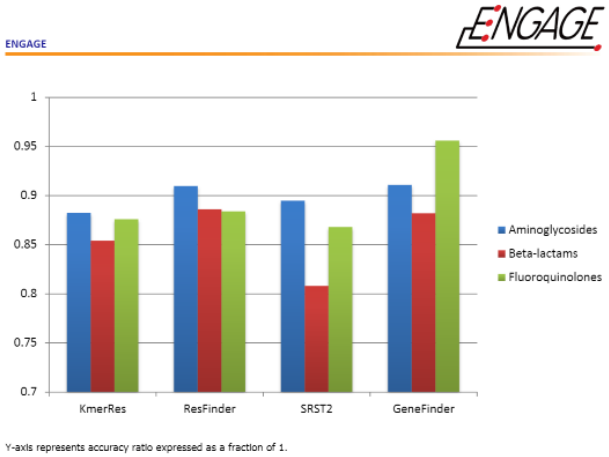
Benchmarking

Only a few studies have benchmarked bioinformatics tools – those previously mentioned

Challenges and considerations in benchmarking

- Origin of the dataset tested
- Sustainable reference datasets
- Quality of the test genomes
- What determinants to include a dataset
- Reference result, expected outcome
- Performance thresholds

Angers-Loustau A et al., F1000Res. 2018



Y-axis represents accuracy ratio expressed as a fraction of 1.

Figure H.1: Accuracy obtained by the benchmarked tools for three antimicrobial classes for the tested *Salmonella* dataset

Y-axis represents accuracy ratio expressed as a fraction of 1.

Figure H.2: Accuracy obtained by the benchmarked tools for three antimicrobial classes for the tested *E.coli* dataset

Final report of ENGAGE, EFSA supporting publication, 2018:EN-1431

Phenotype / genotype concordance

- High concordance (> 96%) between acquired resistance genes / mutations and MIC
- High levels of sensitivity (>87%) and specificity (>98%) have been observed depending of the species analysed

Pathogen	No. of pathogens	AST method	No. of antimicrobials	Bioinformatic tool	Sequencing data	Concordance	Sensitivity	Specificity	Comment	Reference
S. Typhimurium E. coli E. faecalis E. faecium	49 48 50 50	MIC	17 14	ResFinder	Assembled, Velvet	99.74%			Disagreement: 7 isolates: 6 E.coli to SPEC	Zankari etal., 2013
E. coli (ESBL) K. pneumonia (ESBL)	74 69	DD	7	BLASTn, selected panel	Assembled, Velvet		96%	97%	VM rate: 1.2%/ M rate: 2.1%	Stoesser et al., 2013
S. aureus	501	DD/ MIC (Vitek)	12	BLASTn, selected panel	Assembled, Velvet		97%	99%	VM rate: 0.5%/ M rate: 0.7%	Gordon NC et al., 2014
C. jejuni C. coli	32 82	MIC	9	BLASTx	Assembled, CLC	99.2%			Lower concordance to Gen, Azi, Clin, Tel	Zhao et al., 2016
S. enterica	104 536	MIC	14	ResFinder/ ARG-ANNOT/ CARD/ BLAST	Assembled, CLC	99.0%	99.2% 97.6%	99.3% 98.0%	Lower concordance to aminoglycosides / β-lactams	McDermott et al., 2016
E. coli K. pneumonia P. aeruginosa E. cloacae	31 24 22 13	MIC	4	Custom DB based on ARDB/ CARD/ β-lactamase allelles			**87%**	**98%**	Neg. predictive value: 97% Pos. Predictive value: 91%	Shelburne et al., 2017
S. enterica E. coli C. jejuni	50 50 50	MIC	4 6 4	ResFinder/ PointFinder	Assembled, SPAdes	98.4%			Disagreement: 2/2 C.jejuni to FQ/ERY 5 E.coli to COL (pmrB)	Zankari etal., 2017
E. faecalis E. faecium	97 100	MIC	11	ResFinder/ NCBI Pathogen DB/ BLAST	Assembled, CLC	**96.5%**				Tyson et al., 2018
S. aureus	501 491 397	DD / MIC MIC	12	GeneFinder/ Mykrobe/ Typewriter	fastq / assembled, BLAST	98.3%			Disagreements: 0.7% predicted resistant 0.6% predicted susceptible	Mason et al., 2018
M. tyberculosis	10.209	MGIT 960	Isoniazid Rifampin Ethambutol Pyrazinamide	Cortex	Assembled	89.5%			97.1%/ 99.0% predicted R/ S 97.5%/ 98.8% predicted R/ S 94.6%/ 93.6% predicted R/ S 91.3%/ 96.8% predicted R/ S	Walker et al., 2018
H. pylori	140	MIC (E-test)	5	ARIBA	fastq	99%			Phenotype issues to metronidazole	Lauener et al., 2019

Validation of surveillance data – EURL confirmatory testing of MIC data

230 (of 307) strains, 24 antimicrobials → 5520 MIC determinations

AZI: 97.3 % phenotype-genotype concordance
10 resistant strains with *mph*(A)
2 resistant strains with no gene
4 susceptible strains with *mph*(A)
214 susceptible strains with no res. gene

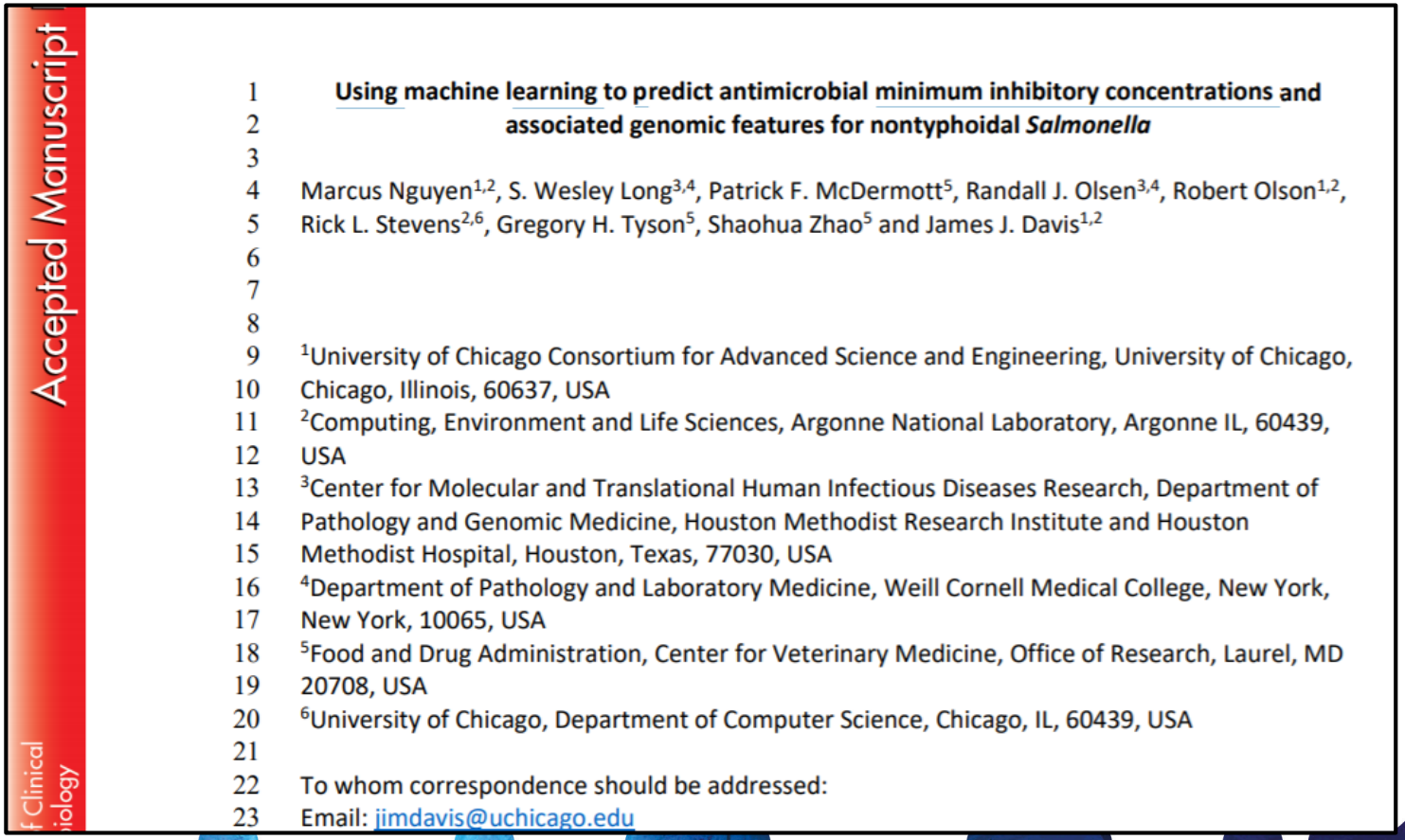
MERO: 100 % phenotype-genotype concordance
3 resistant strains with $bla_{OXA-162}$
227 susceptible strain with no res. gene

COL: 95.6 % phenotype-genotype concordance
22 resistant strains with mcr-1 (n=20), mcr-1.2 (n=1), pmrB V161M (n=1)
10 resistant strains with no res. gene
198 susceptible strains with no res. gene

3rd generation cephalosporins : 99.1 % phenotype-genotype concordance
151 resistant strains with res. gene (bla_{CMY-2}, $bla_{CTX-M-1}$, bla_{SHV-12},up-reg. *ampC*, $bla_{CTX-M-15}$)
2 resistant strains with no res. gene
77 resistant strains with no res. gene

Courtesy of Valeria Bortolaia

Using machine learning to predict MIC or detect novelties



Accepted Manuscript

Using machine learning to predict antimicrobial minimum inhibitory concentrations and associated genomic features for nontyphoidal *Salmonella*

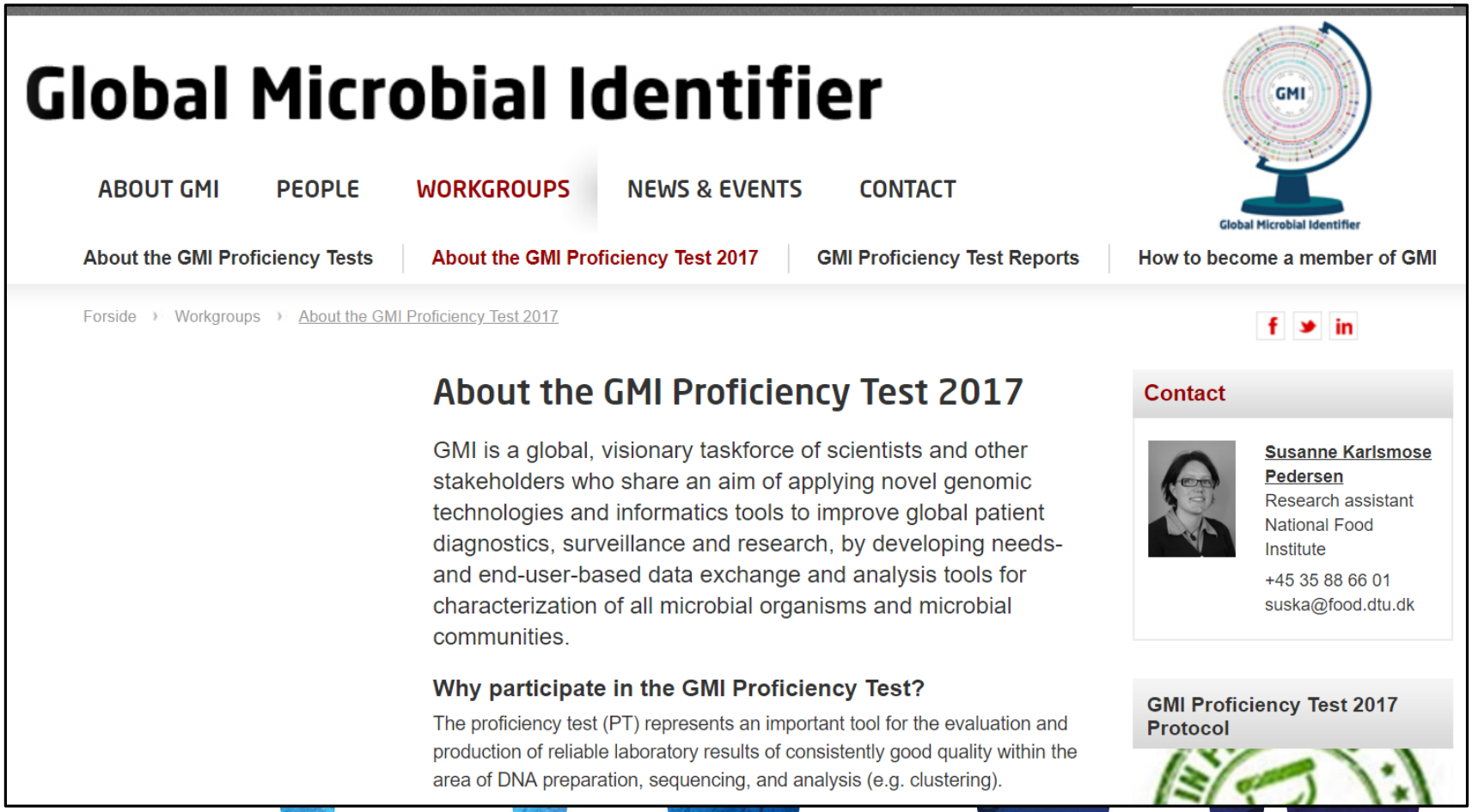
Marcus Nguyen[1,2], S. Wesley Long[3,4], Patrick F. McDermott[5], Randall J. Olsen[3,4], Robert Olson[1,2], Rick L. Stevens[2,6], Gregory H. Tyson[5], Shaohua Zhao[5] and James J. Davis[1,2]

[1]University of Chicago Consortium for Advanced Science and Engineering, University of Chicago, Chicago, Illinois, 60637, USA
[2]Computing, Environment and Life Sciences, Argonne National Laboratory, Argonne IL, 60439, USA
[3]Center for Molecular and Translational Human Infectious Diseases Research, Department of Pathology and Genomic Medicine, Houston Methodist Research Institute and Houston Methodist Hospital, Houston, Texas, 77030, USA
[4]Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, New York, 10065, USA
[5]Food and Drug Administration, Center for Veterinary Medicine, Office of Research, Laurel, MD 20708, USA
[6]University of Chicago, Department of Computer Science, Chicago, IL, 60439, USA

To whom correspondence should be addressed:
Email: jimdavis@uchicago.edu

Nguyen et al., JCM 2018

Quality control of genomes – proficiency testing



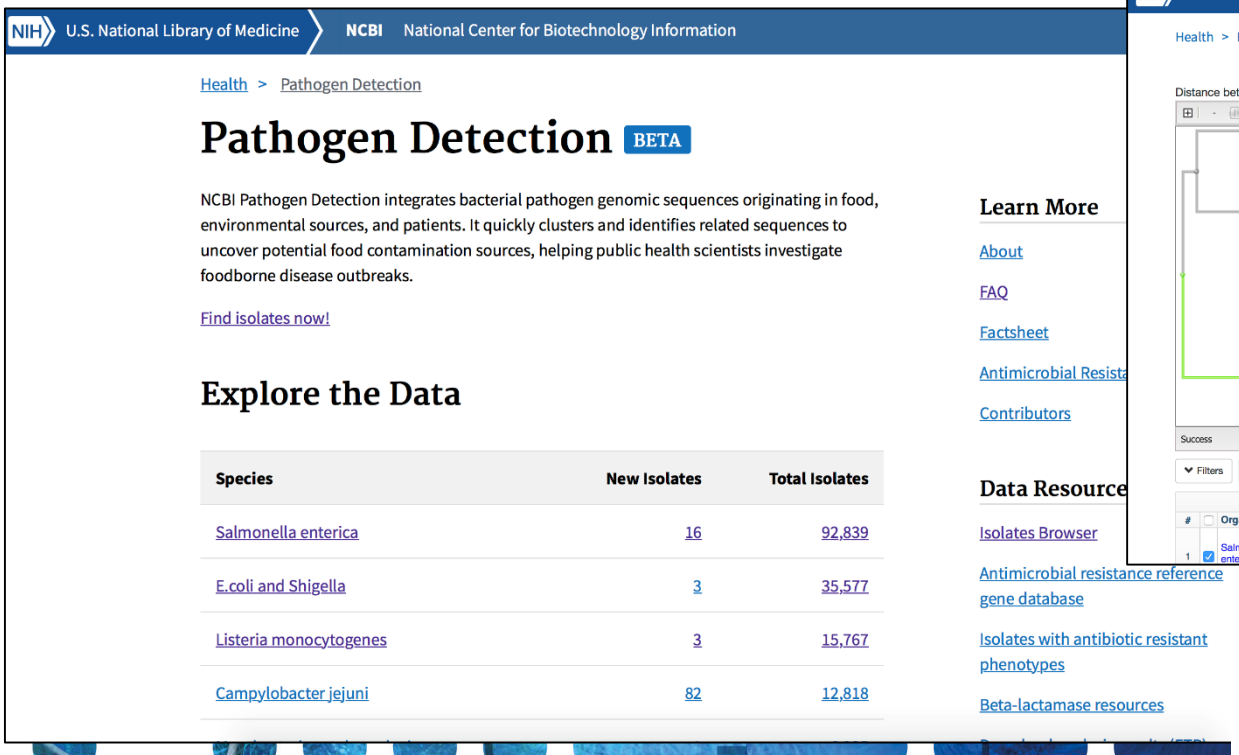
Data sharing

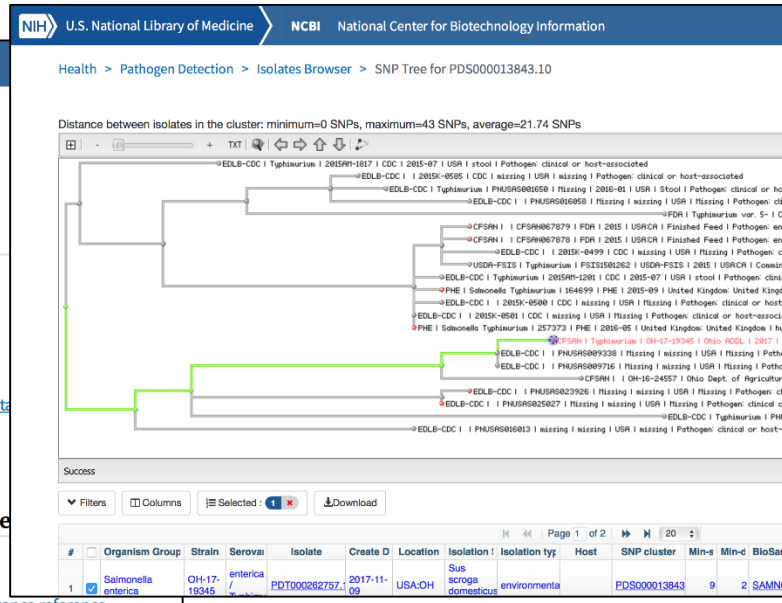
- A huge potential of global sharing to facilitate a global monitoring of AMR and pathogens in general
- Possible to submit and store DNA sequence data in the International Nucleotide Sequence Database Collaboration,
  - AST data is normally stored separately in closed local or national repositories
  - NCBI and EMBL-EBI has created or in development to host and link submitted genome and AST data
- The greatest barrier for global surveillance using genomic data is the fear to share data
  - **Privacy of the data – General Data Protection Regulation**
  - Difficulties to submit
  - Lack of appreciation for its value
  - Access to local or national repositories

Amid et al., 2019, Matamoros et al., 2019

Data sharing - US repository (Open access)

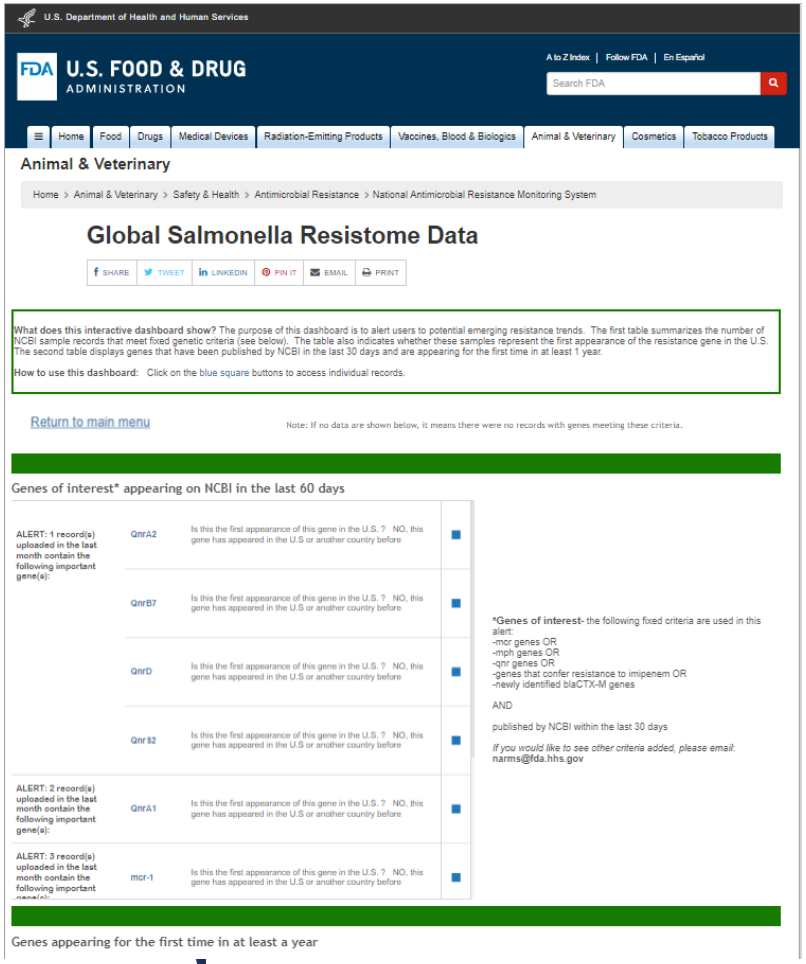
- The number of genome submitted is expected to rise > 100,000 annually from US sources alone
- To facilitate open access, the NCBI Pathogens page was developed to include major foodborne and zoonotic pathogens





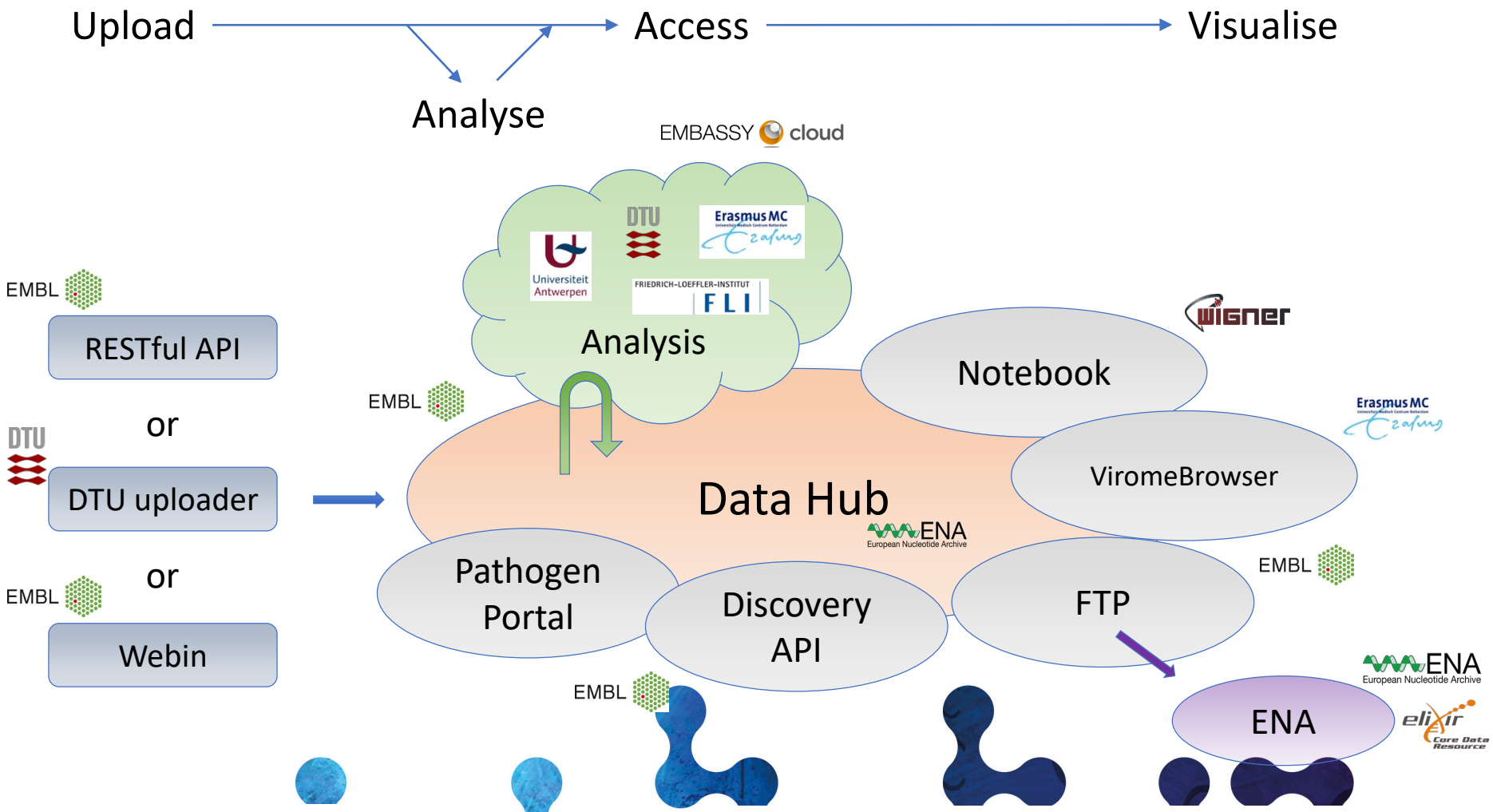
www.ncbi.nlm.nih.gov/pathogens

Data sharing - US repository (Open access)



www.ncbi.nlm.nih.gov/pathogens

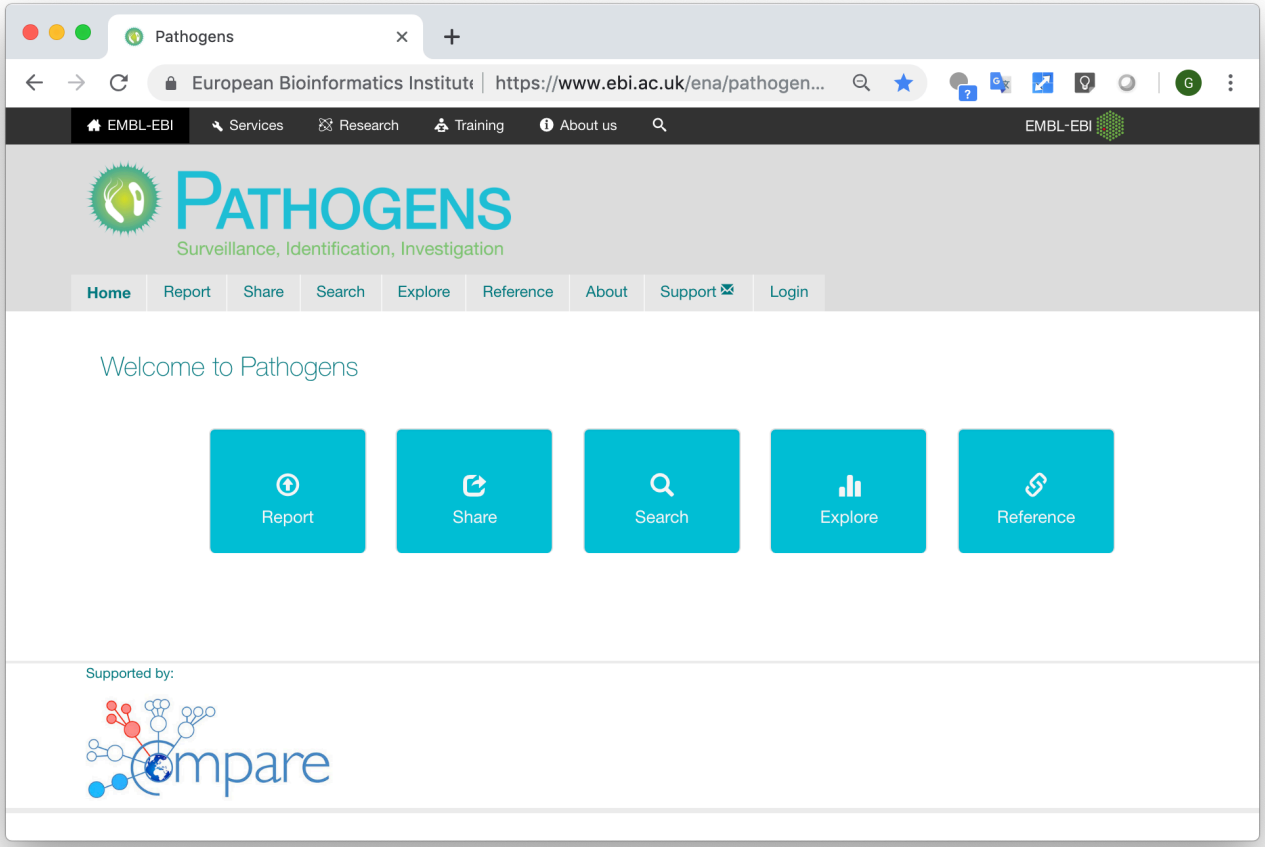
Data sharing – COMPARE platform (Private data hubs)



Courtesy of Guy Cochrane

https://www.biorxiv.org/content/10.1101/555938v1

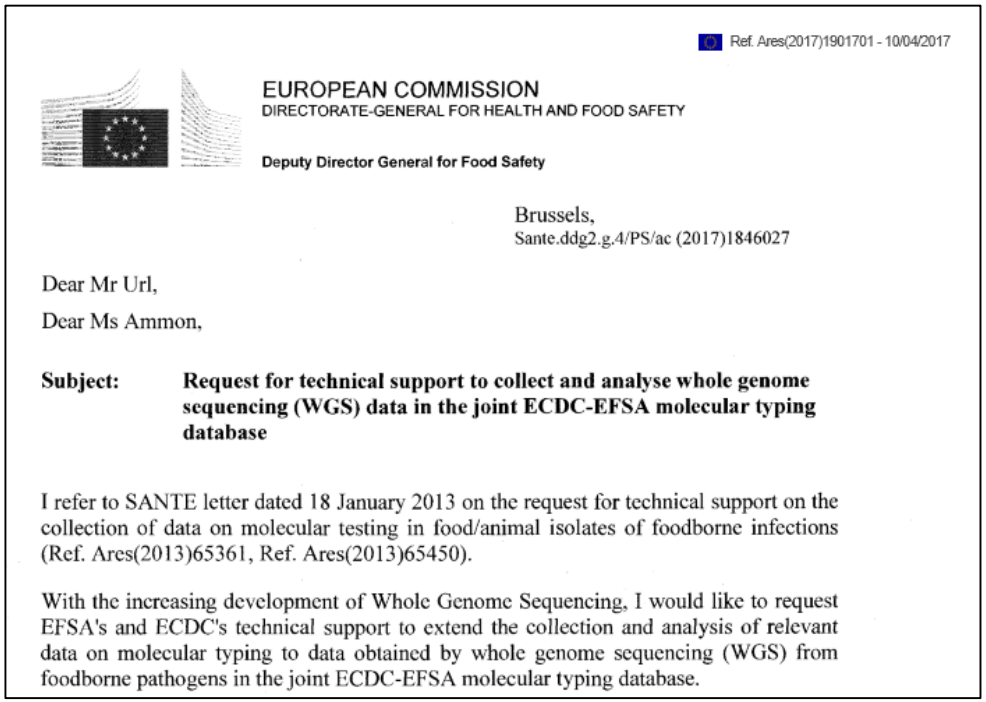
Data sharing – COMPARE platform (Private data hubs)



www.ebl.ac.uk/ena/pathogen

Courtesy of Pataki Bálint Ármin and Csabai István

Data sharing – ECDC-EFSA molecular typing DB



Ref. Ares(2017)1901701 - 10/04/2017

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Deputy Director General for Food Safety

Brussels,
Sante.ddg2.g.4/PS/ac (2017)1846027

Dear Mr Url,

Dear Ms Ammon,

Subject: **Request for technical support to collect and analyse whole genome sequencing (WGS) data in the joint ECDC-EFSA molecular typing database**

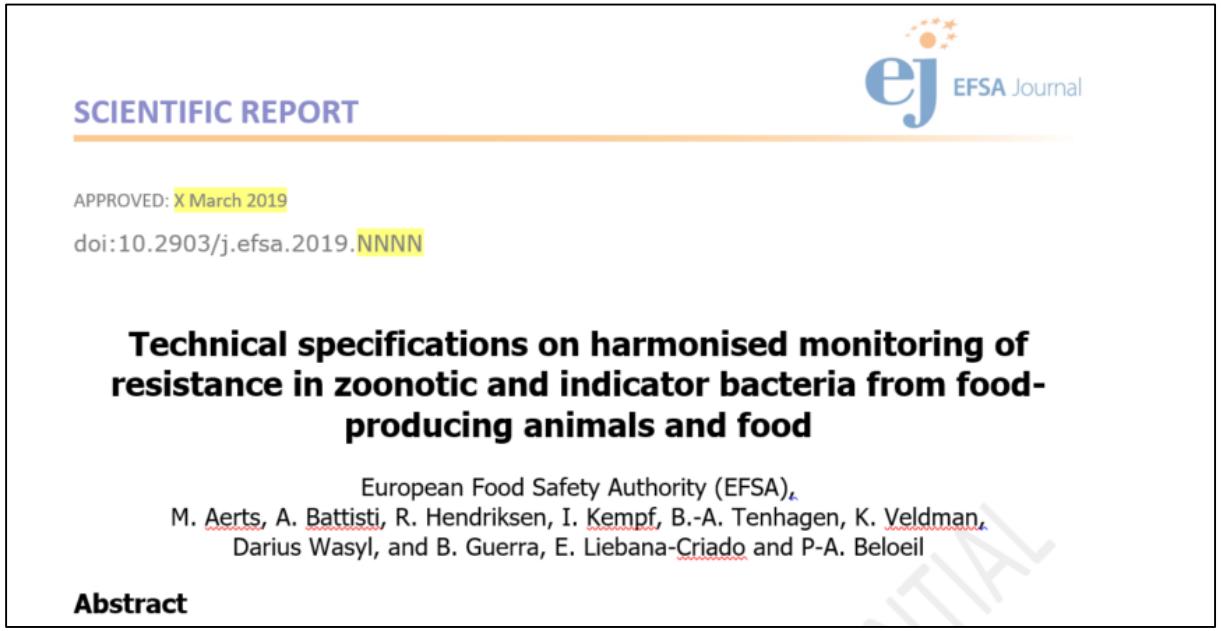
I refer to SANTE letter dated 18 January 2013 on the request for technical support on the collection of data on molecular testing in food/animal isolates of foodborne infections (Ref. Ares(2013)65361, Ref. Ares(2013)65450).

With the increasing development of Whole Genome Sequencing, I would like to request EFSA's and ECDC's technical support to extend the collection and analysis of relevant data on molecular typing to data obtained by whole genome sequencing (WGS) from foodborne pathogens in the joint ECDC-EFSA molecular typing database.

TOR: Conducting a consultation of relevant actors and players to **assess the state of the art of pipelines for collecting and analysing WGS data in Europe**

Future in antimicrobial resistance surveillance (proposal)

Preliminary draft



SCIENTIFIC REPORT

EFSA Journal

APPROVED: X March 2019

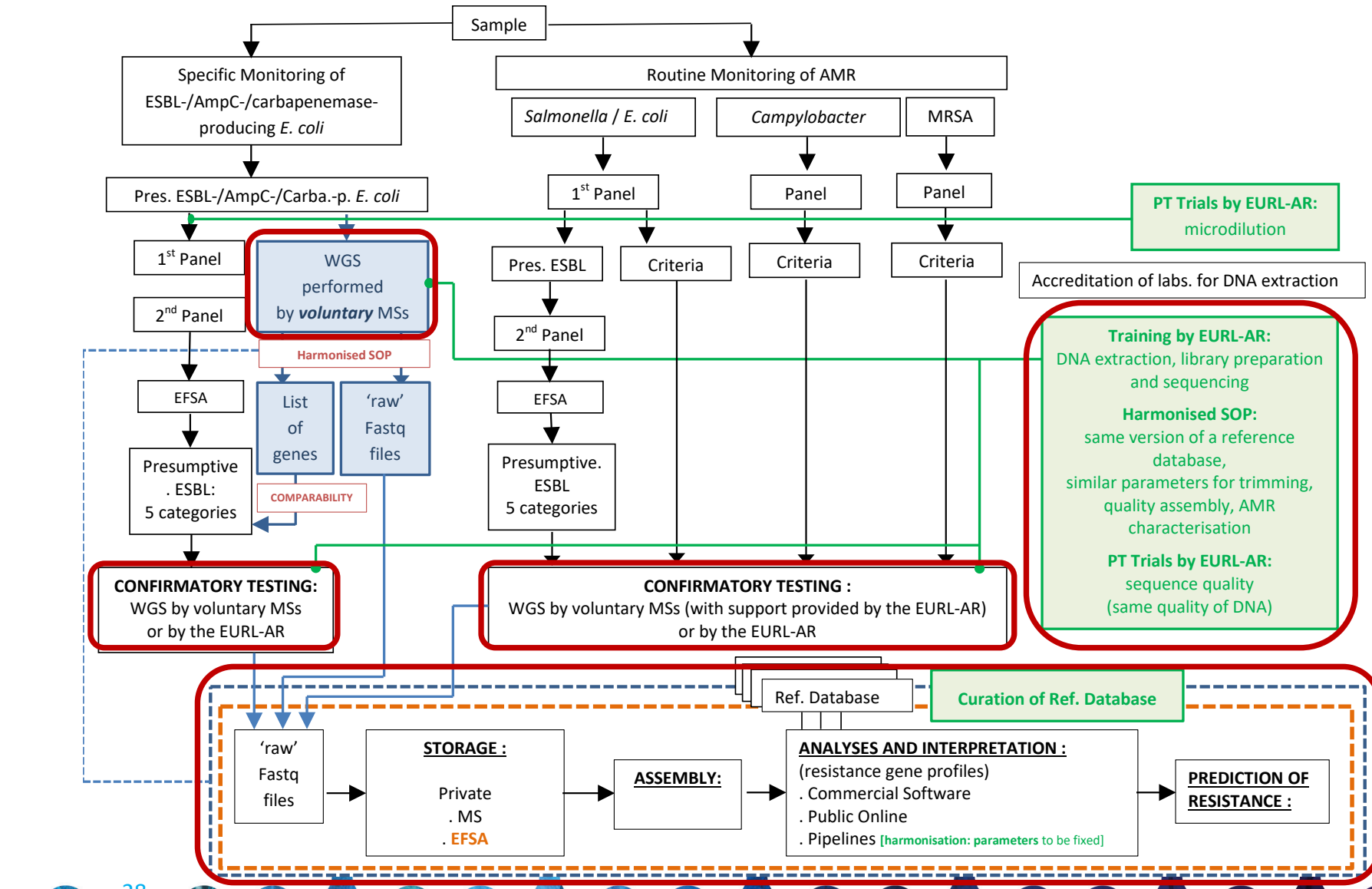
doi:10.2903/j.efsa.2019.NNNN

Technical specifications on harmonised monitoring of resistance in zoonotic and indicator bacteria from food-producing animals and food

European Food Safety Authority (EFSA),
M. Aerts, A. Battisti, R. Hendriksen, I. Kempf, B.-A. Tenhagen, K. Veldman, Darius Wasyl, and B. Guerra, E. Liebana-Criado and P-A. Beloeil

Abstract

Proposal: To achieve the goal of **implementing WGS across the food and veterinary sectors of the NRLs during the up-coming Commission Implementing Decision's validity period (2021-20xx)**, as well as use in the specific monitoring, it also proposed that the participation to the 'Confirmatory Testing' exercise, possibly using WGS on a voluntary basis, with the support of the EURL-AR, becomes mandatory.


Sample
Specific Monitoring of ESBL-/AmpC-/carbapenemase-producing E. coli
Routine Monitoring of AMR
Salmonella / E. coli
Campylobacter
MRSA
Pres. ESBL-/AmpC-/Carba.-p. E. coli
1st Panel
Panel
Panel
PT Trials by EURL-AR: microdilution
1st Panel
WGS performed by voluntary MSs
Pres. ESBL
Criteria
Criteria
Criteria
Accreditation of labs. for DNA extraction
2nd Panel
2nd Panel
Harmonised SOP
EFSA
List of genes
'raw' Fastq files
EFSA
Training by EURL-AR: DNA extraction, library preparation and sequencing
Harmonised SOP: same version of a reference database, similar parameters for trimming, quality assembly, AMR characterisation
PT Trials by EURL-AR: sequence quality (same quality of DNA)
Presumptive . ESBL: 5 categories
COMPARABILITY
Presumptive. ESBL 5 categories
CONFIRMATORY TESTING: WGS by voluntary MSs or by the EURL-AR
CONFIRMATORY TESTING : WGS by voluntary MSs (with support provided by the EURL-AR) or by the EURL-AR
Ref. Database
Curation of Ref. Database
'raw' Fastq files
STORAGE :
Private
. MS
. EFSA
ASSEMBLY:
ANALYSES AND INTERPRETATION :
(resistance gene profiles)
. Commercial Software
. Public Online
. Pipelines [harmonisation: parameters to be fixed]
PREDICTION OF RESISTANCE :

Future in antimicrobial resistance surveillance (proposal)

Table 15: Possible approach to integration of WGS by MSs within harmonised monitoring of AMR over the 2021-2026 period

Year	WGS applied to				
	Specific monitoring of ESBL/AmpC/ carbapenemase-producing *E. coli*	MSs WGS Confirmatory testing	Indicator *E. coli* (a)	*Salmonella*	*Campylobacter*
2021	Voluntary	Voluntary	NA (Phenotypic)	Phenotypic	Phenotypic
2022	Voluntary	Voluntary	NA (Phenotypic)	NA (Phenotypic)	NA (Phenotypic)
2023	Voluntary	Voluntary	NA (Phenotypic)	NA (Phenotypic)	NA (Phenotypic)
2024	Voluntary	Voluntary	NA (Phenotypic)	NA (Phenotypic)	NA (Phenotypic)
2025	Mandatory	Voluntary	NA (Phenotypic)	NA (Phenotypic)	NA (Phenotypic)
2026	Mandatory	Voluntary	TBD	TBD	TBD

Building capacity for genomic-based surveillance

EXTERNAL SCIENTIFIC REPORT

ENGAGE

APPROVED: 8 June 2018

doi:10.2903/sp.efsa.2018.EN-1431

Final report of ENGAGE - Establishing Next Generation sequencing Ability for Genomic analysis in Europe

Rene S. Hendriksen[1], Susanne Karlsmose Pedersen[1], Pimlapas Leekitcharoenphon[1], Burkhard Malorny[2], Maria Borowiak[2], Antonio Battisti[3], Alessia Franco[3], Patricia Alba[3], Virginia Carfora[3], Antonia Ricci[4], Eleonora Mastrorilli[4], Carmen Losasso[4], Alessandra Longo[4], Sara Petrin[4], Lisa Barco[4], Tomasz Wołkowicz[5], Rafał Gierczyński[5], Katarzyna Zacharczuk[5], Natalia Wolaniuk[5], Dariusz Wasyl[6], Magdalena Zając[6], Kinga Wieczorek[6], Katarzyna Półtorak[6], Liljana Petrovska-Holmes[7], Rob Davies[7], Yue Tang[7], Kathie Grant[8], Anthony Underwood[8], Timothy Dallman[8], Anaïs Painset[8], Hassan Hartman[8], Ali Al-Shabib[8], and Lauren Cowley[8]

European Union Reference Laboratory Antimicrobial Resistance

In the project period, ENGAGE has shown that it is possible to implement WGS and the use of bioinformatics tools in laboratories without any prior knowledge of WGS, and that other countries can be supported to do this through partnerships. In addition, ENGAGE has showed that some current phenotypic methodologies, e.g. *Salmonella* serotyping, could in the future be replaced by WGS and the use of bioinformatics tools. The ENGAGE project was successful on many levels both in terms of boosting WGS and analysis capacity and capability across Europe but also in demonstrating advantages of having genome data sets from different sources and different countries for validation and benchmarking exercises as well as investigative analyses. To date there has been little benchmarking of bioinformatics tools for microbial genome analysis and this project has contributed significantly to this which is beneficial to all who use such tools. A limitation to move the WGS

Future in antimicrobial resistance surveillance - Next step - Metagenomics

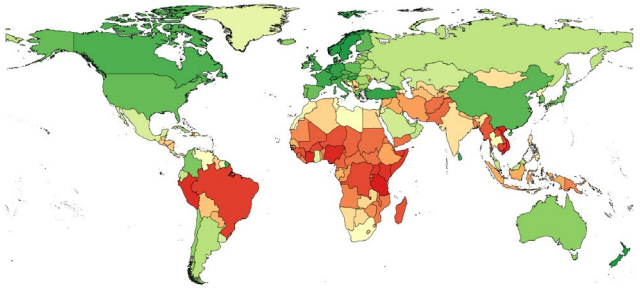
nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-08853-3 OPEN

Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage

Rene S. Hendriksen[1], Patrick Munk[1], Patrick Njage[1], Bram van Bunnik[2], Luke McNally[3], Oksana Lukjancenko[1], Timo Röder[1], David Nieuwenhuijse[4], Susanne Karlsmo, Rolf S. Kaas[1], Philip Thomas Lanken Conradsen Clausen[1], Josef Korbinian Vo, Milou G.M. van de Schans[5], Tina Zuidema[5], Ana Maria de Roda Husman[6], S, Bent Petersen[7], The Global Sewage Surveillance project consortium[#], Clara A, Thomas Sicheritz-Ponten[9], Heike Schmitt[6], Jorge Raul Matheu Alvarez[10], Aw, Ole Lund[7], Tine Hald[1], Mark Woolhouse[2], Marion P. Koopmans[4], Håkan Vig, Frank M. Aarestrup[1]



ARTICLES

https://doi.org/10.1038/s41564-018-0192-9

nature microbiology

Corrected: Author Correction

Abundance and diversity of the faecal resistome in slaughter pigs and broilers in nine European countries

Patrick Munk[1], Berith Elkær Knudsen[1], Oksana Lukjancenko[1], Ana Sofia Ribeiro Duarte[1], Liese Van Gompel[2], Roosmarijn E. C. Luiken[2], Lidwien A. M. Smit[2], Heike Schmitt[2], Alejandro Dorado Garcia[2], Rasmus Borup Hansen[3], Thomas Nordahl Petersen[1], Alex Bossers[2,4], Etienne Ruppé[5], EFFORT Group[6], Ole Lund[1], Tine Hald[1], Sünje Johanna Pamp[1], Håkan Vigre[1], Dick Heederik[2], Jaap A. Wagenaar[4,7], Dik Mevius[4,7] and Frank M. Aarestrup[1*]

Future in antimicrobial resistance surveillance - Next step - Metagenomics

Advantages, challenges and added value by a genomic surveillance

- Seems to be **more reliable** that conventional methodologies to determine antimicrobial resistance
  - Define MDR with a much greater precision
- WGS data stored, **remain easily available** for future investigations
  - Offers the unique opportunity to **re-analyze** previously collected data,
- Data is **easy to share**, but a major challenge due to **GDPR**
- **Standardization and accreditation** of methods may be a challenge
  - ISO/TC 34/SC 9/WG 25 "Whole-genome sequencing for typing and genomic characterization"
- Harmonization
  - Centralized all analysis OR agreements to ensure harmonization
- Capacity building - bring all MSs to a certain level
- Added value of WGS to **extract additional information** about bacterial speciation, typing, plasmid, cluster analysis and to improve the understanding of emerging AMR

Take home message

- Current phenotypic susceptibility methods still being “the golden standard”
- In the last decade, WGS/NGS has entering research and diagnostic with near real time data generation
- Sequencing seems to be a realistic alternative to conventional phenotypic susceptibility methods for surveillance of AMR
    - Assessed and proven by research
    - Considerable large added value
- Infrastructure already created to initiate a full rollout of the paradigm shift
    - A need to build capacity in MS – to the same level as best
        - Incentive – qualify to research grants (investment)
- Perspectives to combine with advanced mathematical modelling for predictions and extrapolations
- Overcome the sharing barrier

Thank you for your attention

Rene S. Hendriksen, PhD

Research Group Genomic Epidemiology
WHO Collaborating Centre for Antimicrobial Resistance in Food borne Pathogens and Genomics
European Union Reference Laboratory for Antimicrobial Resistance

National Food Institute, Technical University of Denmark

rshe@food.dtu.dk