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FACULTY
OF BIOTECHNOLOGY

PORTO

Antibiotic resistant bacteria as contaminants of emerging concern

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2nd Summer School on

Environmental Applications of Advanced Oxidation Processes

***and* Training School** on

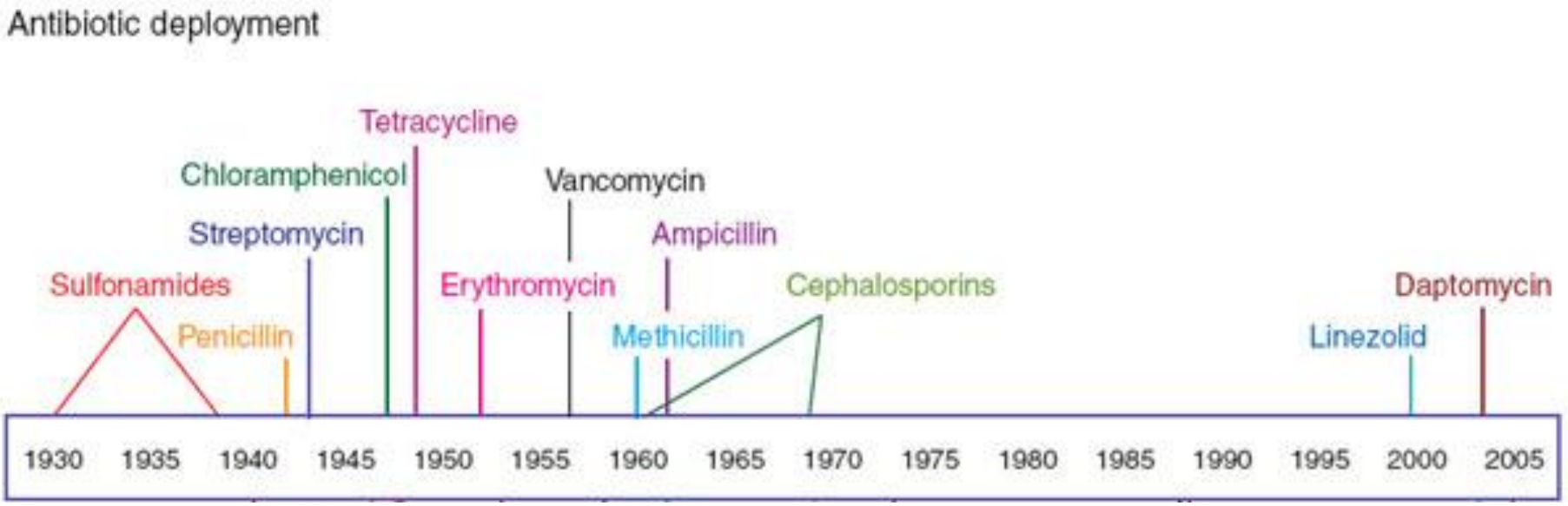
Advanced Treatment Technologies and Contaminants of Emerging Concern

(NEREUS COST Action ES1403)

nereus COST ACTION ES1403

AOPs PhD School

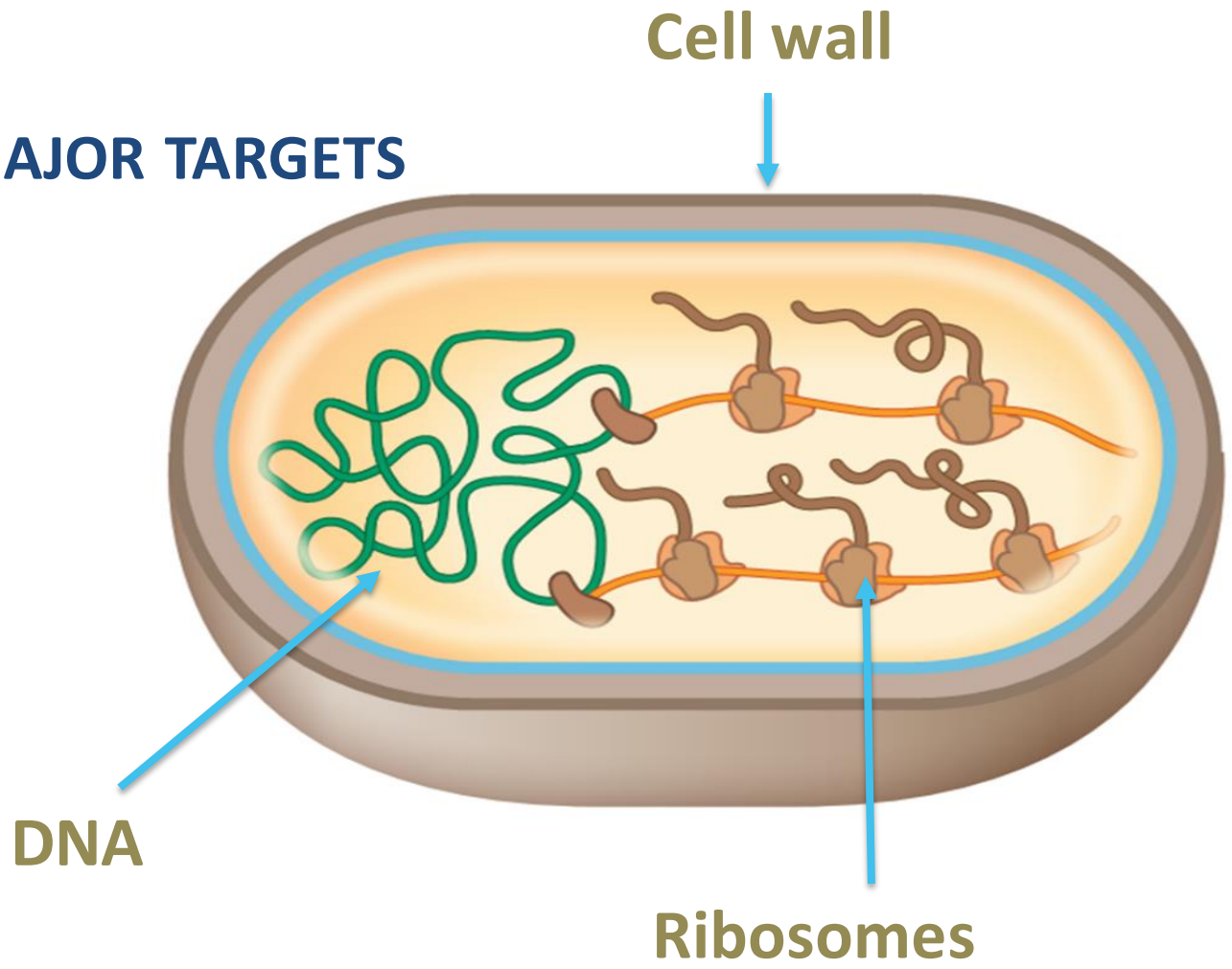
~75 YEARS OF ANTIBIOTHERAPY …



Clatworthy et al. (2007) Nature Chemical Biology **3**, 541 - 548

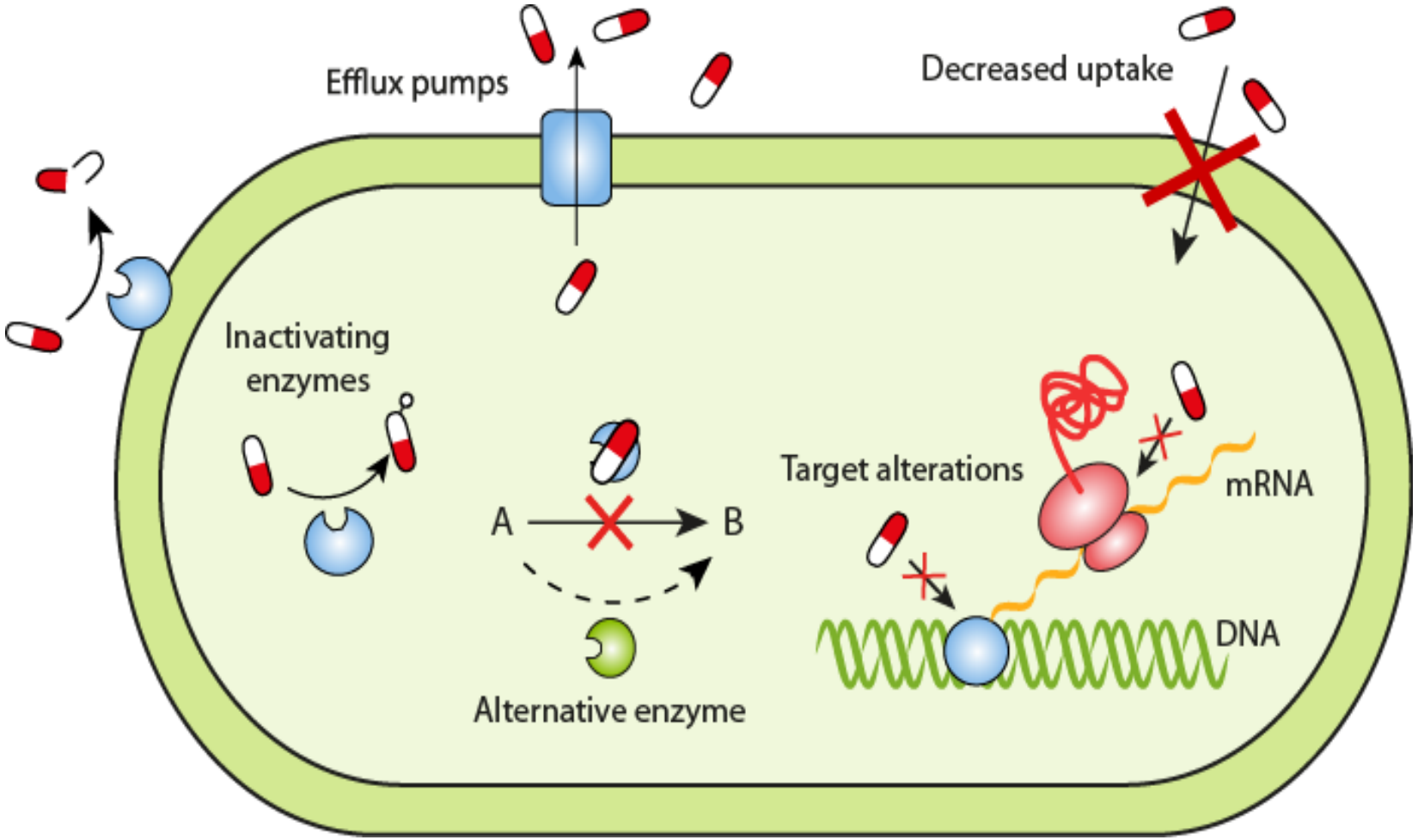
ANTIBIOTICS TARGET SPECIFIC STRUCTURES IN THE BACTERIAL CELL

THREE MAJOR TARGETS



Lewis (2013) Nature Reviews Drug Discovery 12, 371–387

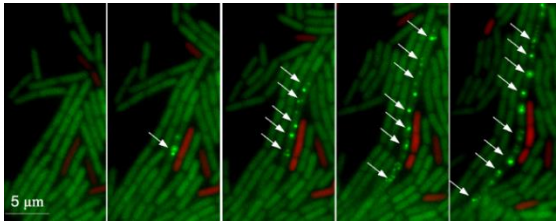
FIVE GENERAL RESISTANCE MECHANISMS



HUNDREDS OF GENES...

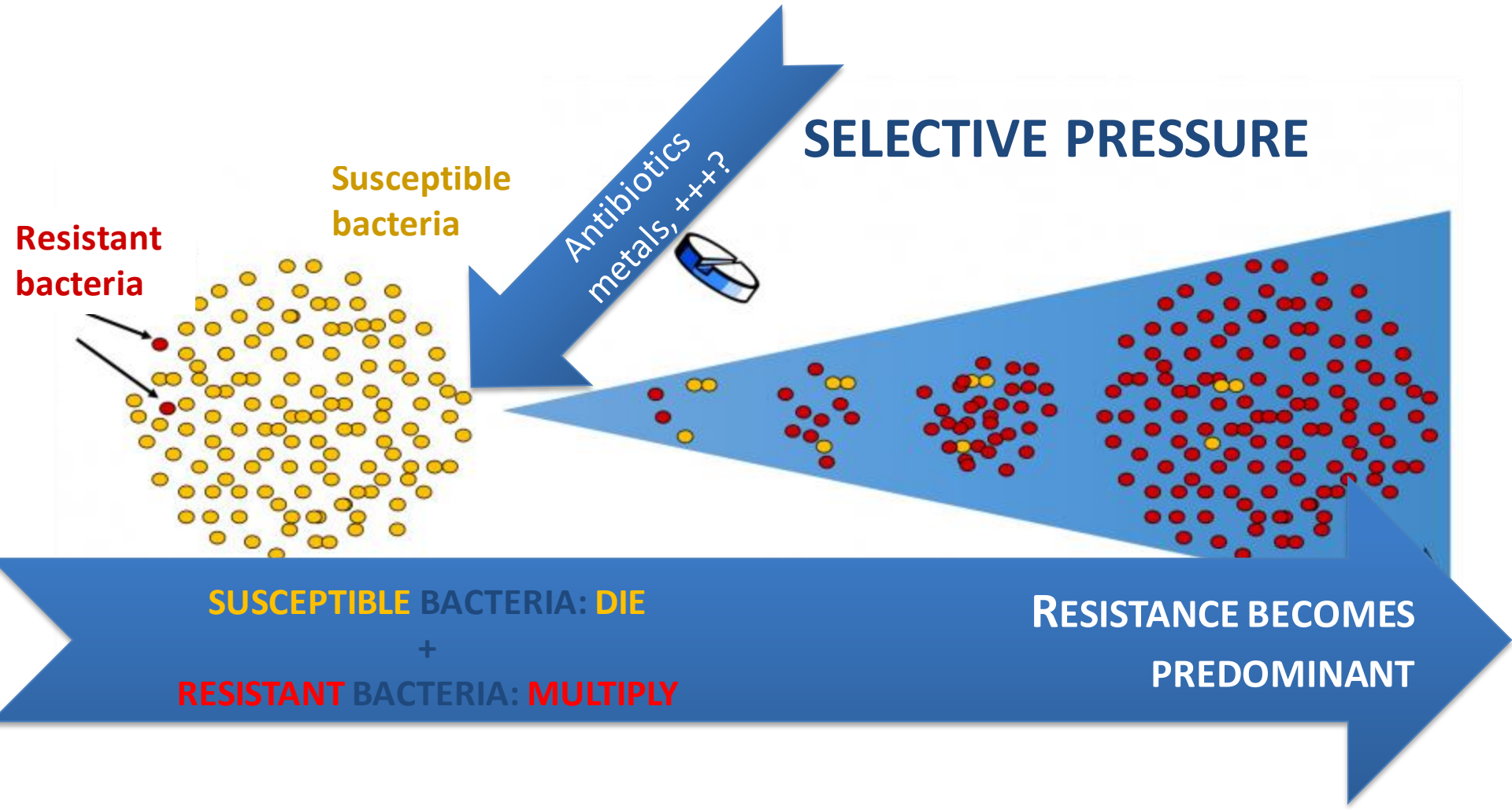
Adaptado de: http://www.reactgroup.org/toolbox/category/understand/the-rise-and-spread-of-antibiotic-resistance/resistance-mechanisms-in-bacteria// (Julho 2016)

HORIZONTAL GENE TRANSFER /MUTATION



Andersson & Hughes (2010) Nature Reviews Microbiology, 8, 260-271

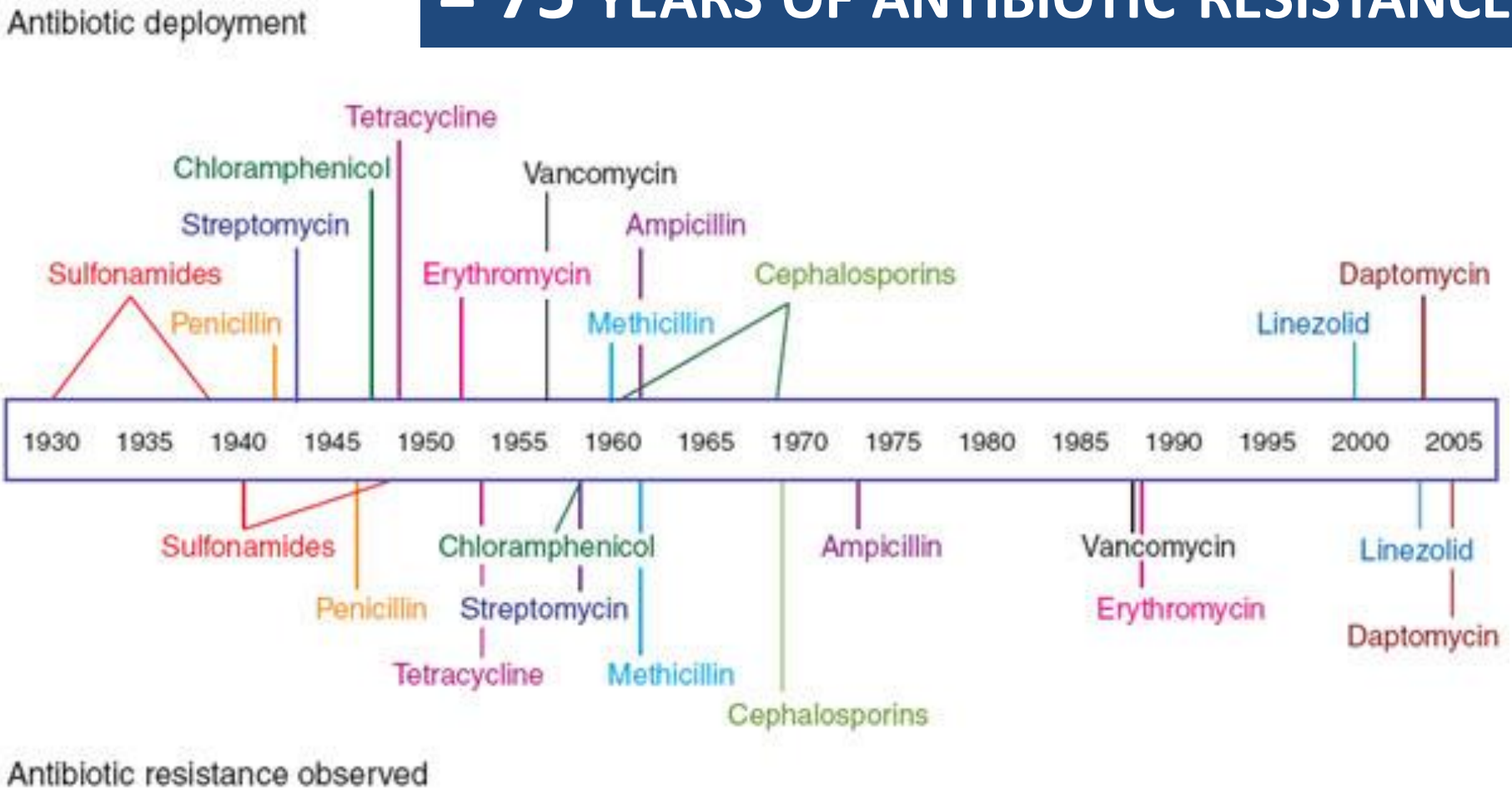
HORIZONTAL GENE TRANSFER
MUTATION
SELECTION



Adapted: http://www.reactgroup.org/toolbox/category/understand/the-rise-and-spread-of-antibiotic-resistance/mutation-and-selection/ (Julho 2016)

~75 YEARS OF ANTIBIOTHERAPY …

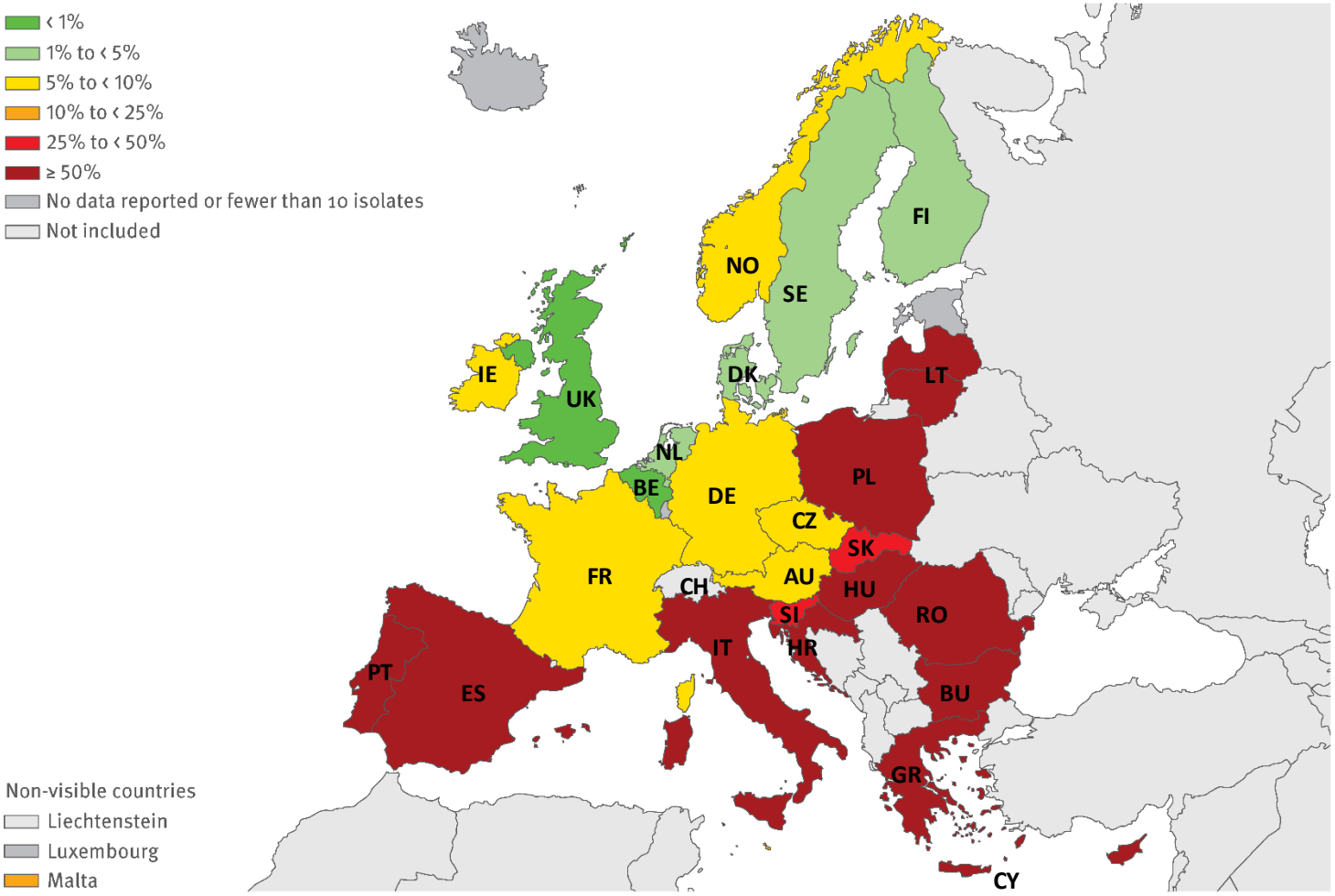
= 75 YEARS OF ANTIBIOTIC RESISTANCE



Clatworthy et al. (2007) Nature Chemical Biology **3**, 541 - 548

ANTIBIOTIC RESISTANCE...

***Acinetobacter* spp.** Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015

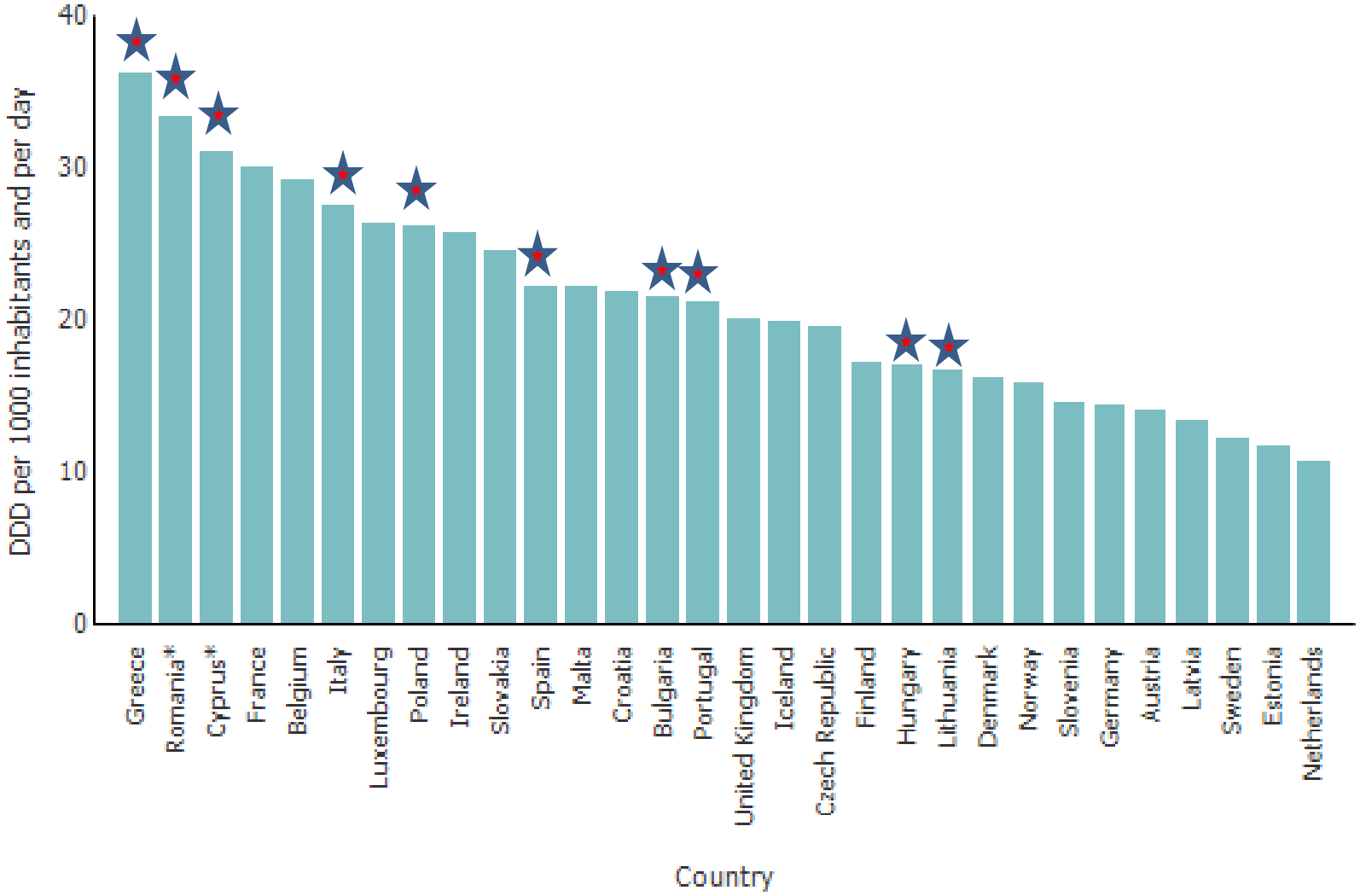


Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Stockholm: ECDC, 2017

© European Centre for Disease Prevention ans Control, 2017

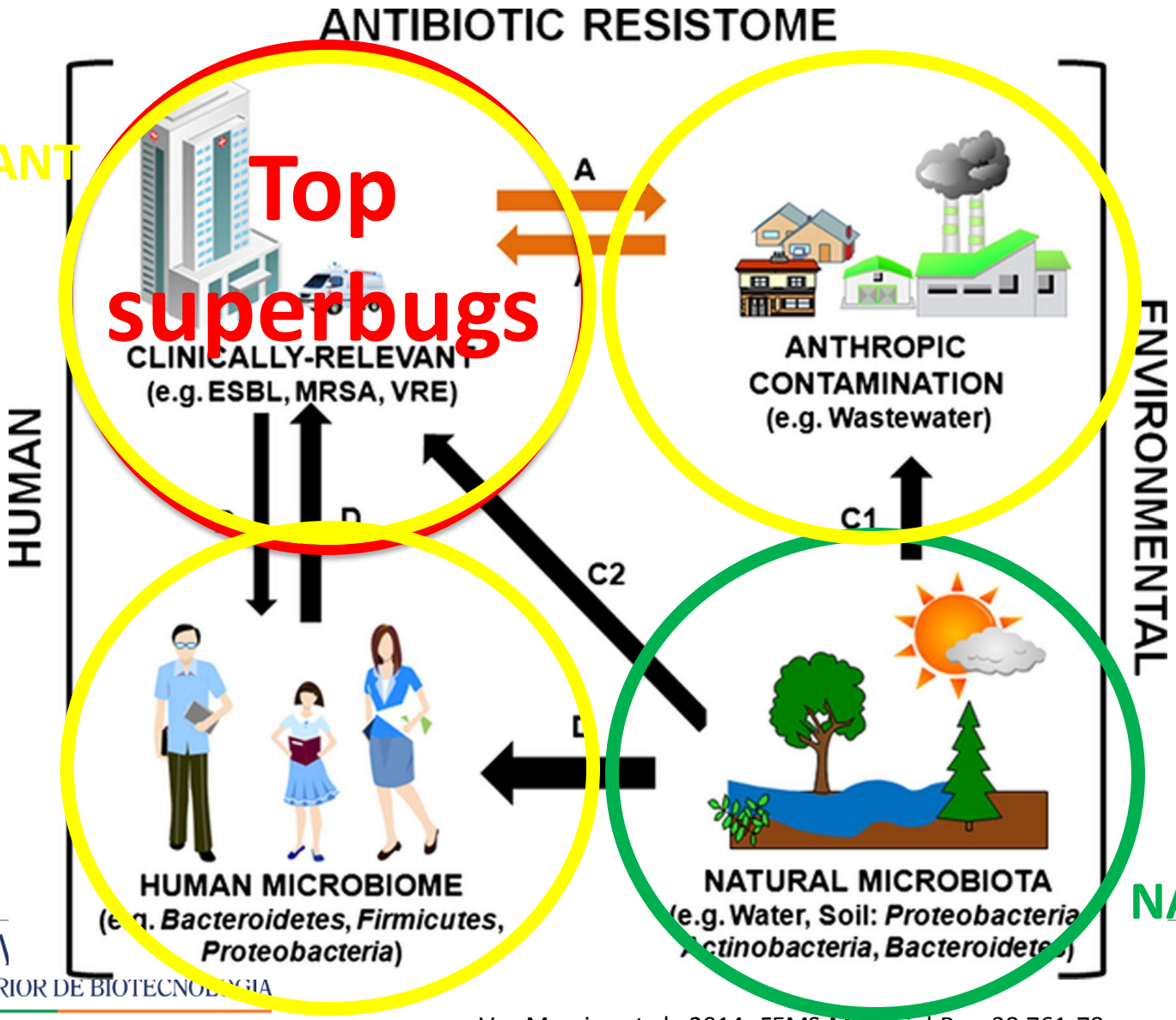
ANTIBIOTIC CONSUMPTION…

Consumption of Antibacterials For Systemic Use (ATC group J01) in the community (primary care sector) in Europe, reporting year 2015



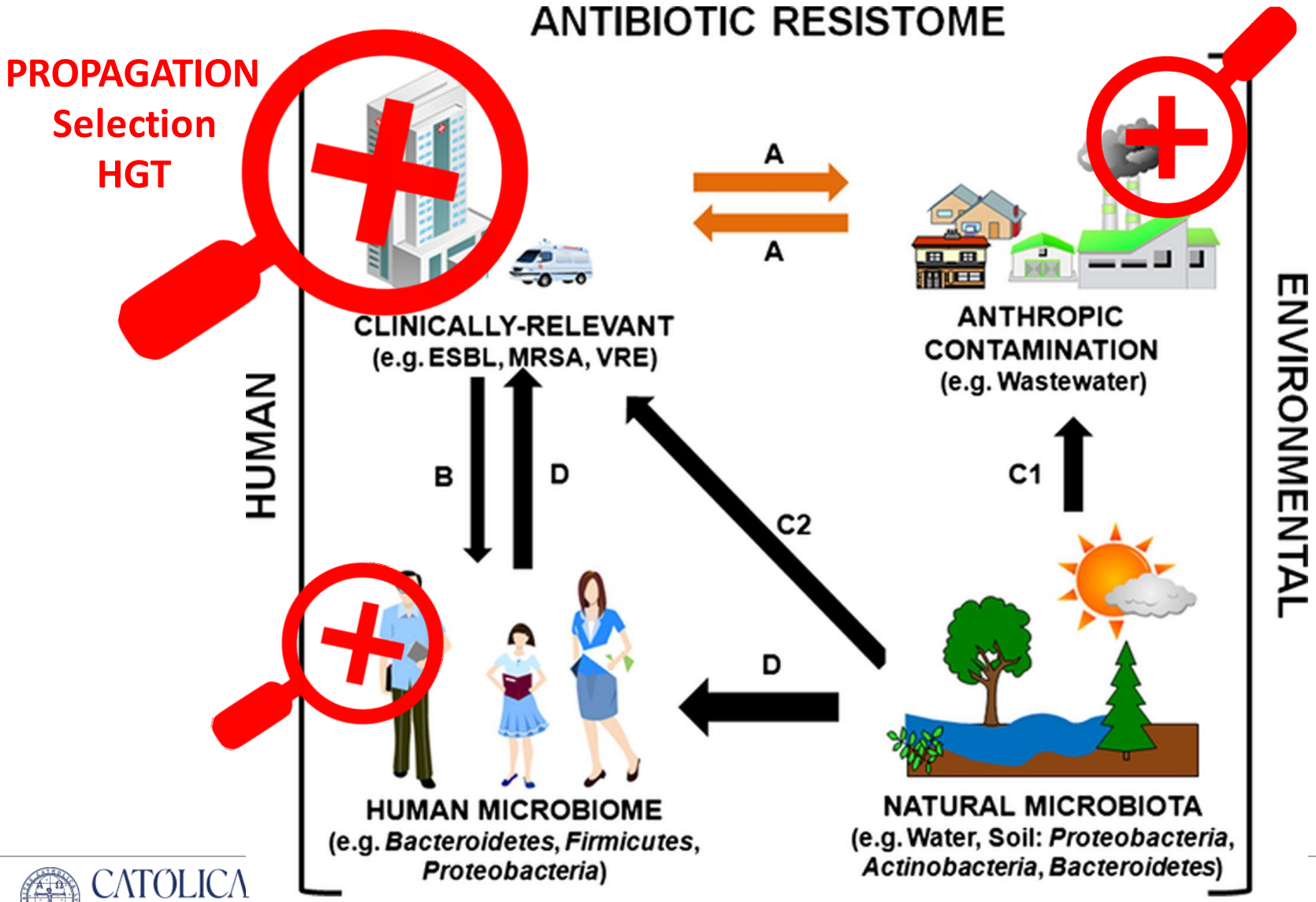
ANTIBIOTIC RESISTANCE IS NATURAL…

AND ALSO… CONTAMINANT



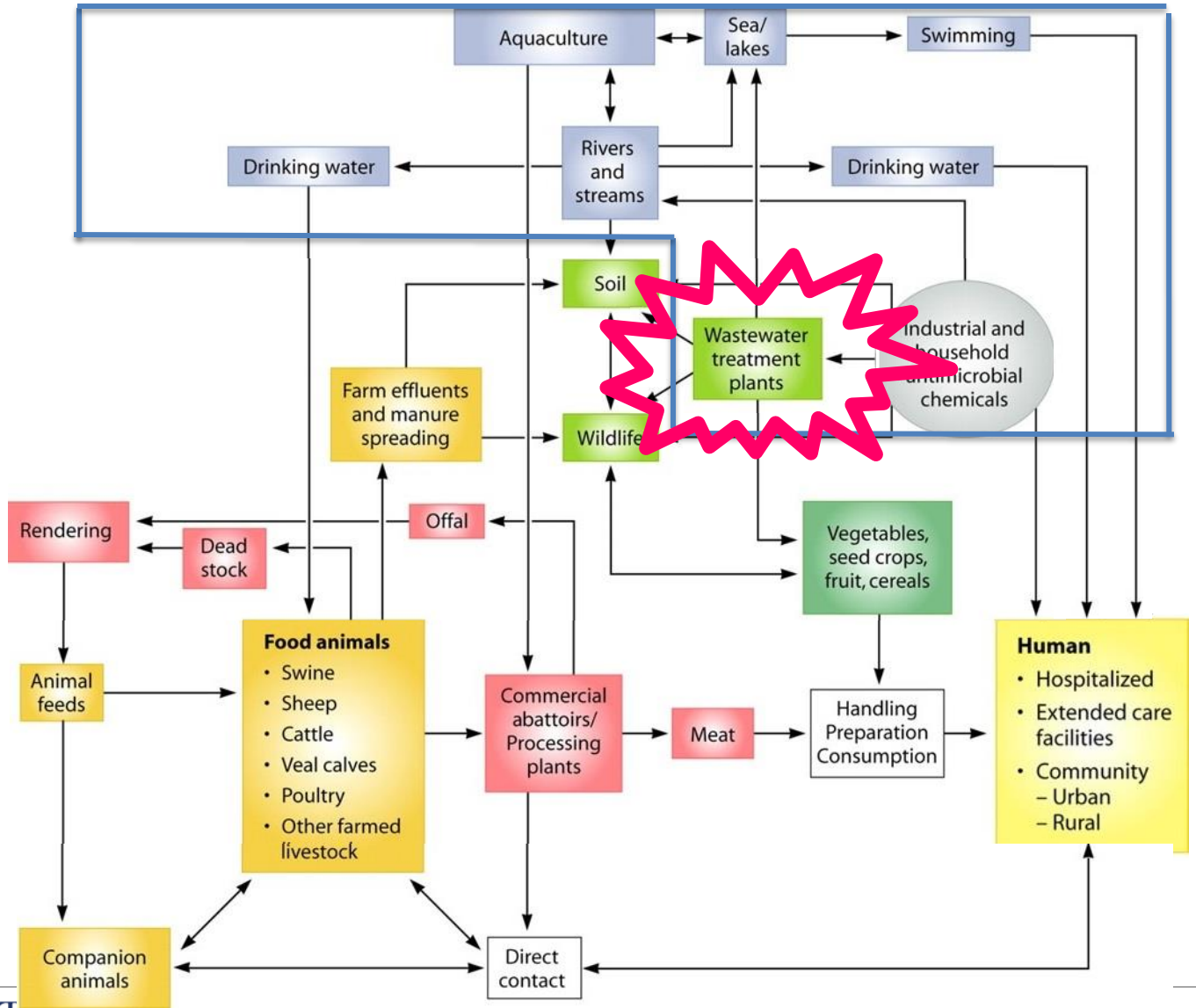
Vaz-Moreira et al., 2014. FEMS Microbiol Rev. 38:761-78

CONTAMINANTS OF (SPECIAL) EMERGING CONCERN



Vaz-Moreira et al., 2014. FEMS Microbiol Rev. 38:761-78

WATER AS A MAJOR ROUTE OF PROPAGATION



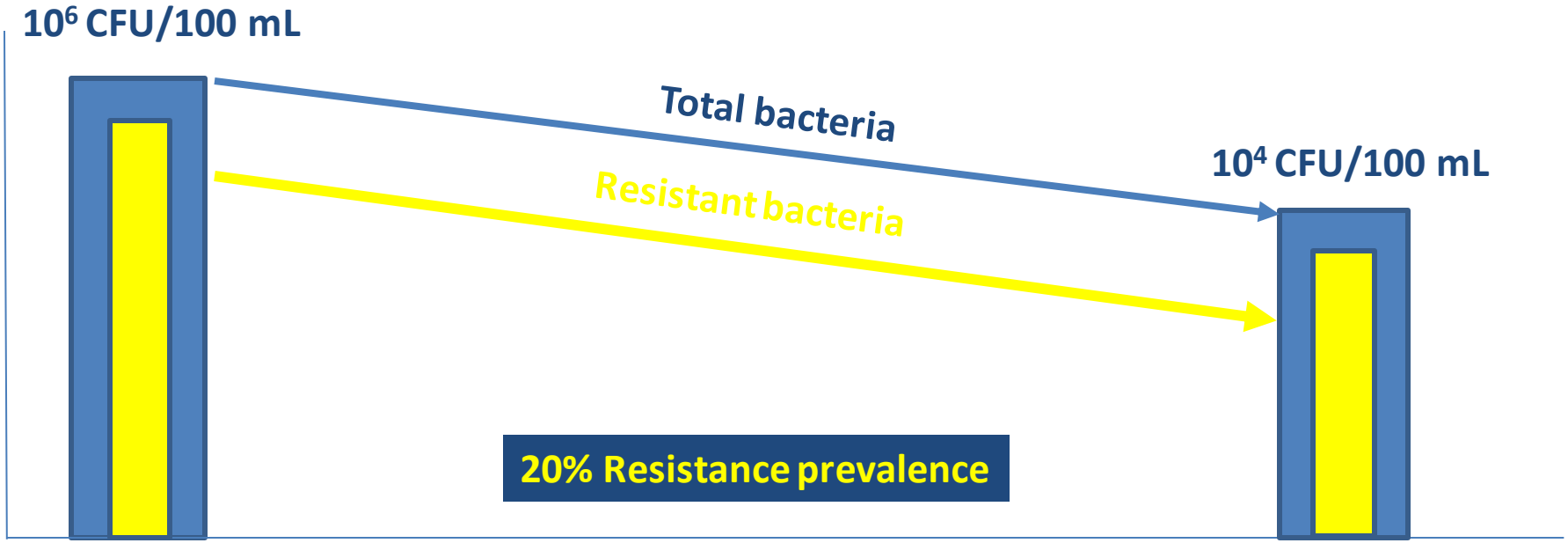
WATER

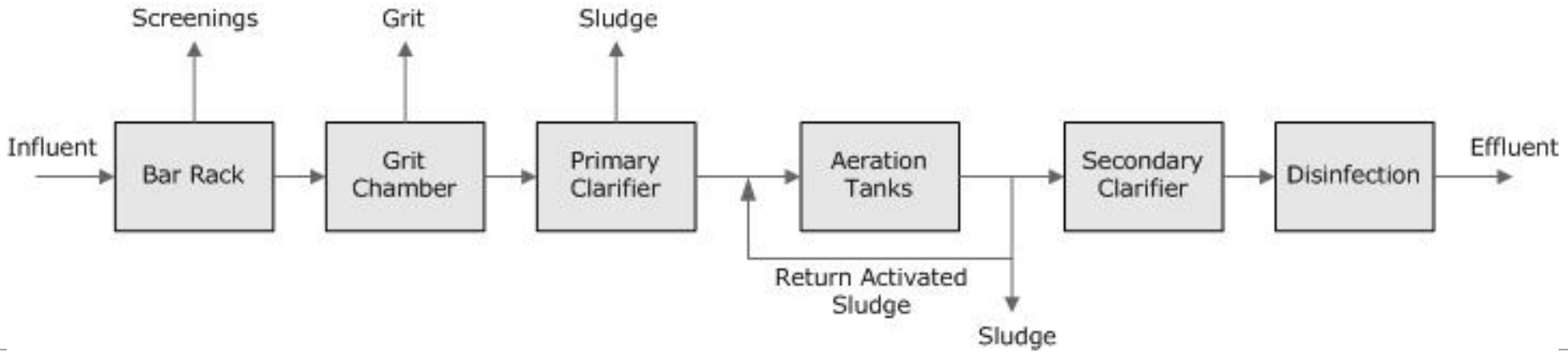
HABITAT

TRANSPORT

Davies and Davies Microbiol. Mol. Biol. Rev. 2010;74:417-433

WASTEWATER TREATMENT IS ESSENTIAL TO REMOVE ANTIBIOTIC RESISTANCE

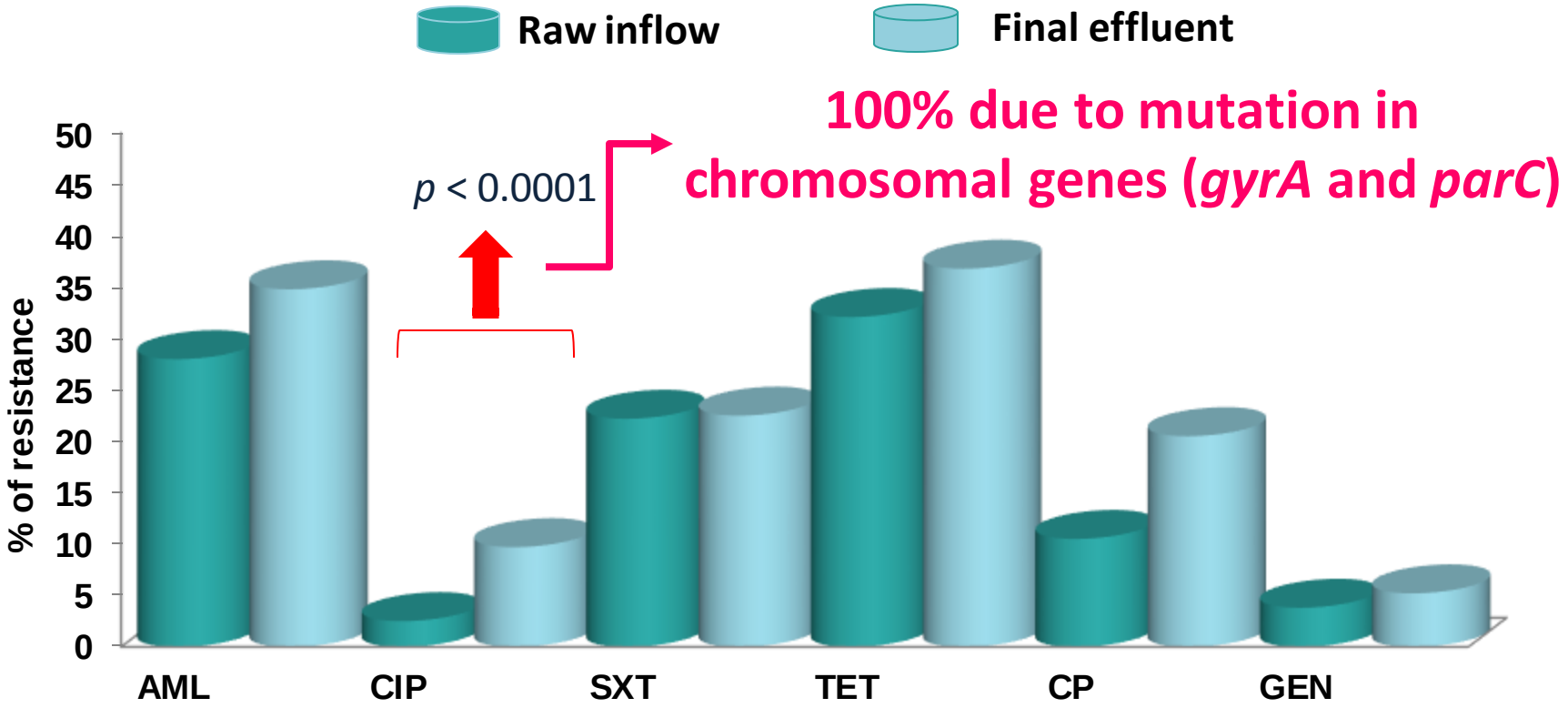




Escherichia coli

Quinolone-resistant

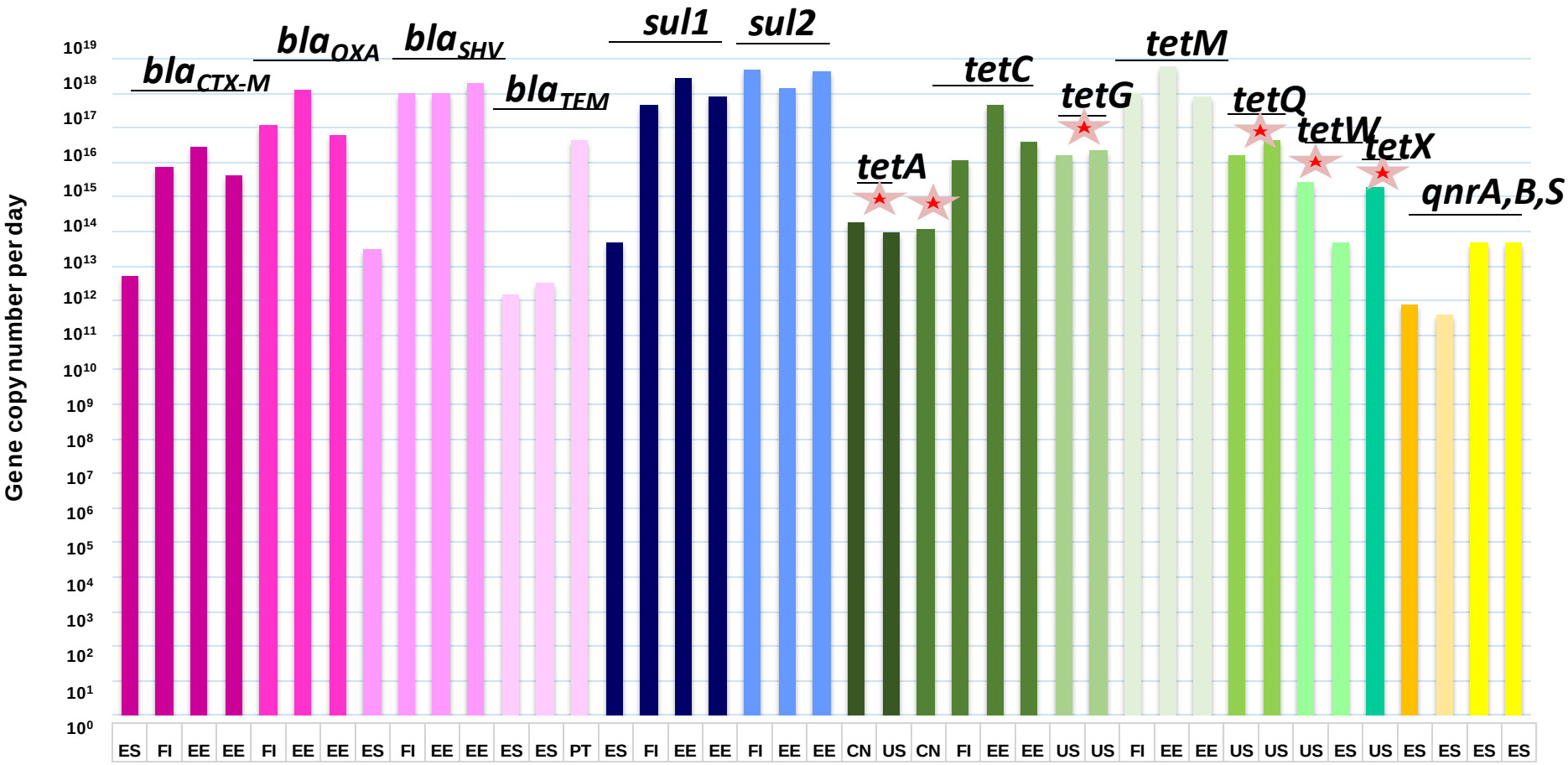
Raw and treated wastewater



Ferreira da Silva, et al. 2007. FEMS Microbiology Ecology, 60:166-176

Figueira et al. 2011 Science of the Total Environment, 409:1017–1023

It is estimated that more than 10^{10} to 10^{14} copies of genes encoding for tetracycline or beta-lactam resistance are released per minute to the surrounding environment



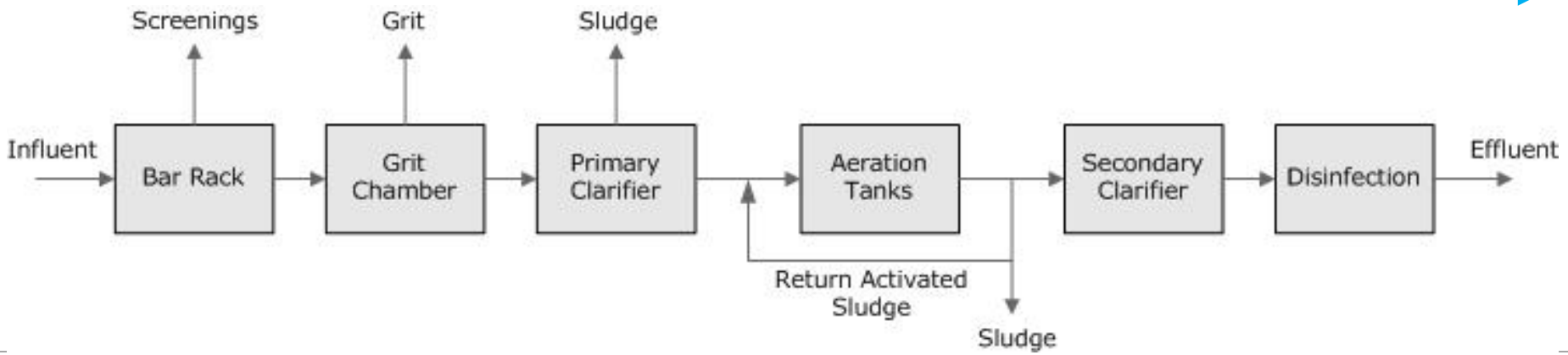
Manaia et al., 2016. Applied Microbiology and Biotechnology. 100:1543–1557

WASTEWATER TREATMENT IS ESSENTIAL TO REMOVE ANTIBIOTIC RESISTANCE

OPERATIONAL CONDITIONS (oxygen, organic matter, sludge age, etc)

SELECTIVE PRESSURES (antibiotic residues, metals, nanoparticles, etc)

INFLUENT QUALITY (hospital, animal production, etc)



SELECTIVE PRESSURES

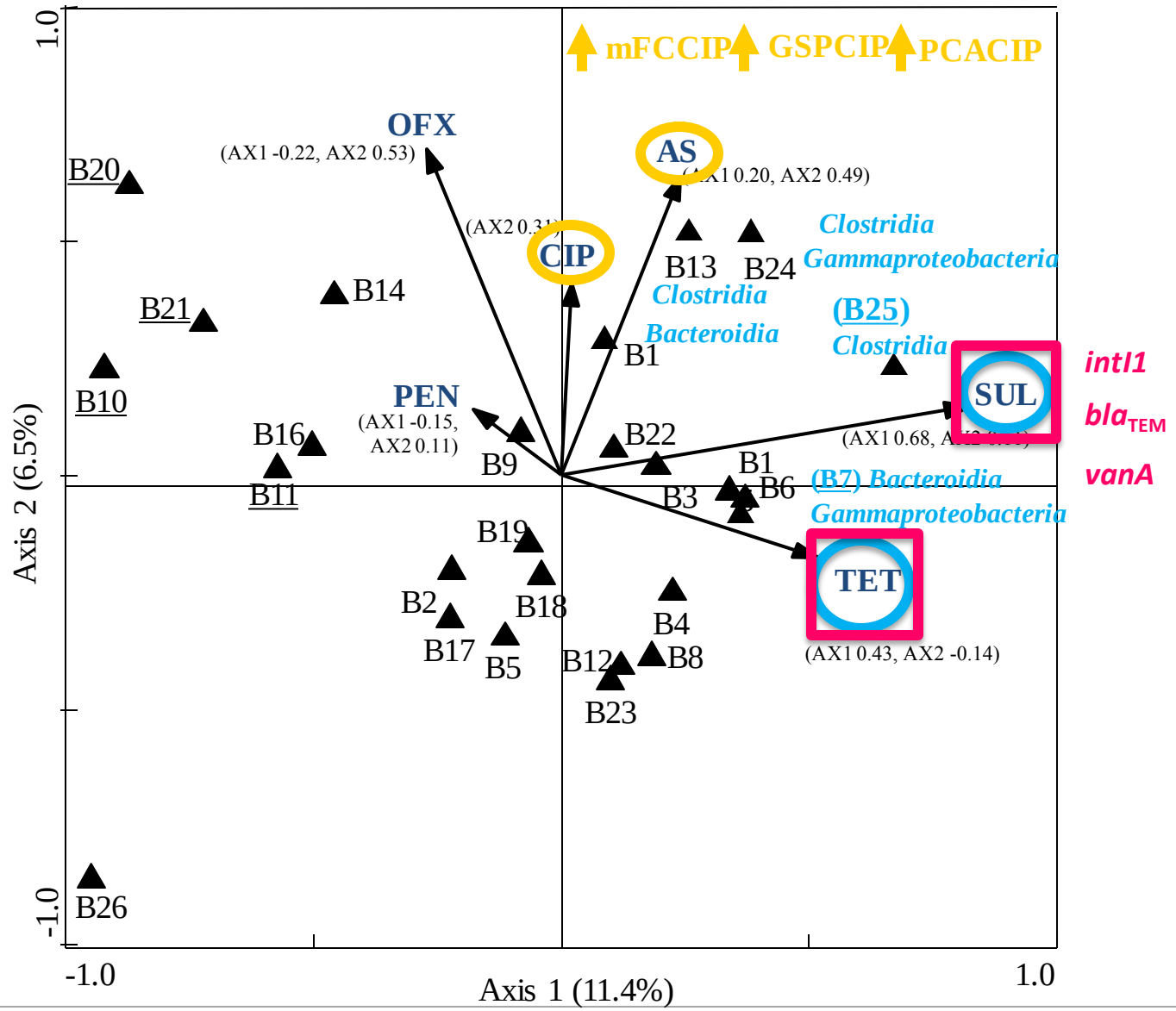
Total bacteria vs. Antimicrobial residues vs. ARG vs. ARB

Antimicrobial Residues

Bacterial Communities

Antibiotic Resistant Bacteria

Antibiotic Resistance Genes



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Varela et al., 2014. Water Research, 54, 327-336;
Narciso da Rocha et al., 2014. Journal of Global Antimicrobial Resistance, 2:309–315

INFLUENT QUALITY

HOSPITAL EFFLUENT VS. THE MUNICIPAL WWTP

*intI*1/*mar*A/bla$_{TEM}$/*van*A - Prevalence / 16S rRNA

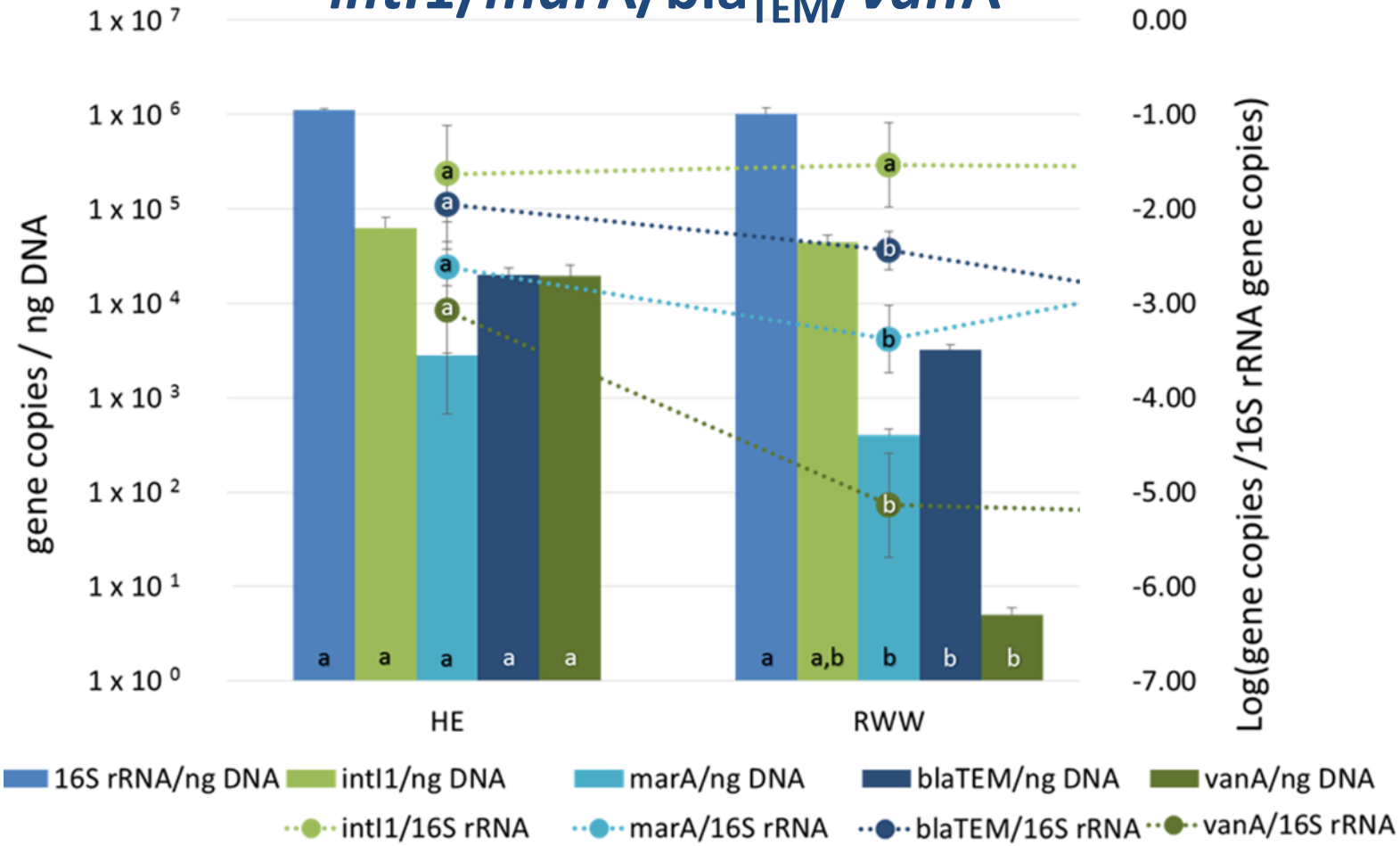
(~2%)

Narciso da Rocha et al., 2014. Journal of Global Antimicrobial Resistance, 2:309–315

INFLUENT QUALITY

HOSPITAL EFFLUENT VS. THE MUNICIPAL WWTP

intI1/marA/bla$_{TEM}$*/vanA*



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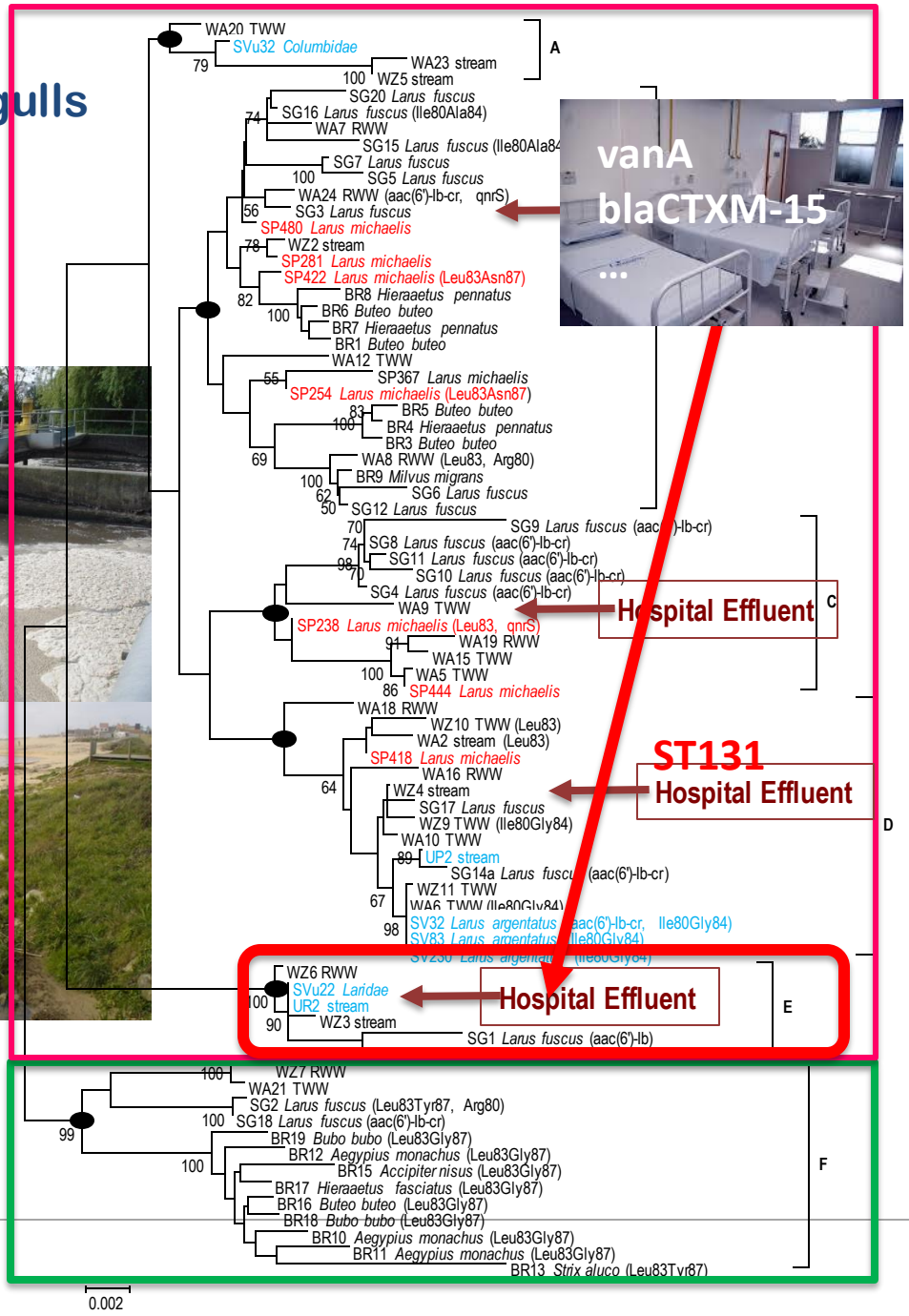
Narciso da Rocha et al., 2014. Journal of Global Antimicrobial Resistance, 2:309–315

Quinolone resistant *Escherichia coli* birds of prey, water environments and gulls Portugal, Spain and Sweden

Gulls
Wastewater
Surface water

Birds of prey
Natural reserve



Hospital Effluent

ST131
Hospital Effluent

Hospital Effluent

ESCOLA SUPERIOR DE BIOTECNOLOGIA

Vredenburg et al., 2014. Environ Microbiology, 16(4):995-1004; Varela et al., J Global Antimicrobial Resistance, 3:286-289 Varela et al. 2015. FEMS Microbiol Ecol. 91(5)

Mitigation measures

I. Assess the risks of transmission from environment to humans

Methods harmonization

Lower the quantification limits

Expand ARG databases

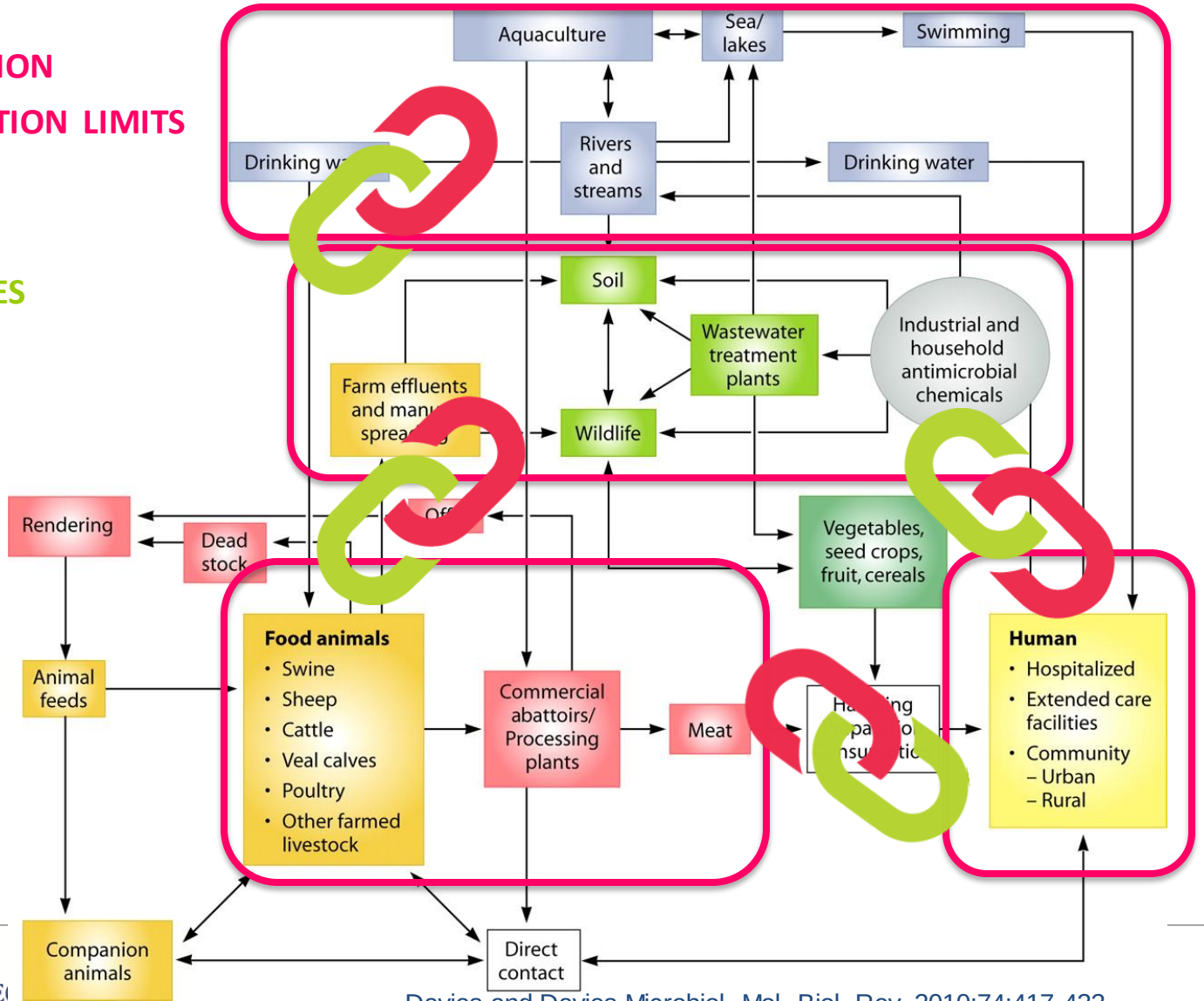
ENVIRONMENT

+

ANIMAL

+

HUMAN

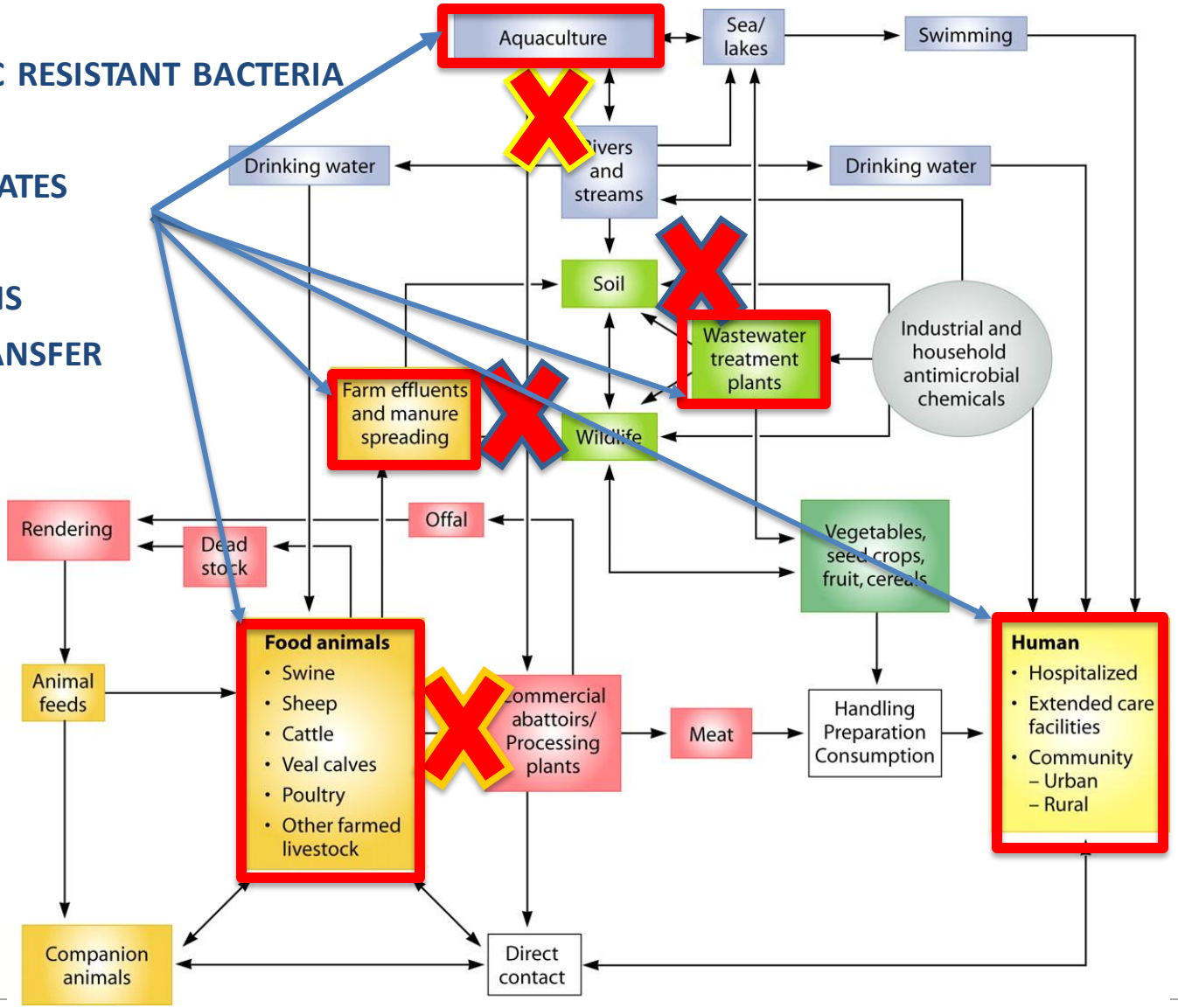


Davies and Davies Microbiol. Mol. Biol. Rev. 2010;74:417-433

Berendonk et al. 2015 Nature Reviews Microbiology. 13(5):310-7.

II. Identification of critical control points

- Income of antibiotic resistant bacteria
- Bacterial growth
- Biofilm/cell aggregates
- Selective pressures
- Adaptative mutations
- Horizontal gene transfer

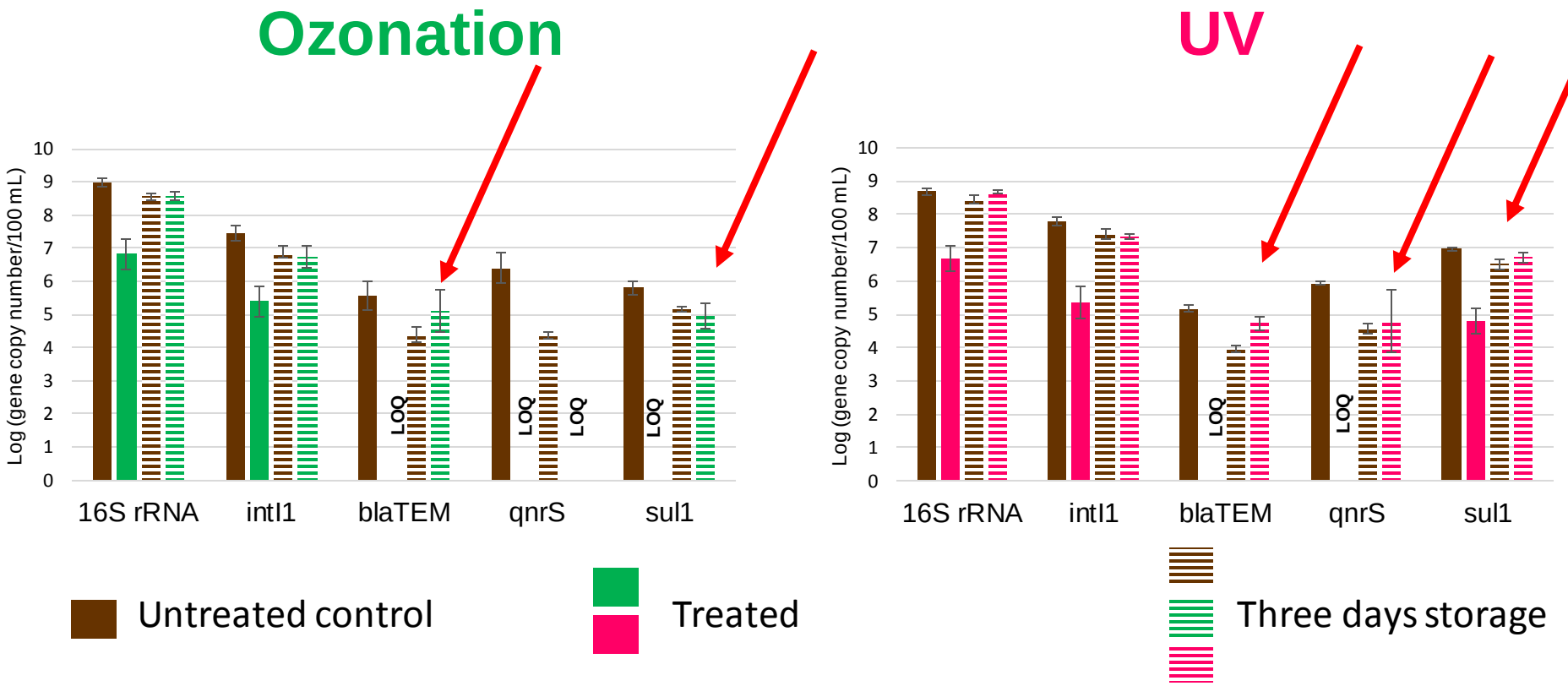


Davies and Davies Microbiol. Mol. Biol. Rev. 2010;74:417-433

Berendonk et al. 2015 Nature Reviews Microbiology. 13(5):310-7.

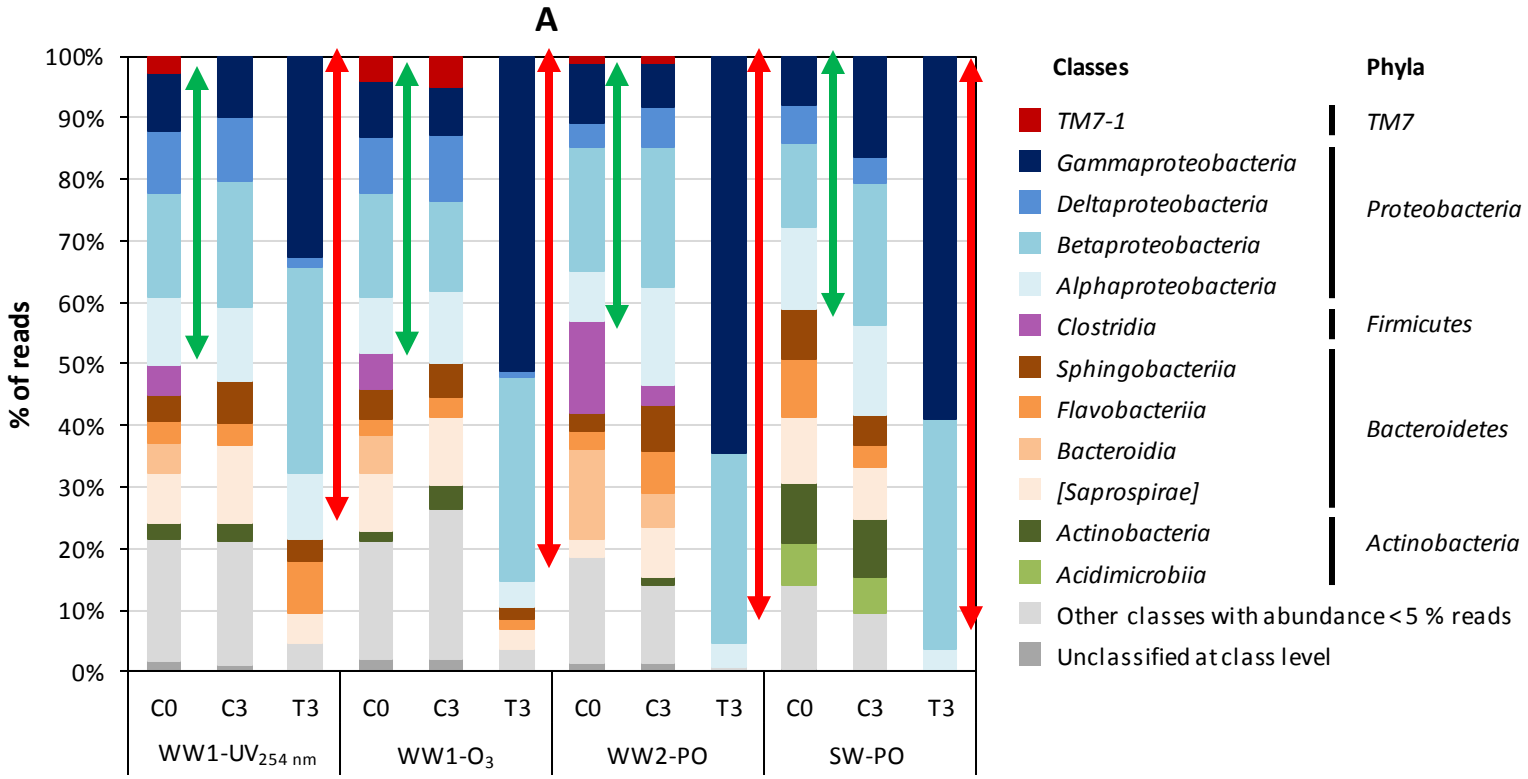
WASTEWATER DISINFECTION

Antibiotic resistance genes



J Hazard Mater. 2017 5;323(Pt A):434-441.

REGROWTH AFTER DISINFECTION



Besides treatment, also storage and transport are key issues in wastewater reuse

Sci Total Environ. 2016 ;573:313-323.

WASTEWATER TREATMENT IS ESSENTIAL TO REMOVE ANTIBIOTIC RESISTANCE

Improved wastewater treatment processes

- ✓ Bacterial removal (disinfection)
- ✓ Environmental friendly *(**low impact** on the environment in particular **on the microbiota**)*
- ✓ Cost effective
- ✓ Wastewater plumbing/storage

StARE
Stopping Antibiotic Resistance Evolution

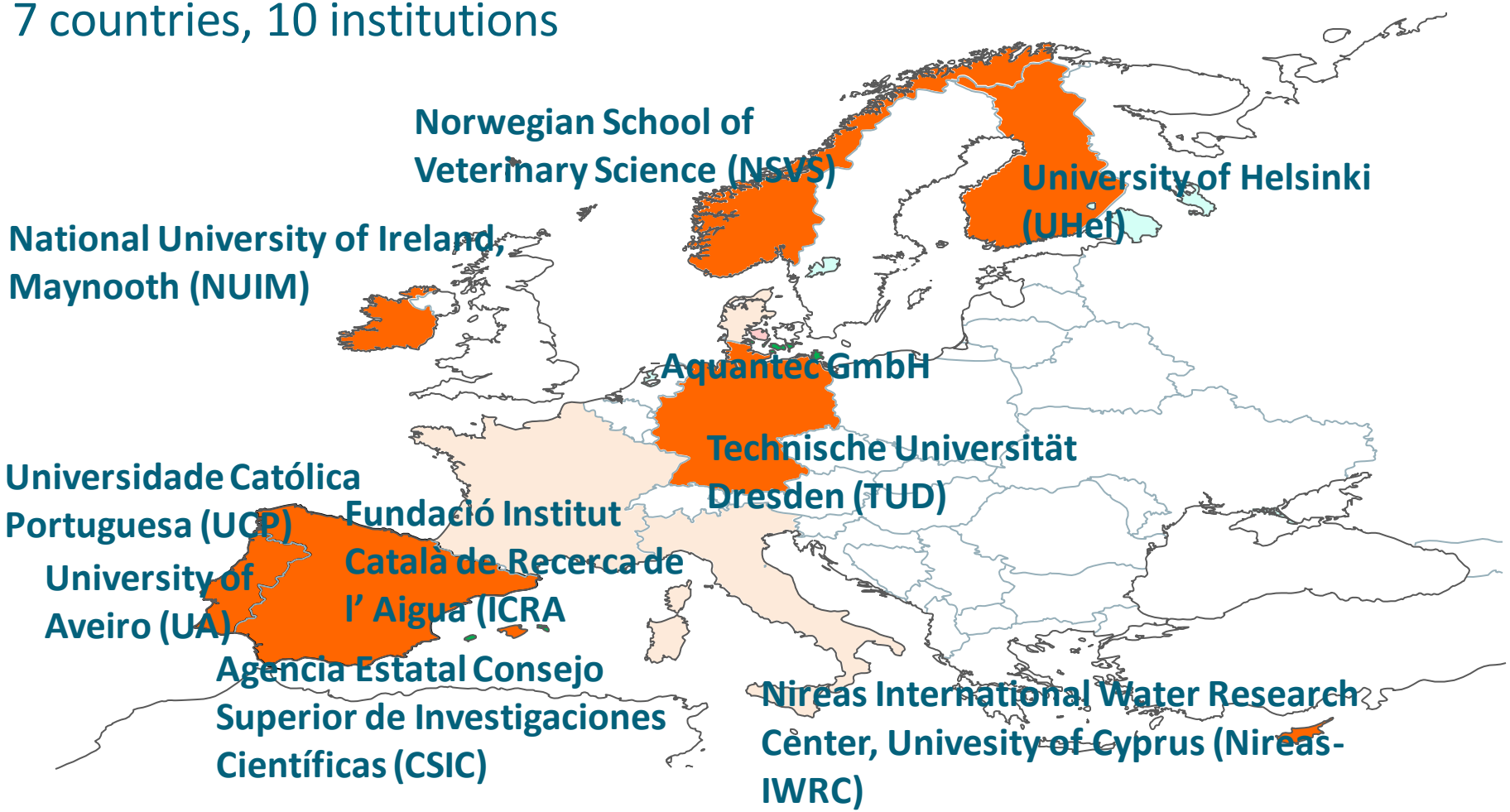
2013 Water JPI Pilot Call focused on
"***Emerging water contaminants-anthropogenic pollutants and pathogens***"

December 2014 – December 2017

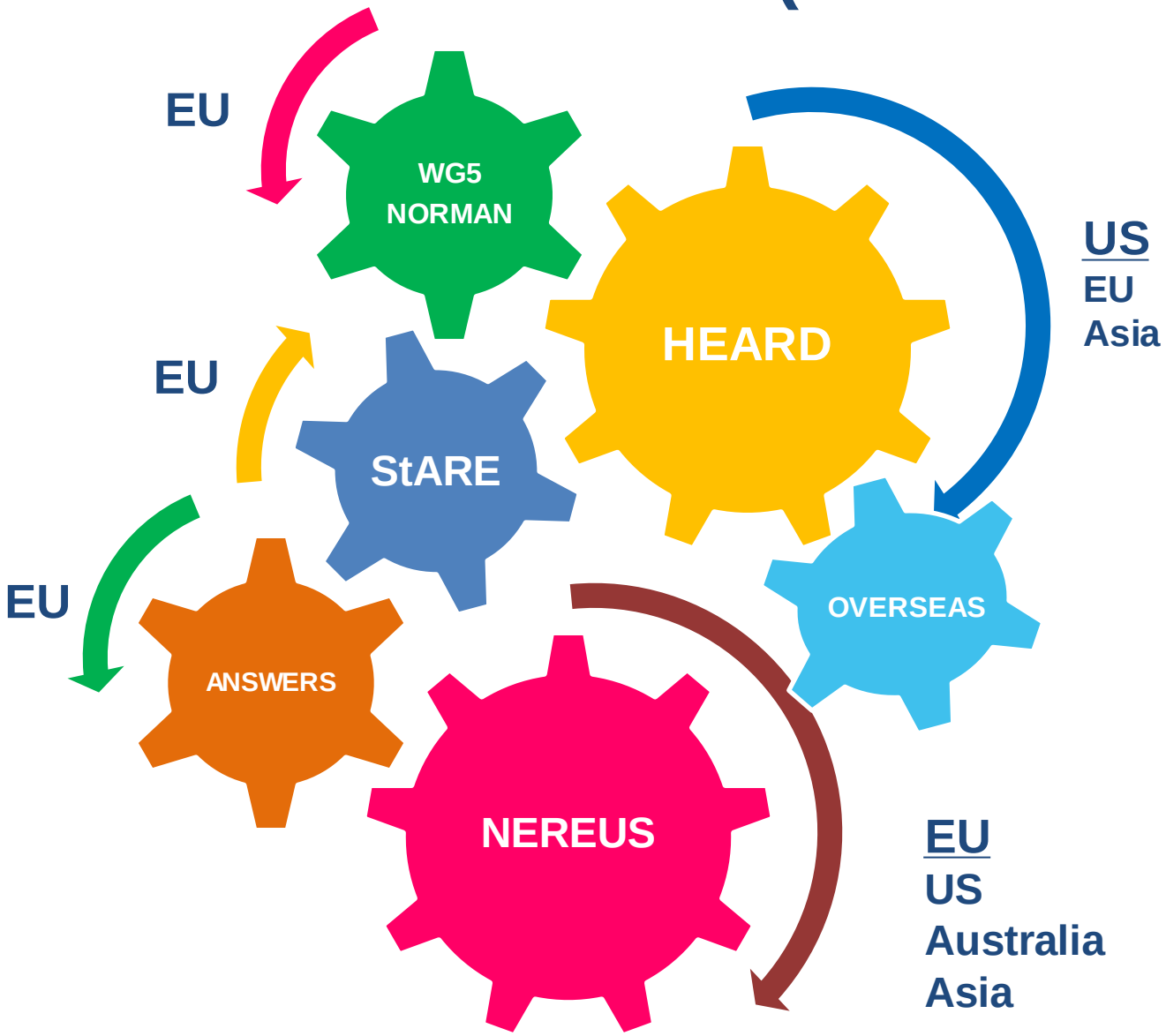
National Funding Agencies
Portugal
Spain
Cyprus
Germany
Ireland
Norway
Finland

Partners

7 countries, 10 institutions



On-going projects on antibiotic resistance in wastewater (and its reuse)



Partners (EU)

Olga Nunes (Portugal)

Paulo Costa (Portugal)

Manuela Caniça (Portugal)

Adrian Silva (Portugal)

Sérgio Silva (Portugal)

Isabel Henriques (Portugal)

Despo Fatta-Kassinos (Cyprus)

Thomas Berendonk (Germany)

Thomas Schwartz (Germany)

José Luis Martinez (Spain)

Sara Rodriguez (Spain)

Marko Virta (Finland)

Fiona Walsh (Ireland)

Henning Sörum (Norway)

Eddie Cytryn (Israel)

Christophe Merlin (France)

Luigi Rizzo (Italy)

Norbert Kreuzinger (Austria)

FCT Fundação para a Ciência e a Tecnologia

MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA

UID/Multi/50016/2013-CBQF

Stopping Antibiotic Resistance Evolution

https://stareeurope.wordpress.com/

COST-European Cooperation in Science and Technology, to the COST Action ES1403: New and emerging challenges and opportunities in wastewater reuse (NEREUS) - http://www.nereus-cost.eu/

ANtibioticS and mobile resistance elements in WastEwater Reuse applications: risks and innovative solutions – ANSWERS. European Commission Horizon 2020 - MSCA-ITN-2015-ETN: Marie Sklodowska-Curie Innovative Training Networks (ITN-ETN)

OVERSEAS (FLAD 298/2015)

Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances - http://www.norman-network.net/?q=node/19

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Bacterial diversity group

ESB-UCP, Porto, Portugal