Removal of antibiotic resistances from hospital effluents

Policy brief - Strengthening EU Action on Antimicrobial Resistance: Addressing Hospital Wastewater

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Abstract

Antibiotic use in hospitals, while crucial, releases residues and resistant bacteria into effluents, thereby promoting antibiotic resistance, a major global health threat. The EU currently lacks specific regulations for pharmaceutical discharge from healthcare facilities, allowing these contaminants to pass through municipal wastewater treatment plants into water sources, where they pose risks to ecosystems and human health. The LIFE GENESYS project offers a decentralised solution for hospitals that combines advanced treatment (membrane bioreactor and UV-LED/H_2O_2) with digital tools for estimating antibiotic load. Initial analyses confirm the presence of antibiotics, antibiotic-resistant bacteria (ARBs) and their associated antibiotic resistance genes (ARGs) in hospital effluents, as well as the limitations of current treatment. This document emphasises the urgent need for specific regulations on hospital antibiotic discharges to protect aquatic ecosystems and human health, and to combat antibiotic resistance, in line with with the EU's ‘One Health’ approach. This policy brief aims to inform policymakers, environmental agencies, and health and water stakeholders, offering initial recommendations for a stronger regulatory framework.

Glossary of Acronyms

AMR	Antimicrobial Resistance
ARBs	Antibiotic-Resistant Bacterias
ARGs	Antibiotic Resistance Genes
CIA	Critically Important Antimicrobials
EPR	Extended Producer Responsibility
HPCIA	Highest Priority Critically Important Antimicrobials
PC	Pharmaceutical Compound
WWTPs	Wastewater Treatment Plants

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Antibiotics in wastewater and bacterial resistance

Hospitals are critical infrastructures for public health and play a key role within the healthcare system. At the same time, they are important points where pharmaceutical compounds (PCs) (including antibiotics), antibiotic-resistant bacteria (ARBs) and their associated antibiotic resistance genes (ARGs) can be released into the environment.[1,2,3,4]

These emerging contaminants can be found in hospital effluents as a consequence of the intensive use of antimicrobial drugs, often without any specific treatment prior to discharge into the urban sewer system.[5,6,7,8] Their presence in wastewater systems is associated with the emergence and spread of antimicrobial resistance (AMR), a phenomenon increasingly recognised as one of the greatest global health challenges of our time.[9]

Antimicrobial resistance threatens medical advancements and contributes to mortality. It directly causes over **1 million deaths worldwide annually**, with nearly 5 million additional deaths linked to its indirect effects. In the WHO European Region, AMR is responsible for about 133,000 direct deaths yearly and is associated with another 541,000 deaths—a burden similar to tuberculosis, influenza, and HIV/AIDS combined.[10]

The point prevalence survey of the **European Centre for Disease Prevention and Control** (ECDC) describes acute **care hospitals** as **key settings** for both healthcare-associated infections and **antimicrobial resistance**, assessing structures and processes for their prevention at hospital and ward level.[11]

"**AMR** currently represents one of the most significant threats to our health, classified by the WHO among the top 10 global health threats. Last September, a study published in the prestigious journal *The Lancet* estimated that, over the next 25 years, antimicrobial resistance would cause **39 million direct deaths,** and approximately **169 million indirect deaths.**"

Maite Martín Ibáñez, PhD – Professor, Department of Cellular Biology, Physiology and Immunology, Faculty of Veterinary Medicine, Universitat Autònoma de Barcelona (Spain). President, One Health Platform.

A critical problem with multiple impacts

- **Persistence of antibiotics**: Many antibiotics are not fully metabolised by the human body and are excreted active in urine or faeces in an active form. These compounds enter sewer networks directly from hospitals.[12]

- **Generation of resistant bacteria in the environment**: Bacteria present in wastewater can develop resistance by coming in contact with antibiotics. This resistance can then be transferred horizontally to other microorganisms, including human pathogens.[13,14]

"Antimicrobial resistance spreads across people, animals, and the environment in many different ways. The presence of these **resistance genes in the environment**, which can originate from different sources, means they may come into contact with environmental bacteria. These environmental bacteria can become opportunistic pathogenic bacteria, which should in principle cause no more than a mild, treatable infection. However, if they have acquired resistance to these antibiotics, treatment becomes more difficult. Furthermore, environmental bacteria carrying resistance genes can come into contact with pathogenic bacteria in humans and thus become what we call '**multidrug-resistant bacteria'**, which are the ones that cause serious problems."

Maite Martín Ibáñez

- **Vulnerable aquatic ecosystems**: Studies have shown that even low concentrations of antibiotics in rivers and lakes can affect the aquatic microbiota, alter ecological processes, and contribute to the emergence of "superbugs" that are resistant to multiple treatments.[5,15]

- **Economic impact**: Beyond its human cost, AMR has significant economic implications. It is estimated to cost the European Union and the European Economic Area around €11.7 billion annually, due to increased healthcare expenses and reduced workflow productivity.[10]

"**AMR** affects the environment, the animals, the soils… it changes ecosystems and reduces their fertility, thereby causing economic losses. This is a broad challenge that requires a **multidisciplinary and multisectoral approach**, which is, ultimately, the essence of the **One Health concept.**"

Maite Martín Ibáñez

Conventional wastewater treatments and emerging challenges

Urban wastewater treatment plants (WWTPs) are essential for safeguarding public health and protecting the environment. While they achieve a high level of performance in removing conventional pollutants, they were not originally designed to specifically target certain emerging contaminants, such as PCs, ARBs or ARGs.[3,5,7,12]

"There is sufficient evidence that, in many cases, **conventional treatments have limited effectiveness in removing** or treating these types of **emerging contaminants**. This means they frequently remain present in the water cycle, contributing to issues such as the spread of antimicrobial resistance. If the objective is to address these emerging contaminants, implementing **advanced treatments becomes necessary.**"

Desirée Marín Navarro - Head of Innovation and Sustainability, Agbar-Veolia (Spain). Expert in sustainable business models and water management.

This gives rise to a significant environmental concern: a considerable portion of these contaminants, including drug residues, personal care products, and resistant microorganisms, manage to pass through the conventional treatment stages of WWTPs. Consequently, these compounds and microorganisms are continuously discharged into bodies of water such as rivers, lakes, estuaries, and aquifers.

The presence of these contaminants in aquatic ecosystems raises several concerns:[16]

- **Impact on human health**: Long-term exposure to low concentrations of PCs can have endocrine-disrupting, genotoxic, or toxic effects[15,17]. Likewise, the dissemination of ARBs and ARGs in the environment contributes to the emergence and spread of antibiotic resistance, which is one of the greatest threats to global health. Recent analyses of 2020 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) estimate that antimicrobial-resistant infections claim **over 35,000 lives each year in the EU/EEA.**[27]

- **Ecological impact**: PCs can affect aquatic fauna, by altering their behaviour, reproduction, or survival. The presence of ARBs and ARGs in the environment can also disrupt natural microbial communities and facilitate the horizontal transfer of resistance genes among bacteria.[13,18,19]

- **Risks to drinking water and the food chain:** If these contaminants are present in receiving bodies used as drinking water sources, they pose additional challenges for drinking water treatment plants, which must implement more advanced technologies to ensure water quality. Furthermore, AMR can enter the food chain when resistance genes present in water are adsorbed by crops irrigated with AMR-contaminated water, or when they accumulate in aquatic organisms intended for human consumption, thereby increasing the risk of human exposure through food.[13,20]

Therefore, it is **imperative** to develop and implement **advanced treatment technologies** capable of addressing the removal of these emerging contaminants more effectively, in order to **protect human health and the integrity of our aquatic ecosystems.**

Key advances of Directive (EU) 2024/3019:

- Quaternary treatment, which is designed to eliminate micropollutants such as antibiotics, pesticides, hormones, and microplastics, will be mandatory by 2034 in WWPTs serving more than 10,000 population equivalents.

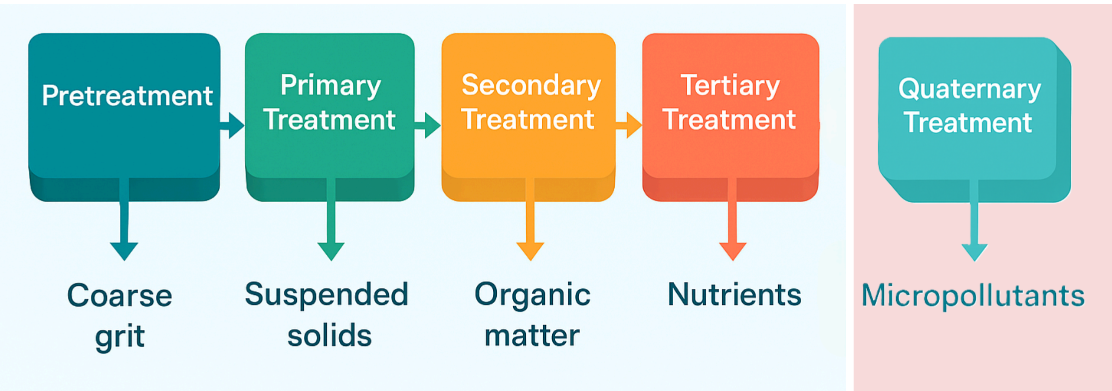

Fig. 1. Treatment stages in conventional WWTPs and novel quaternary treatment.

- Compulsory monitoring of a specific list of pharmaceutical compounds in wastewater.
- Application of the "polluter pays" principle, through an extended producer responsibility (EPR) mechanism, which requires the pharmaceutical industry to contribute to the costs of advanced treatment.
- Reduction targets and strict requirements for the removal of pharmaceutical contaminants in wastewater.

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However, it remains **insufficient**:

- The WHO has identified a comprehensive list of **Critically Important Antimicrobials (CIA)** and **Highest Priority CIAs (HPCIA)**, including carbapenems, advanced-generation cephalosporins, quinolones, polymyxins, aminoglycosides, and macrolides, as critical to human health. However, with the exception of clarithromycin, these compounds have not yet been incorporated into the Directive's monitoring list.[21]
- The Directive does not yet include harmonised **standards**, along with mandatory **monitoring** of **ARGs** and **ARBs** in wastewater.
- A specific normative framework is needed to regulate hospital effluents as a distinct, high-impact source of pharmaceutical emissions, including the establishment of clear discharge limits for antibiotics and other drugs.

What **needs** to be done:

The spread of PCs, ARBs and ARGs into urban wastewater systems would be prevented by targeting these contaminants at hospital level, thereby reducing treatment burdens at municipal plants and mitigating environmental and public health risks. The LIFE GENESYS project, aligned with the EU One Health Action Plan against Antimicrobial Resistance[22] and supporting the Directive (EU) 2024/3019, aims to reduce and monitor AMR by implementing a decentralised treatment of hospital effluents.

> "In the specific case of antimicrobial resistance, it makes the most sense to **tackle the problem at source**. Adopting this integrated vision is **necessary to avoid greater problems or higher costs** elsewhere in the sanitation system."

Desirée Marín Navarro

Initial Evidence from the LIFE GENESYS project

The LIFE GENESYS project, co-funded by the EU through the LIFE Programme (Grant Agreement No. 101147763), will investigate a **decentralised approach** to remove PCs, ARBs and ARGs from hospital wastewater. The project aims to demonstrate an innovative and cost-effective treatment process that combines **membrane bioreactor (MBR) technology and UV-LED/H_2O_2 oxidation**. Additionally, a **digital tool** will be developed to estimate pharmaceutical loads at source.

The GENESYS solution will be implemented at the Parc Taulí University Hospital (Sabadell, Spain). The implementation of on-site treatment will also enable the evaluation of the extent to which reductions in PCs, ARBs and ARGs are reflected at the influent of the Riu Ripoll WWTP. Such evidence will provide further insight into the ongoing discussion between localised and centralised treatment approaches.

"The GENESYS project enables us to take a **comprehensive approach to sanitation**, providing a full understanding of what happens at the point of wastewater generation, throughout the sewer network, and finally how we treat it at the WWTPs."

Desirée Marín Navarro

"**The One Health approach is precisely that**: a global vision that identifies the underlying causes that lead to the emergence of a health risk, in order to **act at source**. This project will do just that by treating hospital wastewater, which is the **point of emission of** those **resistance genes and critically important antibiotics.**"

Maite Martín Ibáñez

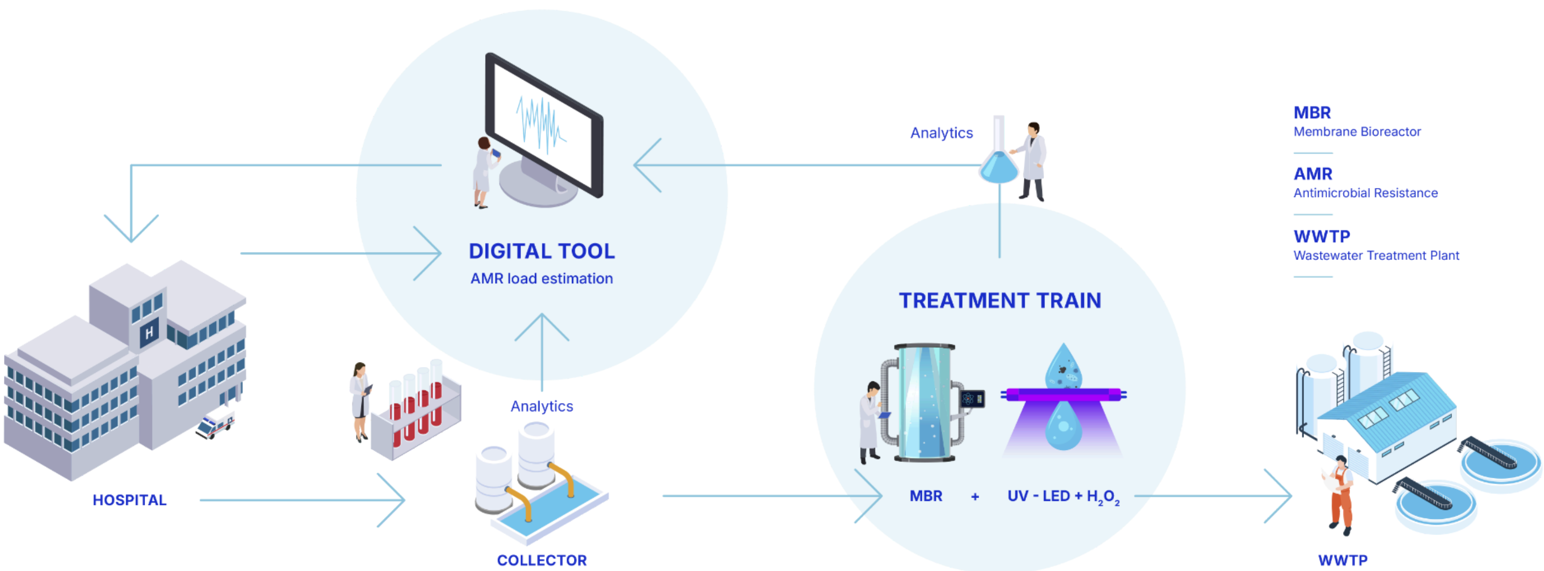
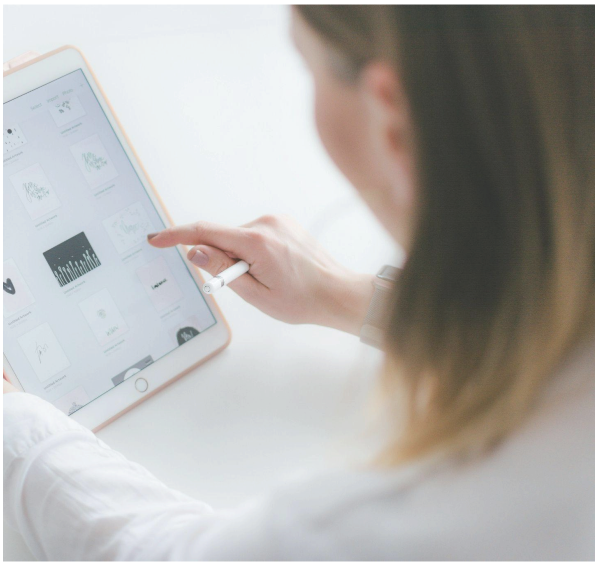


Fig. 2. General diagram of the LIFE GENESYS solution.

Clinical Decision Support Systems (CDSS) have been identified as a high-impact intervention for controlling antimicrobial resistance. CDSS support antimicrobial stewardship by providing healthcare professionals with the latest evidence-based guidelines for antibiotic use, and offering real-time feedback on their prescribing practices, and monitoring at the point of prescription.[23]



"One important aspect will be what is called ***nowcasting***, to infer data that come with delays. Having that control dashboard is an extremely valuable tool because it shifts the paradigm that has been in place so far."

Clara Prats Soler, PhD – Director, Computational Biology and Complex Systems (BIOCOM-SC) research group, Universitat Politècnica de Catalunya (Spain). Expert in modelling and simulation of biological systems.

"Any decision-making process—whether in politics, medicine, or public health—must be grounded in data, with an understanding of the situation and the problem at the appropriate level. If I have access to all the relevant information, including the patient's details, my decision will be much more informed. The patient is actually part of a much broader ecosystem [...] and **the decision I make affects not only the patient, but also the environment."**

Clara Prats Soler

"This **real-time surveillance** tool will **improve decision-making**, by enabling the detection of risks, the implementation of measures , the optimisation of protocols, and the refocusing of attention on hospitals. It is also designed to mitigate the dissemination of resistance genes through the environment."

Maite Martín Ibáñez

"It is important to maintain an integrated vision: what happens in one point eventually has an impact downstream. In addition to treatment, the Project is relevant for the information it provides for mapping, identifying peaks, and cross-referencing data with the health sector. This can help to **make prevention programmes and antibiotic use more objective,** improving them and generating social benefits from wastewater management."

Desirée Martín Navarro

“In contexts where it was not possible to diagnose individuals, **wastewater monitoring** provided information on the incidence’s dynamics of the pandemic at a given time. **Wastewater analysis played a key role** in detecting the emergence of new variants and identifying those in circulation[…], giving us greater **capacity for anticipating or predicting** what might happen in the weeks ahead.”

Clara Prats Soler, speaking about how the City Sentinel tool was used for early detection during the COVID-19 pandemic.

Although the LIFE GENESYS project is still in its first year of implementation, preliminary observations have already been generated that confirm the relevance and urgency of the problem. This **initial evidence highlights the need for decisive political action** at a European level to **control antibiotic residues and resistance genes in hospital wastewater**.

Preliminary results:

- Initial sampling campaigns carried out at the Parc Taulí University Hospital have detected **significant concentrations of antibiotics in hospital effluents**, including substances classified as critical by the WHO.
- **Significant variations** in antibiotics concentrations have been identified **over time**, further reinforcing the need for continuous and tailored monitoring systems.
- **Conventional WWTPs are not specifically designed to remove such compounds** from wastewater, meaning they can subsequently be detected in the receiving environment. This is consistent with case studies reported in several EU countries and elsewhere.[6,7,24,25,26]

LIFE GENESYS is a multidisciplinary consortium coordinated by Cetaqua-Water Technology Centre, and comprising partners LABAQUA, Aigües Sabadell, Parc Taulí University Hospital, Apria Systems, and the Institute of Parc Taulí Research and Innovation Institute Foundation (I3PT).

Initial policy recommendations

➔ Keys to an effective political response to AMR in hospitals

Evidence from the LIFE GENESYS project, together with the strategic insights obtained from expert stakeholders, highlights the pressing need to address existing gaps in the management of antibiotic residues and resistance genes in hospital wastewater.

The following initial recommendations may be considered in the context of ongoing reforms to European environmental and pharmaceutical legislation:

1. **Expand the list of monitored contaminants under Directive (EU) 2024/3019.**

Expanding the list of monitored contaminants to cover all priority antimicrobials identified by the WHO would strengthen the EU framework and ensure better alignment with international health priorities.

2. **Develop a specific regulatory framework for hospital effluents and other high-impact AMR sources.**

A dedicated legal instrument establishing discharge limits for antibiotics and other pharmaceuticals is needed to effectively target critical AMR sources, going beyond the scope of general urban wastewater regulation.

"Hospital effluents contain precisely those **critically important antibiotics** administered to treat difficult-to-combat infections[...]. Thus, in my view, **focusing on hospitals is essentia**l, not so much on the quantitative aspect, but on the qualitative one—that is, to contain the spread of crucial antibiotic resistance genes."

Maite Martín Ibáñez

3. **Introduce mandatory monitoring of antibiotics, resistance bacteria and resistance genes in hospitals.**

Develop harmonised methodologies at the European level as part of environmental AMR control, including parameters such as frequency, sampling points, and priority antibiotics.

"When **developing regulations**, they must be based on data and on information from **data science** and simulation [...]. The **application of regulation** must also facilitate the **collection, storage, and use of data**, providing the necessary resources to measure the set indicators and thresholds. **Data must become part of daily practice and be stored and standardised correctly according to the FAIR principles** (Findable, Accessible, Interoperable, and Reusable). Data collection must be standardised to maximise its value. In addition, **data experts** capable of analysing, combining and using these data to develop explicative and predictive models are needed within the health and environmental ecosystem."

Clara Prats Soler

4. **Incentivise the analysis of the feasibility of carrying out the treatment at source.**

Implementing advanced treatment at source (e.g. in hospitals) could offer operational and economic advantages due to lower flow rates and higher concentrations of pharmaceutical compounds.

"**Economic and governance factors** can facilitate or hinder the implementation of such solutions. This is a public health issue that Europe has identified within the One Health framework [...], but it is not trivial to map everything so that, as a society, we have the most appropriate and **cost-efficient operational solutions.**"

Desirée Martín Navarro

5. **Promote effective coordination between the European Commission departments under the One Health framework and the EU's emerging contaminants strategy.**

Hospital wastewater is a priority environmental vector for the spread of AMR, and therefore requires a coordinated response from the European Commission's Directorates-General for Environment (DG ENV), Health and Food Safety (DG SANTE), and Research and Innovation (DG RTD). Such coordination should integrate human health, the environment, and innovation, in line with the One Health approach.

This coordination should be achieved through joint plans, common technical guidelines, and the alignment of regulatory and financial instruments.

The following table presents the LIFE GENESYS project's proposals to address the identified gaps in the regulation of AMR in European legislation.

Table 1. Gaps of the current regulatory framework and LIFE GENESYS proposal to address them.

Aspect	Current regulatory framework	Closing the gaps: LIFE GENESYS recommendations
Advanced treatment for micropollutants	Mandatory quaternary treatment by 2033 for WWTPs serving >10,000 population equivalents.	Assess the feasibility of carrying out the treatment at source.
Monitoring of pharmaceutical compounds	Mandatory monitoring of selected pharmaceutical substances in wastewater is required.	Expand monitoring to include priority antibiotics (CIA and HPCIA) and antimicrobial resistance bacteria and genes.
Reduction targets	Establishes general reduction targets for pharmaceuticals in wastewater.	Include specific targets by sector (e.g. hospitals) and contaminant type (antibiotics, ARGs, ARBs).
Hospital effluent regulation	Does not explicitly regulate or differentiate the source of the pollution.	Recognise hospitals as critical emission points and establish specific discharge limits within a new regulatory framework.
Antimicrobial resistance in wastewater	Does not address antibiotic-resistant bacteria or antibiotic-resistant genes.	Include standards for monitoring and controlling ARBs and ARGs in line with the One Health approach.

Call to Action

Pollution from antibiotics and resistance genes in hospital effluents represents an increasing threat to public health and environmental sustainability in Europe. Although there have been regulatory advances, such as the new Directive (EU) 2024/3019, the significant role of hospitals as primary emitters of pharmaceutical contaminants and antimicrobial resistance agents has to be effectively addressed.

"Our approach to this issue must be **more ambitious**. While the current actions are moving in the right direction, they are falling short, because the problem of **resistance is a silent threat**. We cannot see it, yet it is evolving and accelerating in the same way that **climate change** is, which in turn is fuelling the generation of resistance. **These are two converging threats**."

Maite Martín Ibáñez

"**A great deal of collaboration is needed** among different stakeholders, including pharmaceutical companies, hospitals, water operators, and the competent authorities."

Desirée Martín Navarro

The WHO has identified antimicrobial resistance as one of the top 10 global health threats. To tackle this issue, action must extend beyond the clinical sphere to include structural interventions in waste management, particularly hospital wastewater.

The LIFE GENESYS project offers an innovative, demonstrable, and replicable solution to eliminate antibiotics and resistance bacteria and genes at source. However, for these solutions to have an impact, it is crucial that legislation, investment, and political coordination are aligned.

"In all respects, **science must be the cornerstone of public policy formulation**. In 2018, the WHO added 'Disease X' to its list of the 10 most important threats, to draw the attention of governments and policymakers to the risk posed by the sudden emergence of a virus, which could lead to a pandemic. The pandemic arrived in 2020. AMR is also one of the major threats. The data support this and the estimates confirm it. We really should be much more ambitious than we currently are."

Maite Martín Ibáñez

Why now?

The window of opportunity is clear: **key EU regulations are being reviewed and implemented**, and international pressure to curb AMR is increasing. Europe can lead by example, addressing this threat with concrete, evidence-based decisions that are supported by innovation.

The **Council Recommendation (2023/C 220/01)** on reinforcing EU action against antimicrobial resistance through a One Health approach urges every Member State to draw up and execute a national AMR action plan, backed by adequate staff and funding.[27]

Without faster and more decisive action, it is unlikely that the EU will meet its AMR targets by 2030.[27] This will lead to an increased burden of hard-to-treat infections and a continued rise in AMR-related mortality.

The **ECDC** has reported only limited progress towards these goals. For example, infections caused by **carbapenem-resistant *Klebsiella pneumoniae* have increased by 50%** compared to 2019. This is in stark contrast to the target of a 5% reduction set for 2030.[27]

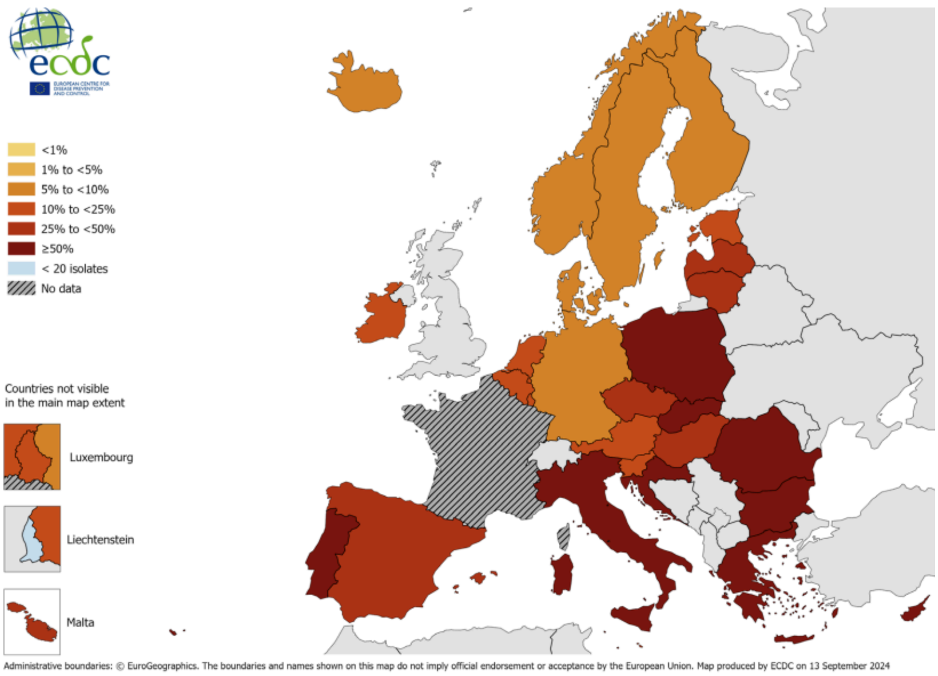


Fig.3. Percentage of invasive *Klebsiella pneumoniae* isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2023[27].

LIFE GENESYS stands ready to collaborate with European, national, and regional institutions, to provide real solutions to transform these environmental and health challenges into opportunities for political leadership.

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