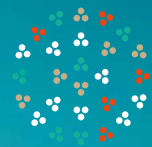




Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections

GLOBAL
AMR R&D
HUB



POLICY BRIEF

INCENTIVIZING ANTIBIOTIC ACCESS AND INNOVATION



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EU-JAMRAI & Global AMR R&D Hub | Policy brief: Incentivizing
antibiotic access and innovation

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POLICY BRIEF

INCENTIVIZING ANTIBIOTIC ACCESS AND INNOVATION



PREDICTABLE ACCESS TO LIFE-SAVING ANTIBIOTICS IS UNDER THREAT

Antibiotic resistance imperils global health, with multi-drug resistant bacterial infections accounting for over 33,000 deaths in Europe alone in 2015. The number of annual global deaths is unknown but predicted to be large. Yet contrary to the public health need, antibiotic innovators and manufacturers are struggling.

New antibiotics are unable to generate revenues large enough to sustain the interest of multinational players and even small developers are failing to cover their costs, resulting in bankruptcies of small antibiotic innovators. Melinta, an American antibiotic innovator went bankrupt in December 2019, after receiving regulatory approval in the United States and Europe for an antibiotic judged as “innovative” against a “critical” priority pathogen by the World Health Organization. Physicians use new antibiotics as a last resort in order to preserve their efficacy. Whereas this is sound stewardship, it dis-incentivizes innovation since unit sales determine revenues.

Simultaneously, shortages of older antibiotics are increasing. Due to antibiotic resistance patterns and prescribing habits, the markets of some essential antibiotics are small, including those for children. Tendering processes based solely on price and automatic price reductions for generic medicines reduce

profitability, leading to a consolidation of supply. The dependency on sole manufacturers may come as a surprise, when there is suddenly no medicine available. For example, in 2017 a fire at a raw material factory in China resulted in a global shortage of piperacillin/tazobactam. During the COVID-19 pandemic, supply chains have been unable to meet demand as well as challenged by supply disruptions due to lockdowns and border closures.

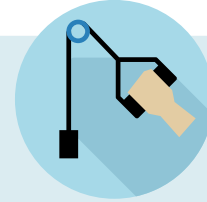
Several prominent reports have assessed the challenges to antibiotic access and innovation and have made recommendations, including calls for “pull” incentives, aiming to increase revenues for marketed, innovative antibiotics. We set out to understand countries’ perceptions of these recommendations, through frank and anonymous dialogue. As a part of the EU Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI) we performed in-depth interviews with policymakers and AMR experts in ten European countries.¹ These insights were made more globally representative with support of the Global AMR R&D Hub who supported the inclusion of a further three countries from other continents.² The aim of the interviews was to understand the barriers and facilitators for implementing incentives that promote antibiotic access and innovation.

¹ European countries interviewed were: Belgium, Denmark, France, Germany, Luxembourg, the Netherlands, Norway, Romania, Spain, and Sweden. We interviewed policymakers from Ministries of Agriculture and Research in nine of these countries.

² Supplementary pool included interviews with the Ministries of Health and other AMR experts in Canada and South Africa, and an interview with an AMR expert in Japan.

PREDICTABLE ACCESS TO LIFE-SAVING ANTIBIOTICS IS UNDER THREAT

EUROPEAN “PULL” MECHANISMS



The Pharmaceutical Strategy for Europe (2020) states that the EU will pilot a pull incentive in 2021. Three countries are already underway:

England will pay an annual fixed payment determined through a health technology assessment (including both patient and societal value) for the supply of a new antibiotic. The payment is not dependent upon sales volumes. The pilot has selected two antibiotics. Target implementation date is Spring 2022.

Germany has revised the way it assesses new “reserve” antibiotics, allowing for higher unit prices in line with the value of the new antibiotic.

Sweden has signed agreements with suppliers of five new antibiotics for an annual revenue guarantee. Swedish hospitals continue to purchase as normal with the funding from the pilot study paying the difference between the guarantee and actual sales. The agreements started July 15, 2020 and will continue for two years.

ELEVEN COUNTRIES EXPRESSED GENERAL SUPPORT FOR ANTIBIOTIC INCENTIVES

Interviewees expressed support for antibiotic incentives in 11 of 13 countries. Yet, it was clear from the interviews that policymakers' support is high-level and general. Almost all countries are uncertain which incentive is appropriate for their country, how to implement an incentive, and how much it will cost. They prefer to wait for evidence from Germany, Sweden, and the United Kingdom (see box). Nine of the 10 European countries interviewed would prefer a common, European or multinational incentive, as long as it is independent from national health technology assessment, medicine pricing, and reimbursement.

Policymakers were clear that incentives should only apply to antibiotics that meet public health needs and that the public health value must be demonstrated through showing benefit in clinical situations against multi-drug resistant infections (see quote).

Whereas policymakers expressed concerns about the lack of antibiotic innovation, this was not the principal driver for support for new incentives. Rather, countries (9 of 11) indicate a preference for a model that ensures access to both old and new antibiotics, with the highest priority for older antibiotics.

“Antibiotics are being approved for indications where there is no intention that they will be used. This sends the wrong signal...would prefer that antibiotics are tested against drug-resistance instead. If the trials need to be done in [high-resistance countries] and they are performed according to existing standards, this is preferable.”



COUNTRIES DO NOT HAVE PREDICTABLE ACCESS TO LIFE-SAVING ANTIBIOTICS

Predictable access to life-saving antibiotics is a common global challenge. Twelve of 13 countries indicated that shortages of existing antibiotics is a serious problem. Eight out of 13 indicated that this resulted in greater use of broad-spectrum antibiotics and thereby potentially increasing antibiotic resistance. As important antibiotics continue to be unavailable, doctors change prescribing habits, potentially away from evidence-informed prescribing guidelines. Interestingly, we also interviewed veterinary counterparts in European countries, who stated that there was no indication of shortages of veterinary antibiotics, despite often being comprised of the same active pharmaceutical ingredients.

National medicines agencies and procurers lack the tools to work proactively to avoid antibiotic shortages. They know which factories produce the raw materials and finished medicines for only their own marketed medicines, but do not have access to data about the global market for a specific medicine. Factory information is generally considered a business secret and cannot be made publicly available. When countries are notified of a supply disruption, it is too late to find a solution if all companies are dependent upon the same raw material supplier. This is a common problem since the world supply of active pharmaceutical ingredients is highly concentrated in a few countries. A lockdown in one geographic region can have significant implications for the world's medicine supply. Trans-

parency is needed to understand supply chain resilience. New Zealand has already taken steps, openly publishing the name and location of raw material and finished product factories for all its marketed medicines.

Unpredictable access is not only a challenge for older antibiotics but also for new ones. New antibiotics are not widely available. For example, the new antibiotic combination meropenem/vaborbactam, judged as "innovative" by the World Health Organization against "critical" priority pathogens, was approved by the European Medicines Agency in 2018 but is currently marketed in only five EU countries.



A lockdown in one geographic region can have significant implications for the world's medicine supply.

SPECIFIC, DETAILED INCENTIVES MUST BE COMMUNICATED TO FACILITATE IMPLEMENTATION

The results of these interviews point to a clear need for specific, detailed incentives that national policymakers can assess, tailor, and implement. These incentives must be designed with the aim of ensuring national access to important antibiotics that meet public health need. EU-JAMRAI aims to publish a recommendation in early 2021.

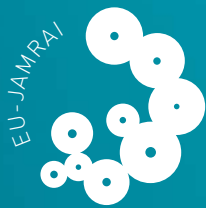
ABOUT EU-JAMRAI

EU-JAMRAI is a European Union Joint Action on Antimicrobial Resistance (AMR) and Healthcare-Associated Infections (HCAI) that brings together 44 partners and more than 40 stakeholders. Our mission is to foster synergies among EU Member

States by developing and implementing effective One Health policies to fight the rising threat of AMR and to reduce HCAI. EU-JAMRAI started in September 2017 and will finish in February 2021.

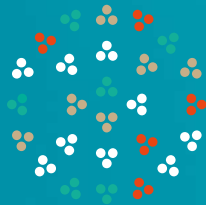
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