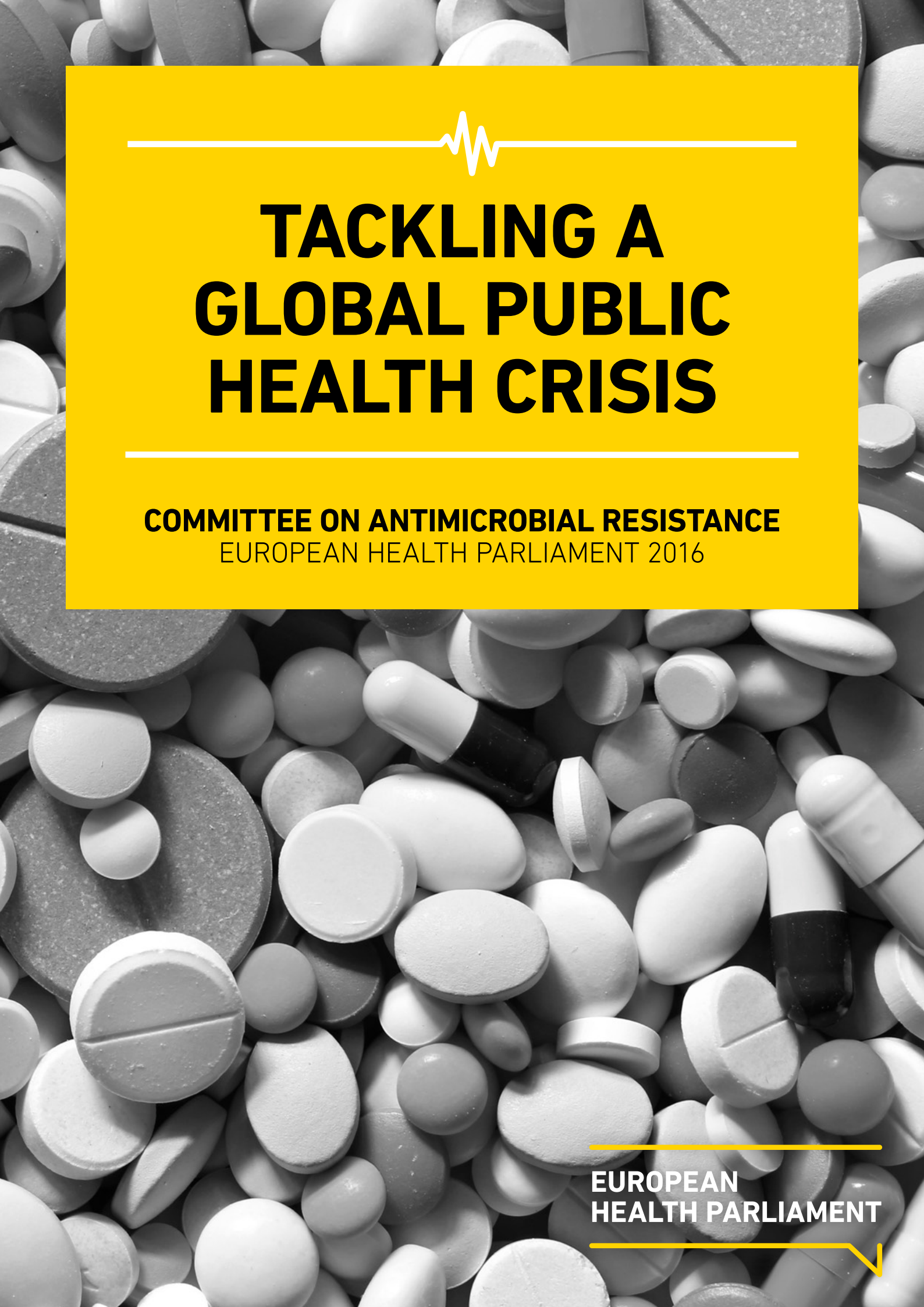

TACKLING A GLOBAL PUBLIC HEALTH CRISIS

COMMITTEE ON ANTIMICROBIAL RESISTANCE
EUROPEAN HEALTH PARLIAMENT 2016

EUROPEAN
HEALTH PARLIAMENT

EXECUTIVE SUMMARY

Antimicrobial resistance (AMR) is the resistance of bacteria and other microbes to previously effective drugs, resulting mainly from the misuse and overuse of antimicrobial drugs. Drug resistance is threatening the ability to treat common infections[1]. Each year, antibiotic-resistant infections lead to 25,000 deaths in the European Union[2] and 700,000 deaths worldwide[3]. If resistance is left unchecked, the death toll is predicted to rise to 10 million people per year by 2050[3].

Global antibiotic consumption grew by 30% between 2000 and 2010[4] and in the EU, overall antibiotic consumption in the community and in hospitals increased between 2010 and 2014[5]. In China and India, antibiotic pollution in rivers and waterways is leading to the proliferation of resistant bacteria, both locally and also worldwide through travel and trade[6,7,8].

This report makes eight recommendations in four key areas:

1. EU Member States should make cross-border healthcare more visible

- *Set up a "European Health Semester": a platform for sharing best practice and country-specific recommendations focusing on cross-border health threats.*
- *Put in place national AMR teams: multidisciplinary teams to ensure effective implementation of national AMR action plans and targets, reporting back to the European Health Semester.*

2. EU Member States should prevent AMR through GP practice intervention and education

- *The EU should encourage R&D into affordable point-of-care diagnostic tools through initiatives such as the Innovative Medicines Initiative 2 (IMI2).*
- *Delayed e-prescriptions should be introduced at Member State level in combination with the use of rapid diagnostic tests.*
- *Member States should introduce a national requirement for healthcare professionals to complete a module on infection control as a part of the renewal of their licence to practise.*
- *Member States should promote health literacy from childhood.*

3. EU Member States should implement manufacturing standards to prevent pharmaceutical pollution that leads to AMR

- *Environmental risk assessments should be conducted on antibiotics manufacturing.*

4. Stakeholders should create access to innovative tools and treatments against AMR

- *Create an AMR Global Access Fund that would ensure access to existing and newly developed AMR tools (antibiotics, rapid diagnostics, and vaccines) for developing countries through the collaboration of international organisations, payers and charities.*

AMR, A GROWING AND GLOBAL THREAT

A POST-ANTIBIOTIC WORLD

AMR is the resistance of microorganisms to an antimicrobial drug originally designed to treat it, meaning that the antimicrobial drug no longer works, or works less effectively. Without urgent action to reduce AMR, it is estimated that 10 million people – equal to the population of Portugal – will die worldwide each year from drug-resistant infections by 2050. This is more than the current death rate from cancer and eight times that of road accidents[3].

Without effective antibiotics, many standard medical procedures will become increasingly difficult to carry out[3]. Hip replacements, chemotherapy and organ transplants are some of the treatments threatened by the spread of resistant organisms. Furthermore, common infections and minor injuries will increase hospital stays and lead to a greater risk of death. The extra healthcare costs and productivity losses associated with AMR are conservatively estimated at €1.5 billion annually for the EU[2], and could cost the world economy 100 trillion USD by 2050[3].

THE FACTORS DRIVING AMR

The development of resistance in bacteria is a natural phenomenon driven by the selective pressure of the bacteria to survive. Several human factors, however, have accelerated its emergence and its spread to unprecedented levels. The main reasons are:

(1) In human medicine, a key driver of AMR is the excessive and inappropriate use of antibiotics[3]. Another is the lack of rapid diagnostic tests, and under-use of existing tests, which makes it difficult for clinicians to determine whether an infection is bacterial or viral, and thus whether antibiotics are needed[9].

(2) In agriculture, a considerable amount of antibiotics are used in healthy animals to prevent infection or speed up their growth. This increases resistance and can subsequently be passed onto humans[3].

(3) Poor infection control practices in hospitals help the spread of healthcare-associated infections (HAIs), a quarter of which are caused by antibiotic-resistant bacteria[10]. In the EU, national training programmes for infection control exist in 55% of Member States for nurses and in 33% for doctors[11]. These differences result in widely varying capacities of healthcare institutions to deal with the surveillance, prevention and control of HAIs.

(4) The presence of antibiotics in the environment can promote antibiotic resistance[6]. For example, the dumping of active pharmaceutical ingredients (APIs) into rivers and waterways used by local populations can lead to the spread of resistant strains around the world through travel and trade. Since most of the world's antibiotic drugs are manufactured in China (which produces 80-90% of antibiotic active pharmaceutical ingredients-APIs) and India[7], the issue goes well beyond Europe's borders.

(5) Across the world, countries show variability in antibiotic consumption, resistance rates and in policy response to AMR[14], which is a problem in the face of the cross-border nature of AMR[7,8].

(6) The lack of long-term investment in research and development into novel antibiotics, preventive approaches and alternative strategies to antibiotics[3] means that there is a gap between the medical need to combat AMR and the size and quality of the therapeutic pipeline. Moreover, equitable and affordable access to innovative tools is lacking, particularly in low- and middle-income countries, some of which have the highest rates of AMR[1].

This paper focuses on resistance to antibacterial drugs or 'antibiotics' because (i) antibiotic resistance has been described by the WHO as the single greatest challenge in infectious diseases today, threatening rich and poor countries alike and (ii) although drug resistance in HIV/AIDS, malaria and fungal infections is also an immense challenge, much effort is already being devoted to research and implementation in these areas[15].

THE POLICY ENVIRONMENT OF AMR

On a national level, there are many examples of valuable AMR-related initiatives. In the Netherlands, mandatory AMR teams in hospitals help ensure appropriate use of antibiotics[16]. In France, nation-wide media campaigns have led to the decrease of overall antibiotic consumption by 10.7% between 2000 and 2013[16].

Many EU initiatives encourage Member States to develop and implement national policies and action plans for countering AMR. Council Conclusions in 2002, 2009 and 2012 set out strategies to contain resistance, put forward measures on general patient safety and healthcare-associated infections, and called for closer collaboration between the human and veterinary sectors. In November 2011, the Commission launched a 5-year EU Action Plan against AMR[17], which is currently being evaluated. Recently, the European Parliament supported restrictions on the use in animals of certain antibiotics that are reserved for the treatment of human infections, and bans on preventive use of these medicines in animals[18]. Whilst the EU has made legislative progress in tackling AMR in the animal sector, action in the human sector has been limited.

Globally, only 25% of countries have implemented a national policy to tackle AMR[14] and less than 40% of countries have put in place infection prevention and control programmes[14]. The WHO has recently adopted a Global Action Plan on AMR, which focuses on five areas for national and international action: awareness, surveillance and research, infection control, antibiotic stewardship, and sustainable investment[19].

This is not an exhaustive list of on-going and planned initiatives. While our Committee applauds these, we call for increased political will to take further action at Member State level and to mandate an increased role for the EU in coordinating efforts.

KEY CHALLENGES AND SOLUTIONS

Based on the causal factors of AMR, our Committee proposes actions in four areas to contain the spread of resistance:

1. EU MEMBER STATES MUST MAKE CROSS-BORDER HEALTHCARE MORE VISIBLE

The impact of EU actions to date has been limited, as acknowledged by Edith Schippers, Minister of Health of the Netherlands, who said recently: "Two EU Council recommendations, several Council conclusions, a European Action Plan, European Commission Guidelines, European Parliament Resolutions. Several reports on economic impact, a strategic research agenda...In the meantime, we still see resistance levels in Europe rising".

RECOMMENDATION #1

We recommend more coordinated action and tangible outcomes in cross-border healthcare in the EU. Health should be placed as high on the EU's agenda as economic policy. The EU should use its coordinating powers where it adds value, but in the meantime respect Member States' own specific challenges.

We recommend the creation of a **"European Health Semester"**, a comparative tool, based on annual cycles of data gathering, country reports and recommendations. The European Health Semester should focus on cross-border health threats, a clear competence of the EU[20]. AMR should be a key element of the Health Semester, given that it is an urgent threat to the achievements of modern medicine[21].

The tool would work as follows. The Commission would collect data from the Member States each year, based on a set of indicators related to health systems and to AMR. These indicators would be based on existing data from the European Centre for Disease Prevention and Control or the Commission's 2014 Communication on effective, accessible and resilient health systems, with the creation of new indicators as needed. Comparability of indicators would have to be ensured.

Member States could thus measure their progress in fighting AMR, based on annual comparisons of their national data with other Member States. An EU advisory panel would also make recommendations each year.

The Commission would draw up the surveys and the recommendations, the Council would discuss/endorse/adapt the recommendations, and the Parliament would be involved in dialogue throughout. The advantage of engaging each institution would be to foster a more collaborative approach.

RECOMMENDATION #2

Member States should set up **national AMR teams** to implement the European Health Semester and increase political will on a national level.

The teams, comprising physicians, pharmacists, infectious disease specialists, psychologists and patients, would ensure effective implementation of national AMR action plans and achievement of targets, and compile the information required for the European Health Semester.

The government would empower teams to set national AMR targets, improve healthcare practices and prevention methods, and to act as the direct link to the European Health Semester. This would ensure political commitment to fight AMR and contribute to successful implementation of national plans. Teams would be in place for as long as necessary to reduce AMR to a level predetermined by the Member States, and to ensure sustainability of changes implemented. As best practice in Lithuania shows[22], such teams were a success in regional coordination and management of AMR.

2. EU MEMBER STATES SHOULD PREVENT AMR THROUGH GENERAL PRACTICE INTERVENTION AND EDUCATION

RECOMMENDATION #3

Rapid diagnostic point-of-care tests can increase diagnostic certainty and may be used to demonstrate to patients that an antibiotic is unnecessary[3].

- We encourage the development and use of rapid tests. The EU should encourage R&D into affordable point-of-care diagnostic tools through programmes such as IMI2.

RECOMMENDATION #4

Behavioural interventions, for example delayed antibiotic prescription, can also reduce unnecessary use of antibiotics[22]. A patient would get tested at the doctor's office, and the doctor would subsequently call the patient once the results arrive – and send an e-prescription for an antibiotic to the pharmacy in the case of confirmed bacterial infection. E-prescription systems can help delayed prescriptions procedures because they would be electronically stored in a database and could be validated once the test results are in, without even the need for the further communication between doctors, patients and pharmacists that is needed with traditional paper prescriptions.

- Delayed e-prescriptions should be encouraged at Member State level in combination with the use of rapid diagnostic tests. E-prescriptions could be uploaded to a national server connected to all pharmacies, or saved on a patient's electronic health insurance card.
- The EU should foster the development of digital prescription systems in all Member States, and encourage the involvement of all stakeholders - doctors, health ministries, IT and insurance companies - to find solutions that fit the needs of each Member State.

EDUCATION AND TRAINING FOR HEALTHCARE PROFESSIONALS AND CHILDREN

It is estimated that intensive hygiene and infection control programmes could prevent 20-30% of healthcare-associated infections, including drug-resistant ones[11].

RECOMMENDATION #5

- We encourage Member States to introduce a national requirement for health professionals to complete a module on infection control (i) every time they renew their licence with the country's authority and (ii) when they apply for their licence to be recognised in another Member State. The licensing authority of each Member State should provide the training, thus preventing additional costs for hospital management or staff.
- We encourage the Commission to update its requirements for the recognition of professional qualifications in the EU to include infection control and AMR for healthcare professionals.

RECOMMENDATION #6

Together with the Committee on Prevention & Self-Care, we jointly recommend the Member States' health, finance and education ministries to develop cross-funded initiatives to promote health literacy from childhood. This would be done by including education on healthy lifestyles and prevention (notably with vaccines) as well as the proper use of medication (and notably antibiotics) in school curricula.

3. IMPLEMENT MANUFACTURING STANDARDS TO PREVENT PHARMACEUTICAL POLLUTION THAT LEADS TO AMR

At present, the regulatory framework for Good Manufacturing Practice (GMP) in the US and Europe pays insufficient attention to environmental safety. Even though supply chains from India and China are regularly inspected, no sanctions can be applied for polluting practices, because verification of this parameter depends exclusively on local governments[23]. To prevent pharmaceutical pollution that leads to AMR, manufacturers should be held accountable for the antibiotics they place on the market and their environmental consequences through the implementation of manufacturing standards. These standards should (i) offer a coherent European solution to address this global issue (ii) integrate all the steps of the supply chain and (iii) be equally applied to medicinal products for both human and veterinary use that are sold in Europe, even when produced in China and India.

The current EU regulatory system requires an Environmental Risk Assessment (ERA) to accompany any application for marketing authorisation of a medicinal product for human use that is submitted since the 'Guideline on the environmental risk assessment of medicinal products for human use'[23] entered into force in 2006. However, antibiotics are predominantly old molecules (many are 30-40 years old) that received marketing authorization before 2006, and most are therefore not affected by this guideline. But there is no scientific evidence that products put on the market before 2006 are of less environmental concern than new products[24].

RECOMMENDATION #7

- We consequently recommend revising the 2006 'Guideline on the environmental risk assessment of medicinal products for human use' in order to require all antibiotics manufacturers, regardless of the marketing authorisation year, to ensure all supply chains comply with the guideline. Requirements to assess the risk for increased antibiotic resistance development should be added to the Guideline.
- A systematic monitoring of the occurrence and effects of antibiotics in the environment, and transparent publication of findings, are needed to fill the current gap in public access to environmental risk data.
- In the long term, environment criteria should be integrated into the overall GMP framework.

4. STAKEHOLDERS SHOULD CREATE ACCESS TO INNOVATIVE TOOLS AND TREATMENTS AGAINST AMR

Research initiatives for new antibiotic drugs and alternatives, such as the Innovative Medicines Initiative or the Global AMR Fund[15], are useful only if the solutions are made accessible in low- to middle-income countries, particularly in those with a high prevalence of antimicrobial resistance[1]. With increased travel and trade, the spread of diseases at Europe's borders is inevitable, and action is therefore needed on a global scale.

RECOMMENDATION #8

- We recommend the creation of an **AMR Global Access Fund** that would ensure access to existing and newly discovered AMR solutions (such as vaccines, diagnostics, drugs and other alternatives) for developing countries, and which would be complementary to the Global AMR Fund proposed by Jim O'Neill[15]. Payers, charities and international organisations would pool their resources to 'buy out' patents from innovators and allow other manufacturers to produce these products through licensing agreements. The initiative would reward innovation, whilst ensuring equitable and affordable access to solutions able to tackle AMR globally.

CONCLUSION

Our Committee realises that the problem of AMR is complex and multi-faceted, and requires an equally sophisticated solution. We have touched here upon current gaps, and proposed ideas that could be implemented as complements to existing initiatives. We encourage the EU and Member States to work together in implementing the recommendations. We look forward to discussing our ideas further with key stakeholders and policy makers.

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