

ADDRESSING A GLOBAL PUBLIC HEALTH THREAT: ANTIMICROBIAL RESISTANCE

What is antimicrobial resistance?

Antimicrobials are medicines to treat and prevent infectious diseases caused by pathogens such as bacteria, viruses, fungi and parasites. Antibiotics, which are used to treat bacterial infections, are one of the most important types of antimicrobials. Antimicrobial resistance (AMR) occurs when a pathogen evolves to survive antimicrobial treatment. While such evolution is inevitable, AMR is developing more quickly due to the inappropriate use of antimicrobials.

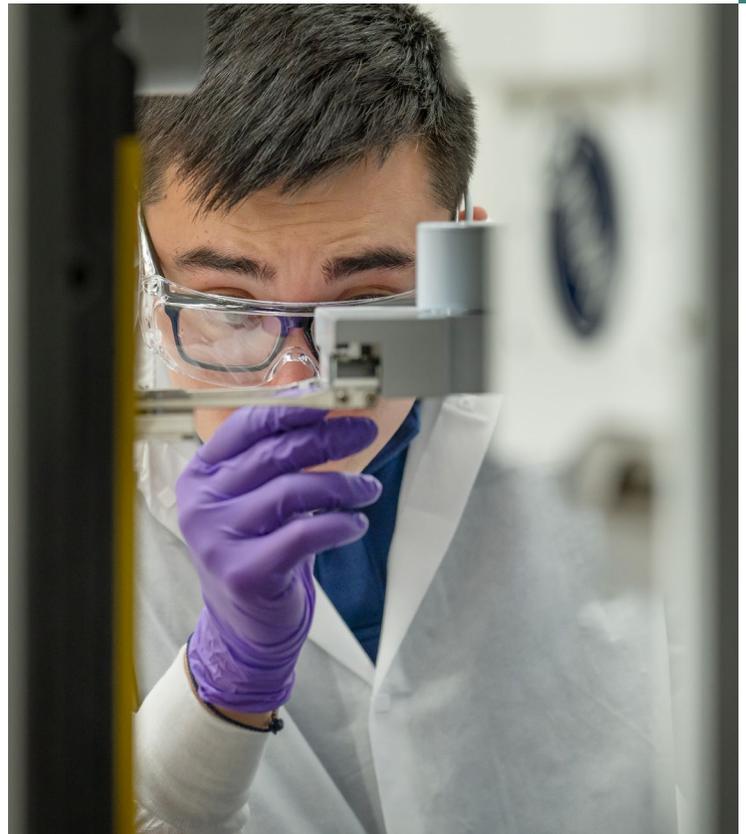
Vaccines and antibiotics have revolutionized modern medicine, saving millions of lives worldwide. Many important advancements including surgery, cancer chemotherapy and organ transplantation depend on our ability to manage infections. Without effective antimicrobials, these medical advancements will carry significantly higher risks for patients. Rising levels of resistance to antimicrobials is a serious threat to public health, a safe and sustainable food supply, and global security.

How should the world address AMR?

Industry, governments, health care providers and others must take steps to ensure our current antimicrobials are used responsibly. A One Health approach – with coordinated action between the human, animal and environmental health sectors – is crucial to slowing the development and spread of AMR so that the available antimicrobials we have can continue to be effective for as long as possible.

There is also an urgent need for new antibiotics to address growing resistance. However, there are relatively few in development. Over the past two decades, there has been a significant decline in the number of companies conducting antibiotic and antifungal R&D due to insufficient returns on investment.

The challenges posed by AMR cannot be solved by individual stakeholders. They require global cooperation, collaborative strategies and a supportive regulatory and political environment. It's necessary to take action to ensure the development and availability of treatments that can help to protect us against the growing threat of resistant bacterial infections.



Society cannot afford to ignore AMR.



The human cost. The European Centre for Disease Prevention and Control estimates that at least 670,000 people become infected with antibiotic resistant bacteria and at least 33,000 people die as a direct result of those infections in the EU each year.¹



The public health cost. In addition to the danger caused by the infection, AMR also endangers the health of our society that depends on antimicrobials in order to benefit from medical advancements, such as organ transplantation, cancer chemotherapy and major surgery.



The economic cost. According to the World Bank, AMR could cause low-income countries to lose more than 5% of their GDP and push up to 28 million people into poverty by 2050.²

ACTION IS NEEDED TO COMBAT AMR

There is no single solution to the complex problem of AMR. Collaboration from multiple stakeholders is needed to slow the threat of AMR. Industry, governments, health care providers and others need to work together to:

Prevent Infections

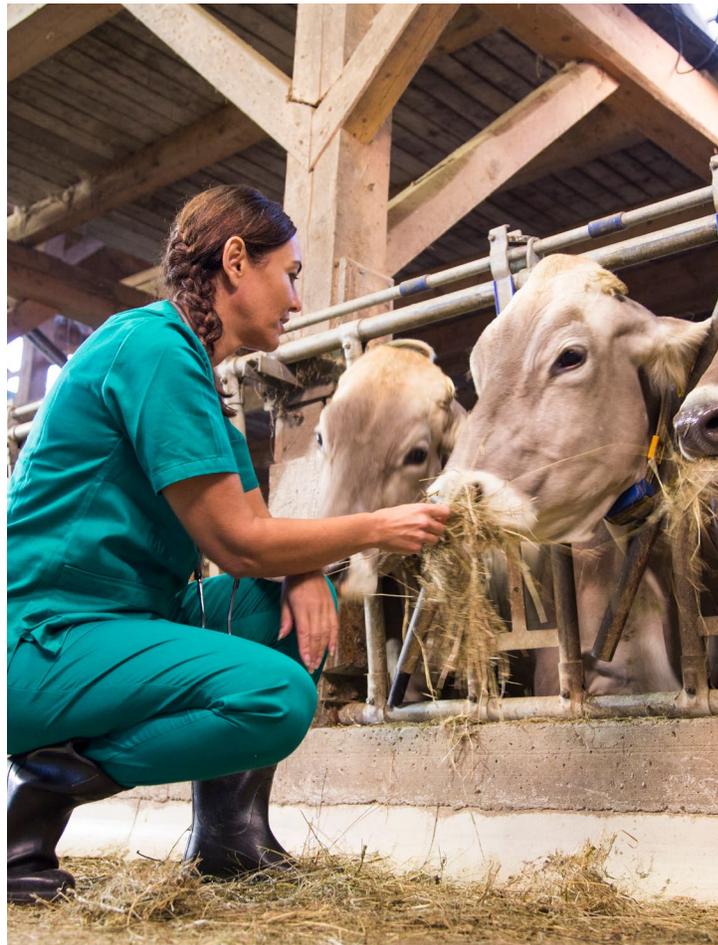
Vaccines are an important tool to address AMR. They prevent infections and can support appropriate antibiotic use in humans and animals, and prevent the circulation of resistant bacteria. Additionally, vaccines have shown to be less susceptible to the evolution of resistance than antibiotics. The role of vaccination in combatting AMR is widely recognized, but concrete policy action is needed to increase the impact of vaccines as a tool to tackle AMR.

Advocate for Policy Solutions That Drive Innovation

It's necessary to overcome the scientific and economic barriers to antibiotic innovation to ensure a sustainable pipeline of new medicines and technologies to address AMR. As a result of the combination of low reimbursement rates and low volume use, many small antibiotic developers have gone out of business entirely, and many large pharmaceutical companies have exited antibiotic development. Government action on incentives is needed to enable sustainable investment in antimicrobial R&D. These reforms are urgently needed to ensure patients have access to effective antimicrobials - now and in the future.

Advance Antimicrobial Stewardship (AMS)

Making meaningful progress against AMR will require both the development of new antimicrobials and the implementation of evidence-based policies to slow resistance to current antimicrobials. Improved diagnostics and responsible antibiotic use can play an important role in treating patients with resistant infections and preserving the effectiveness of antibiotics. Industry leaders, government officials, health care providers, veterinarians and other stakeholders must work together to support responsible prescribing and use of antimicrobials.



Support Global AMR Surveillance

To address AMR, we need to understand it. AMR surveillance studies can be used to identify trends and spot early indicators of resistance. As a result, diagnostic tools can be developed, the responsible use of antimicrobials can be supported, and patient outcomes and overall population health can be improved. It's necessary to work together to strengthen surveillance systems worldwide by enabling them to collect, manage and share AMR data more efficiently.

Protect and Maintain Animal Health and Wellbeing

A safe and sustainable food supply requires healthy animals. Antibiotics are important, life-saving veterinary therapeutic tools to manage bacterial infections in companion and food-producing animals. Expanded use of vaccines and responsible use of antibiotics in animals can help safeguard the efficacy of antibiotics. A One Health approach, addressing human, animal and environmental health, will be critical to addressing AMR and ensuring antibiotics are effective now and in the future for both humans and animals.

VACCINES AND AMR

By preventing infections through the use of human and animal vaccines, many of the key drivers of antimicrobial resistance (AMR) can be reduced. While global stakeholders have recognized the complementary role that vaccination can play in addressing AMR, this recognition needs to be translated into concrete policy action. To maximize the impact of vaccines on AMR, global partners need to come together to:



Strengthen the evidence base. More data and evidence are needed to clearly demonstrate how current and future vaccines for humans and animals can reduce AMR-related morbidity and mortality and limit the economic impact of resistance. Such data can help make the case for additional research, policy reforms, and programmatic and funding decisions.



Incentivize development of new vaccines. New incentives are needed to encourage the development of innovative products that can prevent viral or bacterial infections that drive antibiotic use. A package of incentives, including both push and pull incentives along with health technology assessment and valuation reform, could help address the different challenges across the product life cycle and drive greater investment.



Increase uptake of existing vaccines. More must be done to optimize the use of existing AMR-relevant vaccines. This includes efforts to increase awareness and understanding of the role vaccination plays in tackling AMR and enhancing equitable access across the globe. Stakeholders should work together to ensure AMR National Action Plans prioritize uptake of existing vaccines for humans and animals.



How do vaccines impact AMR?

Effectively tackling AMR will require reducing inappropriate antibiotic use. In both humans and animals, vaccines prevent infections and can support responsible antibiotic use, reduce the need for antibiotic use and decrease the circulation of resistant bacteria. Additionally, vaccines have been shown to be less susceptible to the development of resistance than antibiotics.

Relevant stakeholders must think broadly about the types of vaccines that can impact AMR. New research needs to be funded and conducted on vaccines that treat a variety of infections, including vaccines that prevent bacterial infections, vaccines that prevent viral and parasitic infections (which are often treated inappropriately with antibiotics), and vaccines that prevent infections in animals.

MSD'S LEADERSHIP IN INFECTION PREVENTION

MSD is taking action to support R&D for AMR-relevant vaccines. Vaccine innovation is just one of the many ways we are working to address this global health crisis. For over a century, we've discovered and developed vaccines that have a significant impact on the health and wellbeing of both humans and animals, as well as public health.

MSD is working with a broad range of stakeholders to **expand the evidence base and raise awareness of the wider benefits of vaccination as a strategy to combat AMR.** We are also working with policymakers, health care providers, veterinarians, non-profit organizations, patients and farmers to achieve the broadest access to existing vaccines and facilitate rapid adoption of new vaccines when they come to market.

We have implemented a comprehensive One Health approach to addressing AMR. Our broad infectious disease portfolio and pipeline span both human and animal health. MSD Animal Health is one of the world's largest producers of vaccines for animals, producing over 102 billion doses per year. The company has developed a broad array of vaccines, as well as anti-infective and anti-parasitic therapies, to advance animal health and reduce the need for antibiotic use in animals. **We are commercializing or developing vaccines for all 15 prioritized animal diseases where vaccines could reduce antibiotic use in animals, as recognized by the World Organization for Animal Health (OIE).**



Developing Vaccines with the Potential to Help Reduce Antibiotic Use:

Universal coverage with pneumococcal vaccines have the potential to avert up to 11.4 million days of antibiotic use per year in children younger than five years of age – a 47% reduction in the amount of antibiotics used for treating pneumonia caused by *Streptococcus pneumoniae*.¹ MSD's vaccine development programs include several candidates designed to help protect against *S. pneumoniae* infection in children and adults.

Supporting Access to Affordable Vaccines:

For over a decade, MSD and the Wellcome Trust have worked to develop vaccines targeting the needs of low- and middle-income countries (LMICs) to address gaps in low-resource settings through the Hilleman Laboratories, a non-profit in Delhi, India. Through this first-of-its-kind initiative, we have launched several promising programs, including accessible vaccines for cholera, *Shigella* and Meningococcus.

Introducing Vaccination To Aquaculture in Norway:

In the 1980s, thousands of farmed fish in Norway and other Northern European countries were affected by bacterial diseases, including vibriosis and furunculosis. In 1987 and 1990, MSD Animal Health invented both cold water vibriosis and furunculosis vaccines, respectively. Upon the introduction of these vaccines, the use of antibiotics in fish feed dropped dramatically. Today, the company remains the major vaccine supplier to the Norwegian salmon industry and continues to innovate and develop new technology for automatic salmon vaccination.



1. Laxminarayan R, et al., Access to effective antimicrobials: A worldwide challenge, Antimicrobials: access and sustainable effectiveness, *Lancet*, 2016, 387: 168–75.

INNOVATING TO SECURE OUR ANTIBIOTIC FUTURE

Why are there so few antibiotics in development?

New antibiotics are urgently needed to address the growing threat of resistance; however, there are relatively few in development. Over the past five years, we've seen multiple large research-based pharmaceutical companies exit antimicrobial research and development (R&D). Several other leading biotechs with a focus on antibiotics have also gone bankrupt despite regulatory approval of their products. Others, due to limited return on investment, have been unable to make these products available in certain regions, even Europe and Japan. Today, MSD is one of only a few large pharmaceutical companies that has sustained a focus on antimicrobial R&D for humans.

Antibiotic discovery and development face numerous barriers:

Scientific challenges: Bacteria are resilient and constantly evolving. It is increasingly difficult to develop medicines that effectively kill bacteria while also ensuring an appropriate risk-benefit profile.

Regulatory challenges: While there have been some recent regulatory improvements to facilitate development of antimicrobials, clinical trial enrollment and design still present important challenges.

Economic challenges: The market for novel antibiotics faces unique challenges and dynamics.

- Antibiotics are undervalued relative to the benefits they bring to society.
- Uptake of antibiotics is slow since: (i) they are used sparingly to preserve effectiveness when resistant infections are rare; (ii) clinical guidelines are not regularly updated to reflect newer agents; and (iii) there may be limited diagnostic tools and surveillance data to guide appropriate use.
- Reimbursement systems encourage the use of older, inexpensive treatments, even when a newer antibiotic may in fact be the more appropriate treatment for a particular patient.



Ensuring there is a sustainable pipeline of new antibiotics to address growing resistance will require governments to create market conditions that enable a predictable and sustainable return on investment. **A package of interventions and incentives that address challenges across the product life-cycle is needed to help ensure patients have access to effective antimicrobials - now and in the future.**



Push incentives to reduce the risk of early investment in antibiotic R&D (e.g., grants and tax credits).



A delinked or partially delinked mechanism to reward innovation earlier in a product's life cycle when use is low and increase overall return on investment (e.g., market entry rewards, transferable exclusivity vouchers).



Reimbursement and Health Technology Assessment (HTA) reform to enable appropriate use of antibiotics.



Regulatory reform to streamline, accelerate and reduce the cost of clinical trials and support inclusion of relevant data in product labels globally, further enabling responsible use.



Updated clinical guidelines to support the appropriate use of antibiotics.

MSD'S ADVOCACY TO SUPPORT SUSTAINABLE INVESTMENT IN ANTIMICROBIAL INNOVATION

MSD has a strong legacy in antimicrobial R&D.

For more than 100 years, we have played a significant role in the discovery and development of medicines and vaccines to combat infectious diseases.

However, without substantial changes to the economic landscape, it will be difficult for the company to continue to justify significant investment into new antibiotic R&D programs. We continue to advocate for policies that would enable a predictable and sustainable return on investment for antimicrobial R&D.

MSD continues to focus on antimicrobial and vaccine R&D. Our broad portfolio spans both human and animal health and includes antibiotics, vaccines and approaches to reduce the need for antibiotics. But MSD's ability to continue investing in this area is threatened by the lack of progress on reimbursement reform and incentives.

MSD actively participates in international and country-level initiatives to explore how value-based reimbursement and other models can incentivize sustainable investment in antimicrobial development. The mechanisms to both incentivize R&D and promote appropriate use of antimicrobials need to be well integrated into health systems where these products are used. Across several regions, including the U.S., Europe and Japan, MSD and relevant industry associations are working closely with policymakers, infectious disease societies and other key stakeholders to develop and advance evidence-based proposals to address the challenges of antibiotic R&D.



We collaborate worldwide to ensure changes are made that allow the industry to continue efforts to drive innovation:

AMR Action Fund

In 2020, MSD and a group of more than 20 leading biopharmaceutical companies launched a groundbreaking partnership that aims to bring two to four new antibiotics to patients by 2030. As a lead investor, MSD has committed US\$100 million over 10 years to help bridge the gap between the antibiotic pipeline and patients. We are taking action now to sustain the fragile antibiotic pipeline. But the Fund is a temporary and time-limited bridge that will only work if governments make the necessary reforms to create a sustainable market.

Addressing Regulatory Challenges

MSD is involved in several public-private partnerships to improve clinical trial design, recruitment and streamline regulatory processes.

Supporting Research Into Evidence-Based Policies

Our company, in collaboration with GSK and Roche, supported the Office of Health Economics (OHE) to develop new elements, which could be incorporated into HTA value frameworks for antibiotics. These new elements aim to better capture the societal value of antibiotics in HTA reviews.

SLOWING THE DEVELOPMENT OF AMR THROUGH ANTIMICROBIAL STEWARDSHIP

Making meaningful progress against antimicrobial resistance (AMR) will require both the development of new antimicrobials and the implementation of evidence-based policies to slow resistance to current antimicrobials. Industry leaders, government officials, health care providers, veterinarians and other stakeholders must work together to support the responsible prescribing and use of antimicrobials by:



Ensuring antibiotics are used responsibly to preserve their effectiveness. Hospitals, physician practices, veterinary clinics and farms should have an antimicrobial stewardship (AMS) practice in place that is customized to the local needs and capabilities, ecology and epidemiology.



Developing standardized safety/quality of care metrics. The impact of AMS efforts in both humans and animals should be evaluated using standard measures. It is important that protocols are in place to support the responsible use of antimicrobials.



Investing in diagnostic research. Industry must continue to develop new rapid testing technologies, and regulators should ensure they are reviewed and made available in a timely manner. These tools can advance AMS efforts by enabling more informed health decisions. In addition, diagnostic tools and results can support best practices by prescribing physicians and veterinarians.



Increasing investment in multi-country, multi-sector collaborative approaches to tackle AMR. There are several examples of global initiatives that seek to address AMR from many different angles, including global health security and preparedness; collaborative AMR/AMS research; health systems strengthening; science-based standards; and water, sanitation, and hygiene. Multi-sector representation, including the private sector, is vital for such global initiatives.



What is AMS? And why is it important?

While the development of AMR is an inevitable evolutionary process, the pace is accelerating due to the widespread inappropriate use of antimicrobials. AMS is a principle that seeks to slow the development of AMR by optimizing the use of antimicrobials. The goal is to meet the immediate needs of patients and animals while limiting the long-term impact of AMR on broader human and animal health.

Evidence-based AMS considers human and animal health, agriculture and the environment, infection prevention, surveillance and diagnostic tools, animal identification and monitoring technologies. AMS can:

- Improve patient outcomes, public health and animal health and welfare.
- Preserve the effectiveness of antimicrobials.
- Reduce adverse effects from antimicrobials to improve quality of care of patients.
- Contribute to a safe and sustainable food supply, as well as the wellbeing of companion animals and livestock.
- Decrease health care and societal costs.

MSD'S COMMITMENT TO ANTIMICROBIAL STEWARDSHIP

MSD is taking action to advance AMS. For more than 100 years, we have played a significant role in the discovery and development of novel medicines and vaccines to combat infectious diseases in humans and animals. In addition to developing new antimicrobials, we are making significant investments in global AMS efforts to ensure current treatments remain effective for as long as possible.

MSD's AMS efforts aim to **enhance quality of care and improve global population health.** By focusing on funding AMS education, implementing AMS programs, advocating for policy changes and identifying and supporting unmet research needs, MSD is working to do its part to slow the spread of AMR through AMS.

MSD serves as an AMS resource, helping hospitals around the world to develop and implement patient-centered AMS programs that are customized at the local level based on factors including epidemiology, clinical setting and resource availability. We also provide significant grant funding to support a wide range of AMS initiatives and collaborations.

MSD's internal practices are also aligned with our global AMS efforts. **We have developed a formal framework that describes different aspects of appropriate use, including diagnosis, drug, dose, duration, de-escalation and setting of care.** With this framework, we regularly examine, review and update our promotional practices. We have developed an AMS curriculum that is available for all relevant MSD employees.



The pharmaceutical industry has an important role in supporting the responsible use of antimicrobials:

Establishing AMS Centers of Excellence:

In partnership with organizations around the world, MSD has established regional AMS Centers of Excellence which provide valuable training and implementation support to institutions within a specific region. In Latin America, MSD partnered with CIDEIM to establish an AMS Center of Excellence which provides training, guidance and support to hospitals across the region. Recently published data from this partnership show that the establishment of these regional centers resulted in improved adherence to antibiotic prescribing guidelines, reduced resistance rates and health care cost savings.

Supporting AMS Research: MSD's AMS Investigator Initiated Studies program is the only formalized investigator-based, peer-reviewed funding program supported by a biopharmaceutical company. Since its launch in 2015, MSD has supported 50 studies, including research on the role of AMS in the management of people with COVID-19. The program has generated research supporting the implementation of AMS principles across the globe, including over 20% of studies occurring in low-and middle-income countries. The program supports studies in Latin America, Africa and Asia, including on the impact of AMS intervention in India and two programs in Nepal: an evaluation of an AMS program for wound and burn care and an evaluation of a pilot program for hospital-based post-prescription review.

Another example of research funded through this program includes a manuscript on the role of emergency department-based AMS in the management of community acquired pneumonia (CAP) that was recognized as one of the most impactful AMS-related publications of 2018.

STRENGTHENING AMR SURVEILLANCE IN HUMANS AND ANIMALS

Surveillance is a key tactic in the fight against antimicrobial resistance (AMR). Industry, governments and health authorities need to work together to strengthen these surveillance systems worldwide and improve the effective collection, management and sharing of AMR data.

In particular, there is an urgent need to expand funding for surveillance systems in low- and middle-income countries (LMICs). While these populations are often hit the hardest by infectious diseases, adequate surveillance systems are not in place to understand and predict resistance trends that can help to inform patient care and appropriate antibiotic use.

Additionally, it is critical that microbiology laboratories around the world have the necessary knowledge, tools and equipment to support surveillance efforts. This will improve our collective ability to integrate surveillance systems and provide timely, high-quality data across the animal and human health sectors.

Several of the key long-running AMR surveillance programs are conducted by the multinational pharmaceutical industry. The data from these studies can help to support the appropriate use of antibiotics.

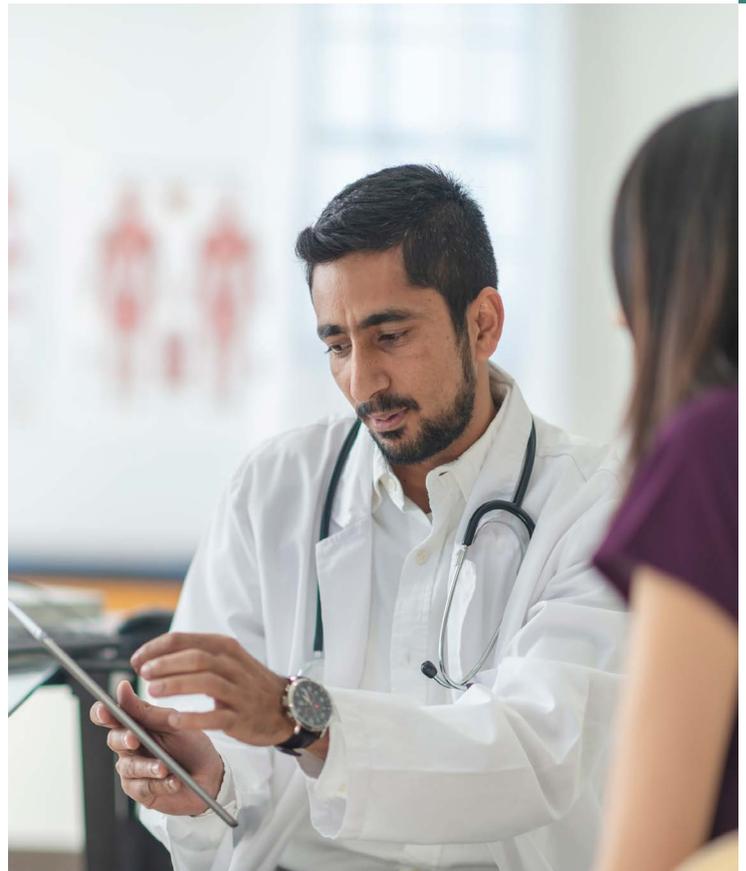
Robust AMR surveillance systems enable health care providers, researchers and policymakers to:



Address major challenges to reporting on resistance and antibiotic usage in human and animal health.



Encourage the development and use of digital tools that improve clinical decision making and improve appropriate use.



Why is AMR surveillance important?

AMR surveillance provides critical information to health care providers, researchers and policymakers about the emergence of resistance. Through these studies, emerging resistance and trends can be identified. This critical information can support the appropriate use of antimicrobials to improve patient outcomes and overall population health.

AMR surveillance systems can help:

- Assess resistance to antibiotics at different levels and in different populations (e.g., at the global or regional level, at the hospital or farm level, in the companion animal population).
- Make informed treatment decisions on an institutional and regional level.
- Better understand and control the mechanisms and spread of resistance within the local environment.
- Determine the early indicators of future unmet medical needs that will guide research efforts to develop new therapeutics.

MSD'S ONGOING COMMITMENT TO GLOBAL AMR SURVEILLANCE

MSD is taking action to support AMR surveillance. For more than 100 years, we have played a significant role in the discovery and development of novel medicines and vaccines to combat infectious diseases. In addition to our work in developing innovative treatments, we recognize the important role surveillance plays in combating AMR and we have taken steps to make our AMR surveillance data accessible to researchers and public health authorities around the globe.

MSD's Study for Monitoring Antimicrobial Resistance Trends (SMART) is one of the largest and longest-running AMR surveillance studies in the world. Launched in 2002, SMART has more than 200 sites across more than 60 countries - with 67 of the participating sites in LMICs. SMART is an important resource in determining pathogen prevalence and antibiotic susceptibility, important data that can be used to support antimicrobial stewardship (AMS) programs and establish regulatory susceptibility breakpoints.

We continuously aim to make our surveillance data more accessible to the scientific community to help providers make more informed treatment decisions to improve patient outcomes. In 2020, MSD launched the new global SMART surveillance website, with expanded functionality as part of an effort to make SMART data more accessible. The website includes heat maps of resistance patterns and improved functionality for SMART investigators.

Additionally, we are working to ensure that researchers around the globe have greater access to these important data. MSD has put in place a mechanism for researchers to request access to anonymized source data on AMR surveillance collected through SMART.



1. El Garch F, et al., Antimicrobial susceptibility of nine udder pathogens recovered from bovine clinical mastitis milk in Europe 2015–2016: VetPath results, *Veterinary Microbiology*, 245. 2. de Jong A, et al., Antimicrobial susceptibility monitoring of canine and feline skin and ear pathogens isolated from European veterinary clinics: results of the ComPath Surveillance programme, *Veterinary Dermatology*, 2020, 31: 431-e114.

AS OF 2020, SMART CONSISTS OF



ENCOMPASSING ALL MAJOR WORLD REGIONS

Recognizing the Urgent Need for Diagnostics:

Increased access to rapid diagnostics may improve patient outcomes and slow the pace of AMR. MSD is collaborating with OpGen to develop new rapid diagnostics and information technology products. Access to MSD's SMART surveillance network data has the potential to greatly accelerate OpGen's development efforts in validating its rapid diagnostic tools, which may be used to guide patient management choices.

Supporting Multiple Surveillance Studies:

MSD is involved in a number of AMR surveillance programs beyond SMART, including STAR (Surveillance of Tedizolid Activity and Resistance) for Gram-positive bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA); as well as local surveillance programs, including CANWARD in Canada and BSAC in the U.K. MSD also supports U.S. and international surveillance programs to monitor ribotype prevalence and antibiotic resistance for *Clostridioides difficile*.

Contributing to Animal Health Monitoring Programs:

MSD continues to sponsor the European Animal Health Study Centre (CEESA) and its 4 pan-European AMR monitoring programs. These industry-sponsored research activities include antimicrobial susceptibility testing and data dissemination. The European Antimicrobial Susceptibility Surveillance in Animals (EASSA) program collects and tests food-borne bacteria at slaughter from healthy animals whereas the pathogen programs VetPath, ComPath and MycoPath focus on target pathogens from acutely diseased companion and livestock animals. CEESA AMS research was published in 2 peer-reviewed papers in 2020.^{1,2}

THE RESPONSIBLE USE OF ANTIBIOTICS IN ANIMAL HEALTH

Effectively addressing antimicrobial resistance (AMR) will require a One Health approach by working collaboratively across multiple sectors to take strategic actions to improve human, animal and environmental health. The animal health industry is a committed partner and brings significant experience, expertise and capabilities to protect and maintain the health and wellbeing of both companion and food-producing animals. Involvement of the animal health private sector in antimicrobial stewardship (AMS) initiatives at the global-, national- and local-levels will be essential to the success of AMR control.

To make progress, relevant stakeholders need to:



Raise awareness of the importance of responsible use of antibiotics among policymakers, animal health professionals, animal caregivers and consumers.



Encourage a One Health approach to better understand the impact that antibiotic use in humans and animals has on AMR.



Scale up the use of vaccines and other preventative practices that reduce bacterial and viral disease in animals through incentives, policies and training for animal health experts, veterinarians and animal caregivers.



Utilize monitoring systems, animal identification and enhanced diagnostic tools that provide animal health professionals with data and analytics to make science based decisions to advance the health of animals.



Foster a regulatory environment with a strong commitment to risk- and science-based decision making.



Why is responsible use of antibiotics important to animal health?

Antibiotics are essential, life-saving veterinary therapeutic tools for the treatment of bacterial infections in companion and food-producing animals. By sharing our homes with us, healthy companion animals enhance our quality of life through the strong human-animal bond. Healthy food-producing animals contribute to a safe, nutritious and sustainable food supply. The expanded use of vaccines, monitoring and identification technologies and enhanced diagnostics can reduce the need for antibiotics and contribute to the responsible use of antibiotics in order to safeguard their efficacy.

When used responsibly, veterinary antibiotics can:

- Manage disease in animals and minimize the time diseased animals exhibit changed behavior, depression and pain, while also preserving the efficacy of antibiotics.
- Reduce the spread of zoonotic disease between animals and humans.
- Contribute to a safe, nutritious and sustainable food supply.

MSD'S COMMITMENT TO PROTECTING AND MAINTAINING ANIMAL HEALTH

MSD has a strong legacy in human and animal health with a broad infectious disease pipeline and portfolio spanning both. We have played a significant role in the discovery and development of novel medicines and vaccines to combat infectious diseases. As one of the few biopharmaceutical companies still engaged in both human and animal health, we recognize the importance of the responsible use of antibiotics, vaccines and preventative health practices in animals. MSD Animal Health's innovative portfolio of products includes animal monitoring solutions, smart data products and services for the management and wellbeing of food-producing and companion animals.

MSD Animal Health is dedicated to preserving and improving the health and well-being of animals through science. We are one of world's largest manufacturers of vaccines for animals, producing over 102 billion doses each year. We are commercializing or developing vaccines for all 15 prioritized animal diseases where vaccines can reduce antibiotic use in animals, as recognized by the World Organization for Animal Health (OIE). In addition, our training programs and strategies help pet owners, veterinarians and animal caregivers protect animal health through robust preventative care practices.

We are committed to helping veterinarians and animal caregivers manage disease development, optimize companion animal and livestock health and preserve the effectiveness of antimicrobials. Supporting responsible use of antimicrobials in animal health is a priority for MSD. As a member of HealthforAnimals, we collaboratively develop responsible use strategies for antimicrobials, support investment into the development of new products and promote vaccination to assist in disease prevention. In recognition of MSD's leadership in both human and animal health, MSD represents industry in the One Health Global Leaders Group on AMR. This group will advise the Tripartite United Nations Organizations on a One Health approach to address AMR.



We work to educate our customers on responsible antibiotic use and work closely with veterinarians, industry stakeholders and livestock producers to develop disease prevention strategies and health programs to ensure the health and wellbeing of animals. MSD Animal Health believes that antibiotics should remain an effective tool to improve and maintain human and animal health, as long as the proper, responsible and targeted use of antibiotics is managed through appropriate channels.

We are leveraging science and technology to support vaccination and responsible use of antibiotics through:

- **“Time to Vaccinate”:** A European program designed to help farmers better recognize the benefits of vaccinating their cattle to prevent disease.
- **Whisper® Veterinary Stethoscope System:** A non-invasive technology that can quickly measure the severity of bovine respiratory disease, allowing appropriate treatment to be selected early and reduce antibiotic use overall.
- **IDAL intra-dermal injection:** An injection system for swine which helps farmers vaccinate large numbers of pigs safely and efficiently while supporting pigs' wellbeing.
- **MSD Animal Health Intelligence:** An operating unit within the company that is focused on digital tracking, data collection and management tools to enable farmers and animal caretakers to optimize the management of animal health and wellbeing.
- **OIE and Codex Alimentarius:** MSD Animal Health has a long-standing involvement in OIE and Codex Alimentarius to develop and advance science based international standards for responsible antibiotic use.