

Position on Antimicrobial Resistance

Background

Antimicrobial resistance (AMR) is one of the defining scientific, health and economic challenges of our time. Without urgent and meaningful action to address specific diseases and system-level issues, patients, families and communities around the world will face a tremendous threat in the years ahead from untreatable infections. While AMR is fundamentally driven by the ability of pathogens to evolve, its impact is greatly amplified by factors that span economic, healthcare and agricultural domains.

The complexity of AMR and its potential for catastrophic impact on people and caregivers worldwide requires that stakeholders across multiple sectors (e.g., government, industry, civil society) work together toward a shared agenda. While the goal is ambitious, successful global efforts around HIV, polio eradication and other health issues show it is achievable. Together, we must improve how we prevent infections in the first place, effectively deploy and deliver current tools across all countries, and spur the development of new innovations.

We must address multiple AMR systemic failures, including lack of early research; the high costs and risks of developing new medications and diagnostics; and the barriers to finding, diagnosing and treating patients across all geographies and economic backgrounds. Solving just one issue in isolation is not enough— incentivizing companies to develop new innovative medicines will not make an impact if health systems are not able to deliver them to patients and steward their effectiveness. And, even the best health systems will not be able to help patients if companies do not continue creating innovative tools.

Relevance

As the world's largest and most broadly-based healthcare company, Johnson & Johnson is committed to changing the course of human health. It is impossible to achieve this goal without addressing the global threat of AMR. We have a diverse set of investments and commitments to address a wide range of AMR efforts.

From a health perspective, AMR is responsible for an estimated 700,000 annual deaths worldwide, including more than 50,000 in the United States and Europe. By 2050, those numbers could increase to 10 million globally—a greater global impact than we currently face from diseases like cancer and diabetes.¹ As a nation's health and wealth are intertwined, AMR is expected to have a catastrophic economic impact as well, drawing parallels to the 2008 global financial crisis. Cumulatively, AMR could cost the global economy more than \$100 trillion between 2014 and 2050.² This makes AMR one of the most significant global health security issues facing nations over the next several decades. These threats have been detailed in several reports, including the [O'Neill AMR Review](https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf), the Access to Medicine Foundation's [AMR Benchmark](#), the World Health

¹ https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf

² *ibid.*, p.7.

Organization (WHO)'s [AMR Global Report on Surveillance](#), the World Bank report on [Drug-Resistant Infections](#), the AMR Industry Alliance's [2018 Progress Report](#), and others.

Resistant pathogens can cause outbreaks locally or be carried within and across national borders. While the impact and threat of AMR are global, the main causes and consequences of AMR play out differently in developing and emerging markets compared to developed countries. That said, three responsive strategies are critical in every context:

1) Preventing individuals from acquiring resistant infections: Broad awareness and education strategies are needed to advance infection prevention. In addition, vaccines play a crucial role in preventing a range of AMR-relevant infectious diseases around the world. Other tailored strategies are needed depending on the local context. In places like the United States and Europe, healthcare-acquired infections (HAIs) are a major driver of AMR-related infections and can be prevented with appropriate tools.

2) Treating existing AMR-related infections: Giving patients with AMR-related infections the best chance at recovery requires preserving and extending the effectiveness of current therapies. To do so, therapeutics must be appropriately used in humans and animals. Surveillance to track prevalence of resistant pathogens and the effectiveness of existing therapies—and also establishing and adhering to environmental protections—are crucial additional components of effective strategies. Success requires that robust health systems be in place to diagnose, track and treat AMR-related infections.

3) Discovering and developing new tools to reverse the trend of growing drug resistance: Infectious pathogens will continue to evolve and develop resistance to new and existing therapies. The unique nature of the AMR market (where product use should be carefully stewarded after approval, so treatments reach the right patients at the appropriate dosages, preventing the development of further resistance) drives the need for tailored incentives to reward innovation and spur further research and development (R&D) investment. Furthermore, new diagnostics are essential to ensure antimicrobial use is limited to those with appropriate infections.

Guiding Principles

Johnson & Johnson's [Credo](#) states: "We believe our first responsibility is to the patients, doctors and nurses, to mothers and fathers and all others who use our products and services."

Our Position

At Johnson & Johnson, we are taking action to be a part of the solution to AMR. We have focused efforts across our business to address many facets of the AMR challenge, and we are championing a new sustainable ecosystem model to work with partners and further change the trajectory of health for humanity.

We are proud to be recognized as a leader among our peers in the fight against AMR for the second time in the [AMR Benchmark](#). The independent report from the Access to Medicine Foundation evaluates 30 pharmaceutical companies on their efforts to bring AMR under control.

Our performance was [recognized](#) in the four core categories of R&D, Responsible Manufacturing, Appropriate Access, and Stewardship. Johnson & Johnson is making the second-largest R&D investment in relevant disease areas as identified by the Benchmark, and is stewarding one of the largest antimicrobial pipelines,

including pediatric formulations of bedaquiline and vaccines to ensure antimicrobials remain a backbone of modern medicine. These efforts are exemplified in our work to tackle drug-resistant tuberculosis (DR-TB).

Timeline of Johnson & Johnson's key contributions to combating AMR:

2012: Through our Janssen Pharmaceutical Companies, we received accelerated approval from the U.S. Food and Drug Administration (FDA) for SIRTURO (bedaquiline), our medicine for the treatment of multidrug-resistant tuberculosis (MDR-TB) as part of a combination therapy.³ It was the first TB drug with a novel mechanism of action to be approved in more than 40 years.

2015: We committed to donate 105,000 courses through a four-year donation program operated in partnership with the U.S. Agency for International Development (USAID) and JSC Pharmstandard.

2017: We implemented our Drug Resistance Emergence Assessment in MDR-TB (DREAM). DREAM is a global drug resistance surveillance to assess the emergence of resistance to bedaquiline. By mid-2018, thousands of bacteria recovered from TB patients from 10 countries were tested and preliminary results indicate that the prevalence of resistance to bedaquiline has remained very low.

2018: Ahead of the first-ever United Nations (UN) High-Level Meeting on TB, we announced a comprehensive 10-year initiative in support of the UN Sustainable Development Goal target of ending the TB pandemic by 2030. Johnson & Johnson will work with partners to improve detection of undiagnosed cases of TB, broaden access to bedaquiline for MDR-TB, and accelerate R&D to discover next-generation TB treatments.

2019: Johnson & Johnson publicly committed to an investment of more than \$500 million over four years in discovery, development and delivery programs to advance the global effort to eliminate HIV and TB by 2030. With co-funding from Europe's Innovative Medicines Initiative, we also launched RESPIRI-TB, an international research consortium to discover and develop new TB antibiotics in collaboration with eight European academic and biotechnology partners.

2020: Together with a consortium of philanthropic, nonprofit and private-sector organizations, we launched the Project to Accelerate New Treatments for Tuberculosis (PAN-TB collaboration), which will focus on treatment regimens comprised of medicines to which there is limited or no drug resistance and that are ready for Phase 3 development.

Read on for more details of our approach to combating AMR, including:

Advocating and partnering for action to combat AMR: We leverage our size and scale to promote shared accountability in addressing AMR. We are a proud signatory to the [AMR Roadmap](#) and the [Davos Declaration on Combating AMR](#), and remain committed to their one-health principles. We have been active members of the [AMR Industry Alliance](#), including contributing to multiple position papers and presentations, and serving on the board. We have also [testified before the U.S. Congress](#) on the topic, and have provided input and support to other international and domestic actions to address AMR, including the [U.S. National Action Plan for Combating Antibiotic-Resistant Bacteria](#), ongoing World Economic Forum AMR working groups, the [EU One Health Action Plan](#) on AMR and the [Global Health Security Agenda AMR Action Package](#).

³ Approval is through Subpart H--Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses.

To help drive standardized approaches to evaluating the environmental, health and safety performance of suppliers across the pharmaceutical industry, including antibiotic suppliers, we are also active members of both the AMR Roadmap Manufacturing Work Group and the Pharmaceutical Supply Chain Initiative. We have reported transparently on our progress in this area through both the Access to Medicine Foundation's AMR Benchmark and the [AMR Industry Alliance Progress Report](#).

See also an [Appendix](#) to this Position that provides further detail on Johnson & Johnson's policy approach to combating AMR.

Delivering medicines, enhancing access and monitoring for tuberculosis:

Globally, more people die of tuberculosis (TB) than any other infectious disease, and DR-TB currently accounts for approximately one-third of all AMR-related deaths. In 2017, DR-TB infected 558,000 people around the world—with cases in nearly every country globally—and claimed 230,000 lives⁴. Currently only one in three people with DR-TB is diagnosed and one in four treated. Every untreated individual can infect up to 15 additional people over the course of a year, posing a global health security threat. In addition to delivering the most widely used treatment for DR-TB, bedaquiline, our actions include:

1. **Simplifying treatment regimens for DR-TB:** Until recently, the standard of care for MDR-TB treatment required a complex regimen of approximately 14,000 pills taken over two years, with daily injections for six months, which had significant side effects and only moderate success. Simpler, safer, and more effective treatments are essential to decrease the overall burden of DR-TB. Johnson & Johnson has invested in these R&D efforts for more than two decades. Bedaquiline is one of the last lines of defense against MDR-TB. To address this, we have taken numerous steps to promote broad, equitable access to bedaquiline while ensuring appropriate use and stewardship in line with WHO guidelines to prevent the development of resistance.
2. **Enhancing access to TB treatment:** We donate bedaquiline treatments in partnership with humanitarian or health agencies, for example, in partnership with USAID and/or other organizations. One hundred and forty countries are eligible to access bedaquiline at a not-for-profit price through the Stop TB Partnership's Global Drug Facility. This price enables us to support manufacturing distribution and surveillance programs to safeguard the antibiotic's effectiveness. We have put in place manufacturing agreements to ensure a steady supply.
3. **Advancing training, monitoring and research:** We work with a variety of local, national and global stakeholders to support healthcare provider training and pharmacovigilance and surveillance activities to monitor resistance to bedaquiline and companion treatments within the same regimen.

Developing additional anti-infective vaccines and therapies: Beyond DR-TB, we have many ongoing research projects to develop new drugs or vaccines for AMR-relevant diseases, in both developed and developing countries. These include projects targeting E. coli, influenza, Respiratory Syncytial Virus (RSV), hepatitis B, and HIV.

Combating healthcare-acquired infections (HAI) prevention: One of the major drivers of AMR-related infections in developed markets like the United States and Europe is HAIs. Many HAIs are preventable with appropriate strategies in place. Across the Johnson & Johnson Medical Devices Companies, we seek to reduce the risk of these infections through a variety of antimicrobial and sterilization tools and technologies. Examples include:

⁴ https://www.who.int/tb/post2015_TBstrategy.pdf?ua=1

- DePuy Synthes' Expert Tibial Nail PROtect, which releases an antibiotic locally into the implant's surrounding tissues;⁵
- Certain DePuy Synthes' bone cements (e.g., SMARTSET GHV and SMARTSET GMV), which contain the antimicrobial gentamicin;
- ETHICON BIOPATCH, a protective disk with Chlorhexidine Gluconate, shown to reduce catheter-related blood stream infection (CRBSI), local infections and skin colonization of microorganisms commonly related to CRBSI; and
- ETHICON Plus Sutures, coated with the antimicrobial triclosan, shown to reduce surgical site infection (SSI).

Supporting access to antibiotics: We use mechanisms such as tiered pricing, partnerships with public health organizations, donation programs, and other mechanisms as appropriate on a country-by-country basis to help achieve broad and timely access to our medicines in a way that is locally affordable. Examples of our initiatives include our program to broaden access to MDR-TB therapy with bedaquiline and our HIV medicines access program.

Supporting work to ensure antibiotics are being used only in patients who need them: Our education efforts for healthcare professionals include topics such as appropriate use, diagnosis, pharmacovigilance, and adverse event reporting and monitoring of side effects. For example, through unrestricted educational grants, we have engaged the International Union against TB and Lung Disease since 2014 to impart medical education programs on MDR-TB in Peru and South Africa. We also supported USAID training on the implementation of a pharmacovigilance program for TB drugs for staff from national TB programs and health authorities in several countries.

Partnering to advance AMR research: We maintain several partnerships to advance AMR research, such as our initiative with the Institute of Microbial Technology in India to help accelerate the discovery of innovative new treatments for TB, and our agreement with the Indian Council for Medical Research to bolster clinical trial capacity in India to support faster development and approval of TB medicines for India.

Minimizing environmental antibiotic exposure from our research and manufacturing: Across Johnson & Johnson, we take a proactive, comprehensive approach to minimizing the environmental antibiotic exposure from our research and manufacturing. Our environmental risk-management strategy aims to reduce the risk of antibiotic discharge during manufacturing. This includes establishing and applying science-based discharge limits and auditing both our own sites and those of third-party manufacturers.

Application

This position is relevant for the Johnson & Johnson Family of Companies, as detailed in our [governance materials](#). We provide updates relating to AMR in our annual [Health for Humanity Report](#) where relevant.

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⁵ As of this publication, this device is not cleared or approved for use in the United States.

APPENDIX to Johnson & Johnson's Position on Antimicrobial Resistance

Anti-infective drugs and technologies have been some of the most effective health innovations in the history of modern medicine, responsible for dramatic gains in life expectancy globally. They are the backbone of modern medicine. And yet, without meaningful, collective action we risk squandering these gains and returning to an era where infection outpaces innovation and patients are left without treatment options. Working together, we can address this threat and change the trajectory of health for humanity.

We advocate for the following approaches to combating AMR, representing a holistic system of policies, mechanisms and actions across sectors:

R&D Incentives to address AMR challenges: The global pipeline for new products targeting resistant infections is not sufficient, given the size and scale of the challenge posed by AMR. We applaud the various mechanisms, such as Biomedical Advanced Research and Development Authority's CARB-X, set up to encourage innovation in this area. We see opportunity for further use of market-based incentives such as:

- **Priority Review Vouchers:** Building on our experience with SIRTURO, we are a strong proponent of the U.S. Priority Review Voucher (PRV) system, which grants companies that successfully develop a drug for certain underserved diseases or populations a voucher for expedited review of another therapeutic candidate. While the market value of a PRV is highly variable and does not in itself provide recompense for a full-scale drug development program, we believe this system should be maintained in the United States and explored elsewhere as an incentive for AMR research.
- **Transferable Exclusivity Vouchers:** Similar to PRVs, transferable exclusivity vouchers could be a powerful motivator for companies to invest in AMR research or other areas of unmet medical need. These incentives would allow companies that develop specific neglected medicines to extend the exclusivity period of a separate product in a defined therapeutic category for a defined time. Like PRVs, they have the advantage of not requiring any appropriated funding from governments. We support further exploration of this model.
- **Market Entry Rewards:** New products targeting resistant infections should be used judiciously, which poses a challenge to market entry in the current landscape where innovator companies have only a limited period in which products have marketing exclusivity. Providing a reward for companies that reach a defined milestone (e.g., bringing a product to market) can overcome this barrier. Implementing this effective solution necessitates that governments or other sources secure adequate funding for these rewards.
- **Special Procurement / Health Technology Assessment (HTA):** We support pre-proposals for special procurement mechanisms or HTAs that address the complexity and unique nature of the AMR marketplace where innovative antibiotics are usually approved by Regulatory Agencies based on non-inferiority clinical trials. These assessments should appropriately recognize the high value that innovative antibiotics bring to patients and society over the older standard of care products by addressing unmet needs and public health issues such as decreasing efficacy over time as resistance grows. HTA should capture the full value of newer antibiotics, including value to society, and consider a wide range of evidence and benefits. Acknowledging this broader value will help better predict demand and encourage investment in future research.

Regardless of the additional incentive models that may be pursued, it is important to maintain existing regulatory exclusivities and intellectual property protections for companies that bring innovations to the

market. As we have experienced with SIRTURO, these protections are a key element of any comprehensive strategy to stimulate innovation and access to new treatments.

Specific incentive tools to address the gap of fit-for-purpose diagnostic tools and technologies are also needed. Finally, we support initiatives like the Coalition for Epidemic Preparedness Innovations and others that seek to incentivize the development and access to new vaccines that can limit the spread of resistant infections.

Promoting appropriate use and access: Ensuring new and existing anti-infective tools and products are used appropriately is paramount to addressing the AMR issue globally. This requires concerted action on several fronts:

- **Health infrastructure and delivery:** A critical factor to addressing the threat of AMR is the existence of a robust health system that can effectively find and treat AMR-related infections, and work to prevent their spread. We have been proud to work with the government of South Africa and others in their accelerated case funding, training and treatment programs. We aim to ensure they have the appropriate technology to promote sufficient access to SIRTURO, and we encourage donors and governments to make the necessary investments to deal with this critical challenge. This includes training healthcare workers and providing them with appropriate infrastructure, ensuring patients have access to essential care and services, tracking and reporting resistant infections, and more. Globally, we are proud to champion the Universal Health Coverage (UHC) movement and believe that actions to address AMR will be most sustainable when taken as part of country-level efforts to achieve UHC.
- **Diagnostics:** As noted by the U.S. Centers for Disease Control (CDC), overprescribing of antibiotics is a significant problem that contributes to drug resistance: more than 40% of outpatient antibiotic prescriptions are for acute respiratory infections, and it is estimated that half of these are not necessary. We support the CDC's recommendations for prescribers and patients to promote appropriate use of antibiotics. Additionally, we believe there is an important need for diagnostics that can help ensure the right treatments are used for the right patients. Beyond the R&D incentives mentioned previously, reimbursement reforms are also needed to encourage doctors and providers to use these diagnostic tools.
- **Medical Devices:** We support the creation and adoption of guidelines that favor use of technologies designed to reduce the risk of HAIs in hospitals, and policies that encourage health workers and hospitals to adopt systematic checklists regarding the use of these technologies.
- **Animal use:** While we do not have an Animal Health business, we do recognize the importance of good antibiotic stewardship in animal populations and support global and local efforts that limit the inappropriate use of antibiotics in these settings. We support ending the use of prophylactic dosing of antibiotics for infection prevention and growth promotion, as well as limiting use in animals of antibiotics that are critical for human use.

Harmonizing regulatory approvals: The approval of therapies targeting resistant infections poses unique challenges in clinical design and evaluation. We commend guideline changes and legislative efforts to streamline regulatory pathways, e.g., ADAPT in the United States and the FDA / European Medicines Agency / Pharmaceuticals and Medical Devices Agency Tripartite Agreement. Building on this progress, we believe further gains can be made by continuing to harmonize regulatory data requirements across countries. Where appropriate, mutual recognition of approvals can expedite access worldwide.

Environmental Considerations: We support the environmental management and transparency principles captured in the Antimicrobial Resistance Roadmap document. We encourage other manufacturers of

antibiotics to endorse, embrace and enact these principles as well, and report on their progress in meeting these principles.

Ecosystem Approach: While we see implementing the policy solutions mentioned above as critical to ensuring additional industry engagement in AMR, they will not be sufficient in isolation. As we learned from our experience with SIRTURO, working collaboratively with all stakeholders in a country is what ultimately creates rapid improvements and drives patient outcomes. Solving for AMR will require a new way of thinking, where stakeholders work transparently in mission-oriented consortia designed to enforce better collaboration and create mutual accountability for results. The incentives of all stakeholders—industry, government and civil society—must be aligned toward reducing the further development of resistant infections and the delivery of better health outcomes for patients and caregivers.

We therefore believe we need a new, sustainable, pathogen-specific ecosystem model to deliver against AMR. Success will require committed leadership across sectors, ambitious yet measurable priorities and targets, detailed execution plans, regular performance management, and public accountability.