

The Sandoz Role in Addressing AMR
Statement of Intent

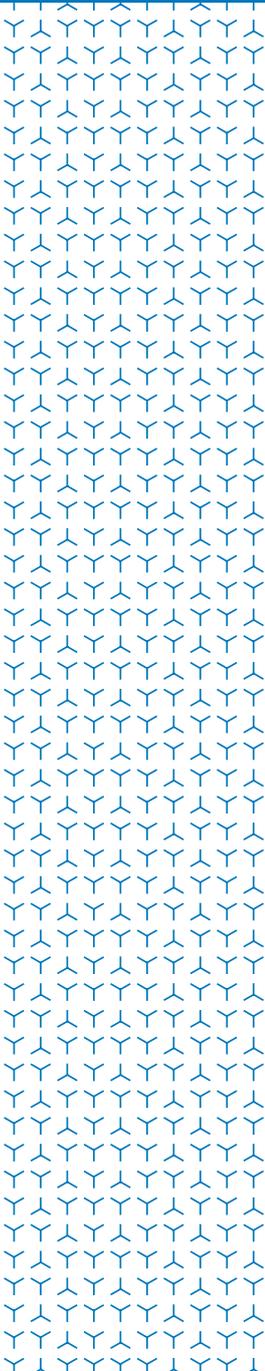
Driving sustainable, multi-stakeholder solutions to combat antimicrobial resistance

Sandoz, the world's largest¹ provider of high-quality affordable antibiotics, is driving practical scalable solutions that deliver meaningful impact in combating antimicrobial resistance



“We are committed to providing reliable access to high-quality affordable antibiotics, and promoting responsible use, while increasing longevity of current antibiotics through innovation. We see local and global collaborations that serve to maximize the impact of our efforts as playing an important role, and are actively seeking new opportunities and new partnerships.”

Harshika Sarbajna, Global Head of Oral Anti-Infectives and AMR Program, Sandoz



Antimicrobial resistance (AMR) is an increasingly serious threat to global public health, according to the WHO². In the Global Action Plan on AMR, it states that, without harmonized and immediate action on a global scale, the world is heading toward a post-antibiotic era in which common infections could once again kill³. In fact, the WHO estimates that AMR could lead to 10 million more deaths annually by 2050⁴.

Antibiotics are the cornerstone of modern medicine and have saved countless lives since their discovery about 90 years ago⁵. They are used to treat and prevent infections caused by bacteria and are crucial to the success of a broad range of medical treatments, including major surgery and chemotherapy. While AMR occurs naturally over time, according to the WHO inappropriate use of antimicrobials drives the development of drug resistance.

Overuse, underuse and misuse all contribute to the problem⁶. As a society we all must do better to safeguard the medicines we have today. We cannot just rely on new antibiotics coming to the rescue. There is a lot more that needs to be done and there is no doubt that we will achieve more working together than in isolation.

Sandoz is the world's largest¹ provider of high-quality affordable antibiotics. Today 90 million patients in 130 countries receive treatment with antibiotics provided by Sandoz for a wide range of infections⁷. Sandoz recognizes the need to find the right balance between improving access to existing antibiotics and ensuring that they are used in a responsible and sustainable way.

Through its parent company, Novartis, it is a signatory to the Davos Declaration on Antimicrobial Resistance⁸, as well as the AMR Industry Alliance⁹, and is focusing its efforts on areas of high unmet need where it can make the biggest impact. To deliver on this commitment, Sandoz AMR initiatives concentrate on four areas which directly address factors known to contribute to AMR. Across all its efforts Sandoz recognizes the importance of collaboration and calls for the AMR community to continue to work together to combat the threat of AMR.

Four areas of focus

Prevention 
Initiatives to drive responsible manufacturing standards that help reduce the environmental impact of the production of antibiotics

Access 
Global and local collaborations with a range of partners to help improve access to anti-infectives

Stewardship 
Global and local initiatives to ensure prescription of the right drug at the right dose for the right duration

Innovation 
Non-traditional research and development to explore innovative solutions to prolong the life of existing antibiotics and improve patient adherence to therapy

¹ Sandoz holds the global number one position in sales of generic antibiotics according to IQVIA data 2017.

² WHO. Antimicrobial Resistance. <http://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance> Accessed August 2018.

³ WHO Global Action Plan on AMR, May 2015. <http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/> Accessed September 2018.

⁴ Tackling Drug-Resistant Infections Globally. The Review on Antimicrobial Resistance Chaired by Jim O'Neill. 2016.

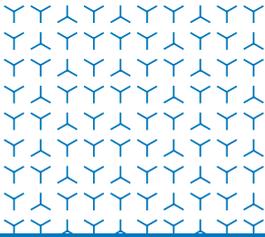
⁵ WHO. Drug Resistance. Microbes and Antimicrobial Agents. Antimicrobial Discovery and Development. http://www.who.int/drugresistance/Microbes_and_Antimicrobials/en/ Accessed August 2018.

⁶ WHO. 10 Facts on Antimicrobial Resistance http://www.who.int/features/infocards/antimicrobial_resistance/en/ Accessed August 2018.

⁷ 2015 Sandoz data on file.

⁸ IFPMA. Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. January 2016.

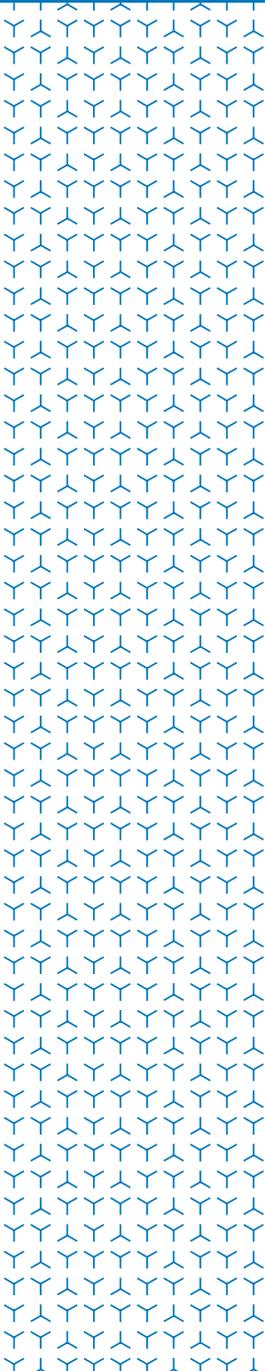
⁹ AMR Industry Alliance. Tracking Progress to Address AMR. January 2018.



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Questions & Answers

Q Why are antibiotics important?

Before antibiotics, even the most minor illnesses and medical procedures posed potentially fatal risks.

Today, the appropriate use of antibiotics means that infectious diseases like tuberculosis and pneumonia are treatable and medical procedures such as chemotherapy and major surgery are less likely to lead to serious infections.

Q What is the Sandoz heritage in antibiotics?

Sandoz discovered the first oral penicillin in 1951 and has been a pioneer in the field for nearly 70 years. Since 1946, the company has been granted more than 150 antibiotic related patents.

Today its integrated supply chain provides a broad portfolio of affordable antibiotics of the highest quality standards. It is the biggest supplier of Penicillin V worldwide and its portfolio covers 50% of available antibiotics and 80% of off patented antibiotics. With these medicines Sandoz reaches 90 million patients in 130 countries around the world¹¹.

Q Why is quality important?

According to the WHO, exposure to poor quality medicines and inappropriate levels of antibiotic can also contribute to AMR. A recent paper suggested that quality assurance measures should be addressed to contain antimicrobial resistance¹².

Q What causes AMR?

AMR happens when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs¹³. These microorganisms then become resistant to the drugs.

Antimicrobial resistant-microbes are found in people, animals, food, and the environment (in water, soil and air) and are difficult, and sometimes impossible to treat, compared to non-resistant microbes.

While AMR occurs naturally over time, a number of factors have accelerated the process: overuse of antibiotics in humans and in agriculture settings, misuse either through incorrect prescription, ingesting low quality drugs or lack of adherence to the treatment, poor access to antibiotics, and lack of infection prevention and control.

Q How serious is the problem of AMR?

AMR is a grave public health problem. It is currently responsible for 700,000 deaths worldwide every year and it has been estimated that it could result in 10 million additional deaths annually by 2050.

AMR threatens the effective prevention and treatment of an ever-increasing range of infections¹³. Key medical procedures that rely on antibiotics in particular (such as gut surgery, caesarean sections, joint replacements, and treatments that depress the immune system, including chemotherapy for cancer) could become too dangerous to perform if the antibiotics lose their effectiveness as a result of AMR¹⁴.

Patients with infections caused by drug-resistant bacteria are not only at increased risk of worse clinical outcomes and death, they also consume more healthcare resources than patients infected with non-resistant strains of the same bacteria¹³.

Q What are the implications of AMR?

Patients with infections caused by drug-resistant bacteria are more difficult to treat and may be sick for longer. It's likely that they may need more expensive healthcare and medications, as well as more complex care and longer hospital stays. They have a higher risk of spreading illness to others. Multi-drug resistant infections can also lead to death¹⁶.

¹⁰Sandoz holds the global number one position in sales of generic antibiotics according to IQVIA 2017. ¹¹2015 Sandoz data on file.

¹²Perspectives, Medicines Quality Assurance to Fight Antimicrobial Resistance Bulletin of the World Health Organization 2018;96:135-137.

¹³WHO. Antimicrobial Resistance. <http://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance> Accessed August 2018.

¹⁴Tackling Drug-Resistant Infections Globally. The Review on Antimicrobial Resistance Chaired by Jim O'Neill. 2016.

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Questions & Answers

Q What is the Davos Declaration on Antimicrobial Resistance?

The Davos Declaration is the Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. It was announced in January, 2016, at the World Economic Forum in Davos, Switzerland. By April 2016 a total of 98 companies, including Novartis, and 11 industry associations in 21 countries, were signatories¹⁷.

Through the Roadmap for Progress in Combating Antimicrobial Resistance, the Declaration set out detailed commitments to address AMR. These were to:

- Reduce the environmental impact from the production of antibiotics
- Help to ensure antibiotics are used only by the patients who need them
- Improve access to current and future antibiotics, vaccines and diagnostics
- Explore new ways of working to overcome the scientific challenges of creating new antibiotics, vaccines, and diagnostics.

Novartis is also a signatory to the AMR Industry Alliance¹⁸.

Q What does the WHO Global Action Plan on AMR recommend?

The 'Global Action Plan on AMR' was developed to ensure continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality assured, used in a responsible way and accessible to all who need them¹⁹. It provides a framework for developing national action plans, including key actions that should be taken within 5-10 years. It was endorsed by the World Health Assembly in May 2015.

Q What is Sandoz doing in response to the Global Action Plan?

All of our work in tackling AMR aligns with the WHO Global Action Plan and the Davos Declaration¹⁷, and the AMR Industry Alliance¹⁸. Our initiatives are concentrated on four areas that directly address factors known to contribute to AMR – Prevention, Access, Stewardship and Innovation – and comprise practical solutions that can make a difference.

Q What impact will the Novartis decision to exit antibacterial and antiviral research have on Sandoz activity to address AMR?

The announcement in July 2018 from Novartis on the decision to exit new molecule research in the antibacterial and antiviral space in no way changes the Sandoz commitment to tackle AMR. Efforts to address AMR will continue.

Q Why has Novartis decided to exit antibacterial and antiviral research?

Novartis announced the decision to exit antibacterial and antiviral research in July 2018. While the science for these programs is compelling, the company decided to prioritize its resources in other areas where it believes it is better positioned to develop innovative medicines that will have a positive impact for patients. The need for these types of medicines is clear and, to maximize the chances that these programs will one day help patients, Novartis is actively engaged in out-licensing discussions with companies focused on developing medicines in these areas.

Through Sandoz, Novartis has stated that it remains committed to drive change to tackle antimicrobial resistance. Novartis will also continue to look for solutions for malaria, identified by the WHO as an area at risk from AMR.

In April 2018 Novartis announced a five-year USD 100 million commitment to advance the Novartis malaria pipeline through 2023 and to complete a comprehensive global clinical trial program for its novel antimalarial drug candidates KAF156 and KAE609 (currently in Phase IIb and Phase IIa respectively).

¹⁵Sandoz holds the global number one position in sales of generic antibiotics according to IQVIA 2017.

¹⁶WHO. Antimicrobial Resistance. <http://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance> Accessed August 2018.

¹⁷IFPMA. Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. January 2016.

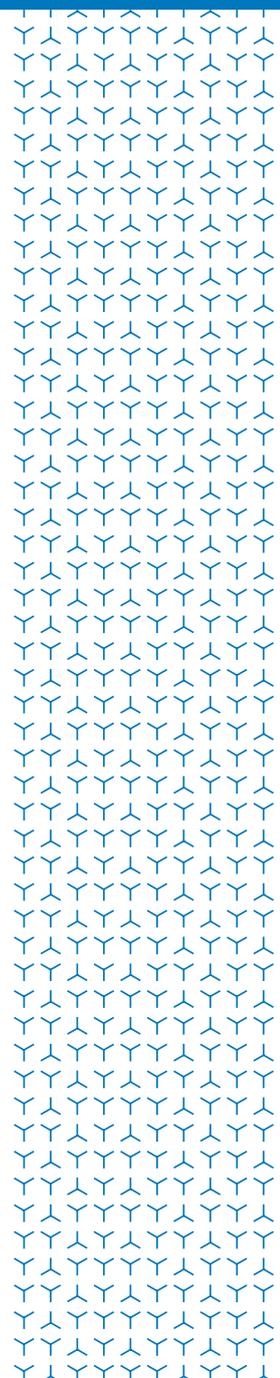
¹⁸AMR Industry Alliance. Tracking Progress to Address AMR. January 2018.

¹⁹WHO Global Action Plan on AMR, May 2015. <http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/> Accessed Sept 2018.

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Initiatives to address AMR

All work undertaken by Sandoz in tackling AMR aligns with the WHO Global Action Plan and the Davos Declaration²¹, as well as the AMR Industry Alliance²², of which we are a signatory through our parent company Novartis. Our initiatives are concentrated on four areas that directly address factors known to contribute to the rising incidence of AMR, namely Prevention, Access, Stewardship and Innovation, and comprise practical solutions that can make a difference.

Area of focus: Prevention

Sandoz is actively driving responsible manufacturing standards that minimize environmental impact of production.

Initiatives

Commitment to high-quality antibiotics for optimal outcomes

Novartis, the parent company of Sandoz, owns one of the largest vertically integrated antibiotic facilities in Western Europe employing state-of-the-art manufacturing processes.

All antibiotics provided by Sandoz are of the highest quality and provide optimal therapeutic levels for the best possible treatment outcomes when taken in adherence with the correct prescriber instructions.

Reinforcing environmental excellence to promote real change

The Novartis Supplier Code sets out the high environmental standards we expect our suppliers to comply with and apply to our own operations everywhere we operate.

All potential suppliers are required to meet the Health, Safety and Environmental (HSE) standards specified in our Supplier Code and by the Pharmaceutical Supply Chain Initiative (PSCI).

During 2018, all our Indian suppliers are due for HSE re-evaluation and AMR assessment, in line with the defined framework set out by the Roadmap for Progress in Combating Antimicrobial Resistance.

Area of focus: Access

Sandoz is involved in global and local collaborations with a range of partners as part of its commitment to improve access to critical existing antibiotics for use whenever and wherever they are needed, irrespective of broader economic concerns.

In areas where infrastructure and logistics issues create barriers to access, we form collaborations with global NGOs and UN organizations such as UNICEF, WHO and Save the Children.

Initiatives

Combating the scourge of childhood pneumonia worldwide

In 2014 Sandoz made a long term commitment to make pediatric Amoxicillin treatment available to developing countries in response to WHO Guidelines on the preferred treatment for pediatric pneumonia. Pneumonia is the leading cause of death from infection in children, killing approximately 2,400 children a day²³. So far, one million treatment courses have been delivered to UNICEF, with 450,000 as part of a country-specific UNICEF program in Yemen²⁴.

Addressing the global Retarpen shortage

Retarpen (penicillin G benzathine) is a WHO Essential Medicine and the only approved treatment for congenital syphilis as well as a first-line medication against rheumatic heart disease. Globally, more women that are pregnant suffer from syphilis than from HIV, resulting in more than 500,000 adverse pregnancy outcomes annually.

Given the worldwide shortages of the active pharmaceutical ingredient (API) for Retarpen, Sandoz is actively exploring options to re-start manufacturing of this critical medicine.

Driving access to tuberculosis treatment options

Sandoz is working tirelessly to increase access to second-line treatments for tuberculosis (TB), one of the top 10 causes of death worldwide²⁵. Cases of TB have increased due to AMR.

²⁰Sandoz holds the global number one position in sales of generic antibiotics according to IQVIA data 2017.

²¹IFPMA. Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. January 2016.

²²AMR Industry Alliance. Tracking Progress to Address AMR. January 2018. ²³UNICEF data, <https://data.unicef.org/topic/child-health/pneumonia/Accessed August 2018>.

²⁴Sandoz data on file, June 2018. ²⁵WHO Tuberculosis Key Facts. <http://www.who.int/news-room/fact-sheets/detail/tuberculosis> Accessed August 2018.

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Area of focus: Stewardship

Sandoz is actively involved in global and local partnerships to ensure responsible and appropriate use of existing antibiotics in line with WHO guidelines.

Initiatives

Supporting responsible use in Latin America

In 2015, Sandoz in Latin America created "Better Care More Health" or "Mejor Cuidado, Más Salud", – an ongoing multi-media educational campaign on responsible antibiotic use, aimed at physicians and pharmacists. It reaches eight countries in Latin America and includes an e-learning site for healthcare professionals and a website in three languages for patients to learn more about antibiotics.

Providing access to education on AMR for healthcare professionals

Sandoz is currently partnering to create a website and mobile app on AMR. Both will address prescriber needs for continuous medical education on AMR, as well as simple efficient access to prescribing guidelines. The site will be continually updated to ensure it remains current.

Sharing medical information with healthcare professionals across Central and Eastern Europe, and Middle East and Africa

Sandoz regularly organizes events to share medical information about appropriate antibiotic use across different regions, including remote locations. It uses multichannel platforms to reach healthcare professionals with cutting-edge medical information shared by recognized scientific experts.

Area of focus: Innovation

Sandoz is intensifying its focus in the area of non-traditional R&D to explore innovative solutions that prolong the life of existing antibiotics and improve patient adherence to therapy to safeguard future antibiotic effectiveness.

Initiatives

Driving innovative solutions for improved access and responsible use

Sandoz has seven centers with experts working on anti-infectives, including two development centers and five process improvement centers.

Current options being explored include new diagnostic tools, medications and digital applications.

One development project aims to meet the need for a convenient and palatable mode of delivery of amoxicillin/ clavulanic acid, a combination treatment for bacterial infections of the respiratory tract in children aged 3-12 years. The dispersible tablet form was launched in Russia in April 2018 and will be rolled out in other countries.

²⁶Sandoz holds the global number one position in sales of generic antibiotics according to IQVIA data 2017.

²⁷FPMA Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. January 2016.

²⁸AMR Industry Alliance. Tracking Progress to Address AMR. January 2018.