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MYLAN: DOING WHAT'S
RIGHT TO PROTECT
THE ENVIRONMENT AND
ADDRESS THE RISE
OF ANTIMICROBIAL
RESISTANCE

 Mylan®

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Among the greatest breakthroughs in medicine was the discovery in 1928 of penicillin by Andrew Fleming. Capable of killing a wide range of harmful bacteria, this “miracle drug” gave rise to the golden age of antibiotics in the 1950s, 1960s and 1970s. During this period, multiple varieties of anti-microbial drugs were discovered, saving millions of lives all over the world and effectively eliminating infectious disease as the leading cause of human death.

So effective were these drugs, which include antibiotics, anti-virals, anti-parasitics and anti-fungals, that they were – and still are – used liberally. Over time, this practice gave rise to antimicrobial resistance, or AMR.

AMR is an example of natural selection in action, where the strong members of a group are more likely to survive, reproduce and pass on their genes, while weaker members perish. The prevalence of antimicrobial medicines, particularly antibiotics, has resulted in the emergence of strains of bacteria that are difficult, if not impossible, to kill.

Growing awareness of this threat is prompting various stakeholders, including policymakers, industry, healthcare professionals and the general public, among others, to examine current practices and explore opportunities to address the continued rise of AMR. This is especially important given that demand for antibiotics is expected to rise significantly over the next several years as essential medicines become more accessible, particularly in developing countries.

One main cause of the rise of AMR is the inappropriate use of antibiotics in or by humans, for instance, through over-prescription, prescription for non-bacterial illnesses, failure to complete a course of treatment.

The other main cause is the use of antibiotics in intensive livestock farming, e.g., to promote growth and prevent infection. Up to 90% of the antibiotics given to animals are excreted in urine and stool, then widely dispersed through fertilizer, groundwater and surface runoff¹.

AMR antimicrobial resistance



Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria.

U.S. Centers for Disease Control and Prevention

A much smaller contributor to the rise of AMR is the release of antibiotics into the environment by factories. A 2013 study, for instance, pointed to manufacturing effluent as contributing only 2% of pharmaceuticals found in the environment in Europe².

Although the increase of AMR ultimately is a collective problem, there are no silver bullets or one-size-fits-all solutions given the multitude of regulatory arrangements, economic systems and priorities, social norms and healthcare practices in use around the world. For instance, in many countries, antibiotics are available without a prescription.

Solutions need not be daunting. Preventing infections, viral and bacterial, through proper sanitation and vaccination is a good example of a powerful, yet simple tool. By mobilizing all stakeholders in a sustained, multidisciplinary response to the threat of AMR, we can address it and help ensure a safe and healthy future for generations to come.

Since Mylan's founding more than 50 years ago, our mission has been to provide people access to high quality medicine. Along the way, we have stood fast by our pledge to always "Do what's right, not what's easy." This stance is why we so often have gone above and beyond to raise the bar within the pharmaceutical industry and, more recently, to set new standards in healthcare.

Mylan's many responses to date to the growing threat of AMR reflect our commitment to taking the high road and challenging the status quo. Broadly speaking, our responses include manufacturing responsibly and providing leadership with respect to public policy and education.



new standards in healthcare



\$100T OF GLOBAL GROSS DOMESTIC PRODUCT AT RISK

Unless effective action is taken, drug-resistant strains of tuberculosis, malaria, HIV and certain bacterial infections could by 2050 be claiming 10 million lives each year. This would come at an economic cost of \$100 trillion wiped off global gross domestic product over the next 35 years.

The Review on AMR

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MANUFACTURING RESPONSIBLY

Mylan began proactively addressing concerns about pharmaceutical discharge into the environment long before AMR became a major public focus.

For instance, we began implementing zero liquid discharge (ZLD) wastewater treatment systems at our active pharmaceutical ingredient (API) manufacturing facilities in Hyderabad, India, before doing so was made mandatory by the region's State Pollution Control Board (SPCB). Today all of our manufacturing plants in Hyderabad feature it.

These plants are operated 24 hours a day, seven days a week by qualified individuals and have been visited by various regulatory and environmental authorities, including SPCB, which often showcases our sites to third parties as best-in-class ZLD units. The plants also have been audited by the multinational companies to which we supply APIs.

Effluent from Mylan's ZLD facilities is recycled and reused in non-potable applications; there is no discharge to the environment or to common effluent treatment plants. All solid wastes generated go to authorized disposal sites. Further, many of Mylan's facilities are ISO 14001 certified and go through regular audits from certifying agencies.

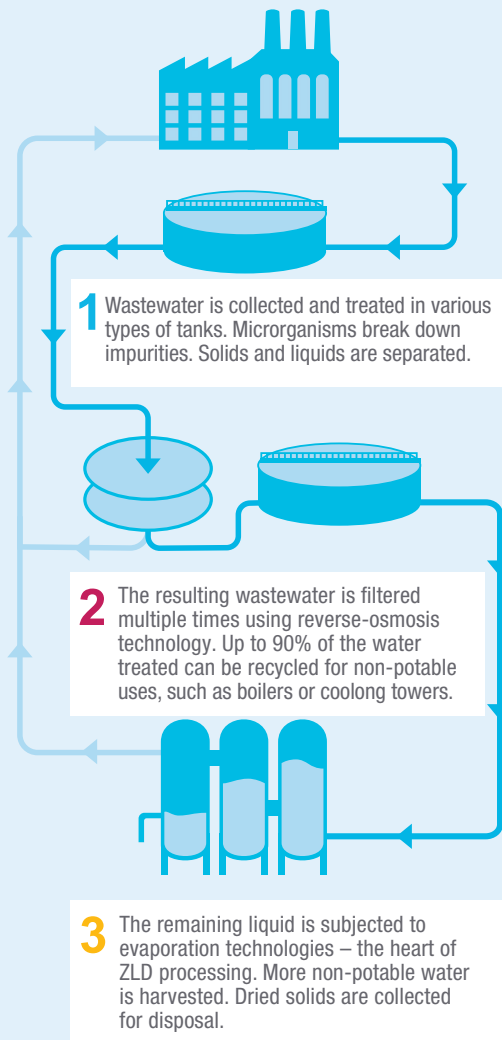
Mylan's use of ZLD technology helps eliminate the discharge of antibiotics and keep other APIs and AMR-contributing compounds out of the environment.

Further, we continue to invest in and expand the technology to other facilities throughout India, which lacks sophisticated water-treatment infrastructure and is home to approximately half of Mylan's production sites around the world. Sadly, the expense and effort required to implement ZLD often leads companies to avoid complying with local regulations.

Even in countries that have more advanced municipal water-treatment infrastructure, Mylan typically goes above and beyond to protect the environment. We employ a variety of proven technologies, such as membrane bioreactors and sequencing batch reactors, and have established good working relationships with appropriate government agencies regarding proper treatment methods.

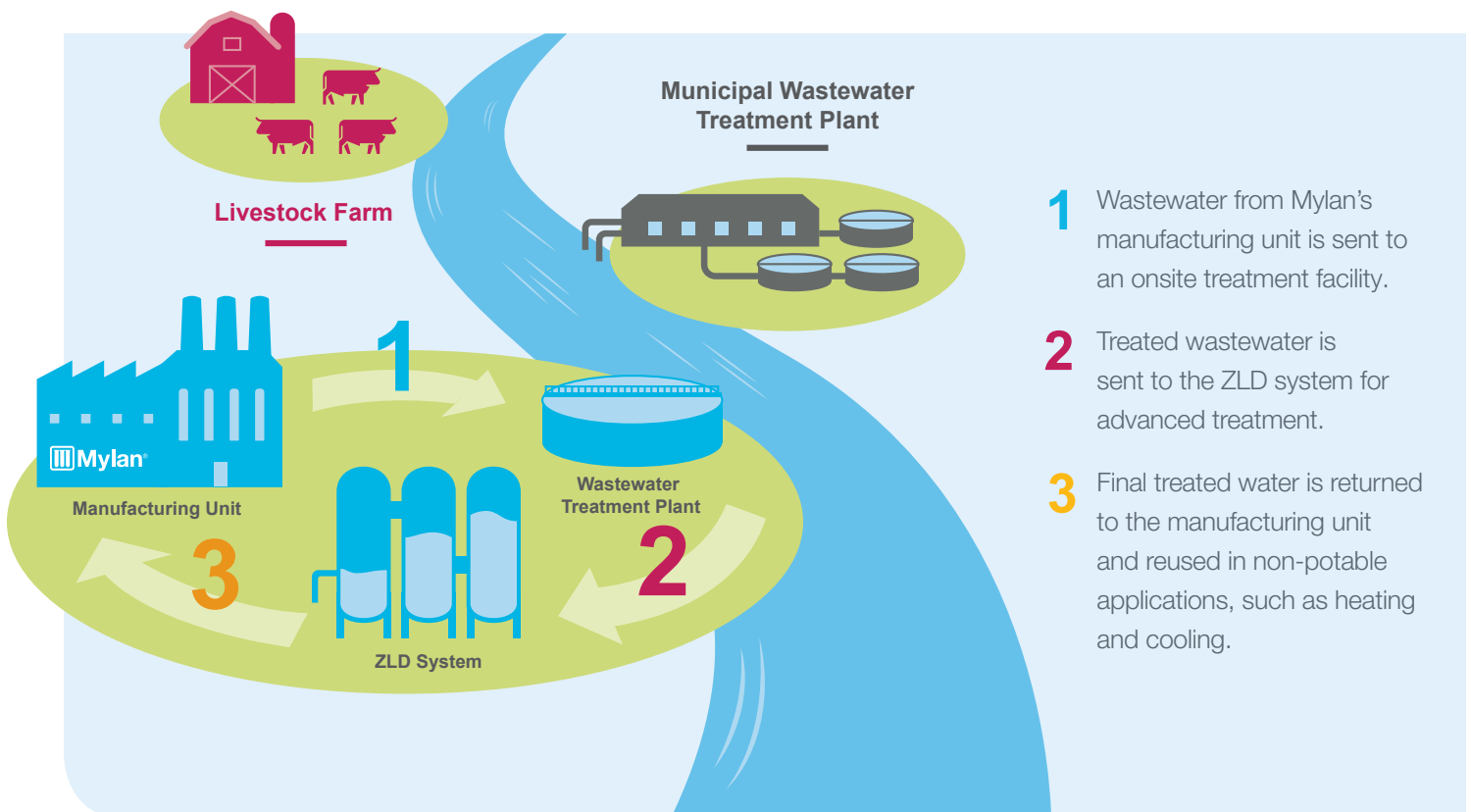
We also continue to evaluate emerging treatment options, such as chemical oxidation, ultraviolet systems and ozone systems, with an eye to implementing them once it's clear they're technically and commercially viable.

Zero Liquid Discharge Processing



Fast Facts

- > Municipal wastewater treatment plants receive effluent from a number of sources, including residential communities, hospitals, medical and veterinary clinics, and other sources that contain pharmaceuticals, primarily from the excretion of product from people.
- > Antibiotics are used extensively in agriculture, primarily to promote growth and prevent infection in livestock. Animals metabolize as little as 10% of antibiotics given to them. The rest is excreted, contaminating waterways, groundwater and soil.
- > On average, high-income countries treat 70% of their wastewater, middle-income countries treat 28% of their wastewater, and low-income countries treat 8% of their wastewater⁹.
- > Limited scientific data exists about the characteristics of pharmaceutical manufacturing effluent. Further, technology to detect and remove drug compounds from treatment-plant wastewaters is not technically or financially feasible for the majority of applications. This is especially true for municipal systems that receive large quantities of anti-microbial compounds.
- > A more practical approach to keeping such compounds out of the environment is to prevent them from being discharged at all. Indeed, that is the goal of ZLD technology.



- 1 Wastewater from Mylan's manufacturing unit is sent to an onsite treatment facility.
- 2 Treated wastewater is sent to the ZLD system for advanced treatment.
- 3 Final treated water is returned to the manufacturing unit and reused in non-potable applications, such as heating and cooling.

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Mylan supports and is a signatory to the 2016 Davos Declaration on AMR.

PROVIDING PUBLIC POLICY AND EDUCATION LEADERSHIP

Mylan always has taken seriously its responsibility to provide industry leadership – both independently and by engaging with government leaders, trade associations and other health-focused organizations around the world. Currently, our CEO, Heather Bresch, is on the board of the U.S. Association of Accessible Medicines, and the head of our business in Europe, Jacek Glinka, is president of Medicines for Europe, which represents drug companies supplying the largest share of medicines across the region.

Mylan supports and is a signatory to the 2016 Davos Declaration on AMR. We also were engaged during the development of the “Industry Roadmap for Progress on Combating Antimicrobial Resistance,” laid out subsequently by a small cohort of Declaration signatories, and we will continue to participate in the dialogue. Per the Declaration, Mylan supports efforts to:

- > **Reduce the development of antimicrobial resistance.** To this end, we support the rational use of antibiotics, limiting prescription and use to patients who need them, and continued associated education for clinical professionals. We encourage infection control via improved hygiene, vaccination and preventive treatments. We support measures to reduce environmental pollution from antibiotic manufacturing, along with a “one health” approach towards prudent and responsible use, including a global reduction of unnecessary antibiotic use in livestock.



According to the World Health Organization, immunization is one of the most successful and cost-effective health interventions, preventing between 2 million and 3 million deaths every year⁴.

Vaccines are safe and beneficial. They provide “herd coverage,” for example, which indirectly protects individuals who have poorer access to healthcare or who cannot be vaccinated, such as newborns. Vaccines also are a key tool in combating AMR.

Pharmacies can play an important immunization role. The International Pharmaceutical Federation, for instance, estimates that community pharmacies have the potential to vaccinate at least one in eight people globally⁵.

Still, more education and awareness of vaccine effectiveness are needed to increase immunization rates.

education leadership

- > **Invest in R&D to meet public health needs with new innovative diagnostics and treatments.** Examples include innovative antibiotics; vaccines; methods to distinguish bacterial and viral infections; technologies and diagnostics for resistant infections; and determining how to overcome the significant scientific difficulties of antibiotic discovery. We support research in academia and elsewhere on new and repurposed antibiotics. We support new ways of working, such as open collaborations between industry and public researchers. We also stand ready to work with payers and policymakers on new valuation mechanisms and commercial models that specifically address the unique challenges facing the antimicrobial market.
- > **Improve access to high-quality antibiotics and ensure that new ones are available to all.** We support mechanisms to ensure affordable access to new and existing antibiotics to the patients who need them, in all parts of the world and at all levels of income. We recognize the success of programs to improve global access to HIV/AIDS, tuberculosis and malaria drugs and call for similar collaborative efforts to address issues of access to antibiotics.

These commitments are informing our current work on AMR.

For instance, through our position on the Board of the Global Fund to Fight AIDS, Tuberculosis and Malaria, we continue to raise the strategic risk of AMR in the global fight against these three infectious diseases. We have pushed for greater action to address this risk given the identification of drug and insecticide resistance as a high and growing threat in the organization's risk register.

We are an active participant in the Inter Association Initiative on Pharmaceuticals in the Environment, a cross-industry group in Europe working together to address key issues related to the environmental impact of pharmaceuticals.

We met with Lord Jim O'Neill's team to discuss their Review on Antimicrobial Resistance's final recommendations (published May 2016). We discussed ways Mylan could help address AMR through our various related product areas, such as essential antibiotic products, antivirals and vaccines.

We have convened educational events for the medical community, government officials and media to raise awareness of AMR and the various tools necessary to address it. Such tools include appropriate use of vaccines, such as those against influenza.

Sources

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