



## Antimicrobial Stewardship Issue Brief

### Importance to Elanco and our Stakeholders

Consumers want to understand how and where their food is made, including what medicines are used to treat food animals and how that may impact human health. As a company dedicated to the health and welfare of animals, we have a responsibility to help answer these questions. Antibiotics in the food supply can impact human interactions with antibiotics. Proper antimicrobial stewardship is critical for human health.

### Background

Even when best practices are used to manage appropriate hygiene, vaccination status and biosecurity, animals (like people) can still get sick – and antibiotics are sometimes needed.

Using antibiotics responsibly means treating sick animals with the right dose of antibiotics at the right time to help them get better. It also means using antibiotics to control the spread of infection among a group of animals, when there is a threat and healthy animals are at risk.

In addition, there may be times when a healthy animal is at an elevated risk of getting sick. For example, it is stressful to wean young animals from their mothers. That stress can decrease immunity and increase the animal's risk of getting sick. In such cases, antimicrobials may be administered as a preventative against illness.

Treatment, control and prevention are collectively defined as 'therapeutic use' by international institutions such as the World Health Organization (WHO), United Nations' Food and Agriculture Organization (FAO) and World Organisation for Animal Health (WOAH) as well as by government regulatory agencies such as the United States Food and Drug Administration (US FDA) and European Medicines Agency's Committee for Veterinary Medicinal Products (EU/EMA/CVMP).

When used appropriately with good animal care practices, antibiotics can enhance animal welfare and overall food safety. Non-science-based decisions to limit therapeutic use through broad-based bans or severe restriction would greatly restrict veterinarians, farmers and pet owners from best protecting animal health in a manner reasonable and effective in the circumstances, mitigating suffering from disease and reducing animal mortality.

### Our Action

Antibiotic stewardship has been an Elanco priority for more than two decades.

While we appreciate that antibiotics are critical, Elanco strongly supports the idea that they are just one of many tools available to maintain human and animal health and welfare. We're focused on finding solutions and alternatives to combat antimicrobial resistance – and to bringing greater clarity and collaboration to issues around antibiotic stewardship.

We're working with leaders across industries and across the globe – including farmers, veterinarians, scientists and health care industry leaders – to develop long-term, responsible solutions. And we're actively engaged in shaping science-based recommendations on responsible antibiotic use, animal welfare and the long-term sustainability of the food system.

Internally, we're encouraging greater innovation to protect the long-term effectiveness of antibiotics. We've intentionally shifted our business to align with the following tiered approach to antibiotic stewardship – positioning us to continue recognizing progress in this important, collaborative effort:

- **Reduce the need for antibiotics** - Farmers and veterinarians use many methods to keep animals healthy and prevent disease, including balanced diets for strong immune systems, well-maintained housing and good animal care. Elanco's industry-leading technical data, when combined with support from our technical experts, helps farmers make well-informed management decisions to support animal health and welfare.
- **Promote responsible antibiotic stewardship** - When therapeutic use of antibiotics is required, non-medically important (animal-only) antimicrobials are the preferred – and most responsible – first choice. These products were developed expressly for therapeutic use in animals and are not useful in human medicine. Their use does not create human health risk.
- **Replace antibiotics with alternatives** - Elanco has intentionally expanded our vaccine and nutritional health capabilities since 2015 to provide alternative solutions – including nutritional health products like enzymes, probiotics and prebiotics, parasiticides and vaccines. Eliminating the pathogen at the source reduces the need for antibiotic use in humans.
- **Monitor the efficacy of antibiotics in livestock and pets** – Elanco has been an active participant in the monitoring of antibiotic susceptibility, as elaborated below.
- **Actively engage and educate** – Elanco's Chief Medical Officer, Dr. Shabbir Simjee, provides regular training and information on AMR, participates in the development of global regulation and helps execute national AMR action plans across the globe.

### **Animal Health Strategy**

As noted, "Preventing infections in the first instance is the best way to achieve reduction and to minimize the need to use antimicrobials, as reducing the number of infections reduces the number of treatments needed. This approach is supported by the Animal Health [Strategy](#), as it is fully in line with the principle promoted by the philosophy that prevention is better than cure. A reduction in the instance of animal disease and zoonotic infections should also minimize the need for, and use of, antimicrobials."<sup>1</sup>



The following measures help prevent disease and reduce the need for antimicrobials in all species:

- Hygiene and biosecurity measures: hand washing, disinfection of facilities, quick removal of mortality and applying an “all in - all out” system
- Improved husbandry: appropriate housing, ventilation and environmental conditions
- Establishing production systems to avoid the need to buy and mix animal populations and prevent transportation of animals with unknown disease status
- Avoiding animal stress
- Implementing other zotechnical treatments to minimize disease and decrease use of antimicrobials
- Introducing herd-specific health plans and prevention of prophylactic antibiotic administration
- Implementing programs to control specific animal diseases (both viral and bacterial) by means of vaccination
- Using scientifically proven, effective and safe alternatives to microbials
- Using only safe high-quality feed and water
- Providing incentives to farmers and encouraging them to adopt effective prevention measures to improve animal health and welfare standards and to monitor pathogens and their sensitivity at group level.

### **Antimicrobial Stewardship Milestones**

Through our pipeline, policies and advocacy efforts, Elanco seeks to protect the benefits of antibiotics in human medicine – while responsibly protecting the health and welfare of pets and farm animals and the safety of our food supply. We have made significant strides to advance antibiotic stewardship efforts globally:

## ELANCO'S ANTIBIOTIC STEWARDSHIP MILESTONES

<p><b>8-Point antibiotic stewardship plan announced</b></p> <p><b>2015</b></p>	<p><b>Removed</b> growth promotion claims from nearly 100 product labels from our shared-class antibiotic molecules globally</p> <p><b>Removed</b> over-the-counter use from 67 product labels to require the oversight of a veterinarian in the countries where over-the-counter uses remained and veterinary infrastructure exists</p> <p><b>Invested</b> substantially in developing alternatives to antibiotics, entering nearly 25 new antibiotic alternatives into our development pipeline to help producers replace antibiotics when possible</p> <p><b>2017</b></p>	<p><b>Elanco expands R&amp;D commitment</b>, collaborating with AgBiome to develop swine nutritional health products, and acquiring Prevtec Microbia, which specializes in the development of vaccines that help prevent bacterial and viral diseases in food animals.</p> <p><b>2019</b></p>	<p><b>Elanco achieved approval of poultry vaccines in Latin America</b>, helping control salmonellosis and further preventing potential need for antibiotic treatment in poultry raised in this region.</p> <p><b>2021</b></p>
<p><b>2016</b></p> <p>Elanco convenes <b>OneHealth Summit on Antibiotic Stewardship</b></p>	<p><b>2018</b></p> <p>Elanco joins <b>CDC &amp; HHS Antimicrobial Challenge</b></p> <p>Partners with <b>Novozymes for Nutritional Health Innovation</b></p>	<p><b>2020</b></p> <p><b>Through the acquisition of the Bayer Animal Health business</b>, Elanco expanded the portfolio of preventative products and disease treatments for pets, furthering the company's contribution to OneHealth outcomes. Also published Antibiotic Stewardship Guiding Principles.</p>	

### Principles Toward Better Antimicrobial Stewardship

Antimicrobial resistance is a [One Health](#) issue impacting both human and animal medicine. We support the layers of protection in place to facilitate use of antibiotics in animals that pose minimal risk to human health. We work closely with regulators, veterinarians, animal health companies, farmers, pet owners, government and environmental health stakeholders as well as research and academic institutions to ensure – where allowed– antibiotics are used under strict professional supervision, to minimize the potential risk of resistance development.

Pet owners and farmers need innovation to address unmet health needs. Our aim is to prevent disease by supporting veterinarians and farmers with new and innovative products for disease prevention, survivability and early diagnosis of diseases. Our vision is to move from treatment to prevention, while championing awareness and technologies that promote health and survivability even before an animal's life begins. With increased knowledge and expanded access to data, a growing product portfolio and precision application, antibiotic alternatives such as vaccines, enzymes and probiotics are expected to contribute to more reliable and effective approaches.

Elanco's guiding principles for responsible antibiotic use include:

- **Food chain stakeholder engagement:** Helping stakeholders across the food chain better understand and implement responsible antibiotic guidelines

- **Global antibiotic classifications:** Considering international, national and regional ranking recommendations
- **Disease treatment:** Supporting the administration of an antibiotic to an individual or a group of animals showing clinical signs of an infectious disease
- **Disease control:** Supporting the administration of antibiotics for disease metaphylaxis/control in animals identified by a veterinarian
- **Disease prevention:** Supporting the administration of antibiotics for disease prevention/prophylaxis where determined by a veterinarian that animals are likely to get sick
- **Utilization of risk assessment:** Following a risk assessment process, where regulations allow, to support the use of non-medically important antimicrobials for performance indications
- **Concomitant use:** Supporting the approach that two medically important antibiotics of different classes should not be used at the same time, for the same disease indication (unless approved by the regulatory agency or supported by scientific evidence and/or veterinarian experience)
- **Aquaculture:** Restricting use of antibiotics in aquaculture to areas where environmental exposure of the antibiotics can be sufficiently controlled, to avoid environmental impact or risk of resistance development
- **Recording of antibiotic therapy:** Supporting veterinarian and/or farmer recordkeeping for antibiotic use in farm animals

### **Healthy Animals and Safer, More Sustainable Food**

Animal health is fundamental to animal welfare. Healthy animals are more efficient, helping to reduce the environmental footprint of livestock production.

Elanco helps veterinarians and farmers deliver safe and healthy meat, milk, fish and eggs to consumers by providing a wide portfolio of antibiotics – as well as alternatives such as vaccines, probiotics and nutritional solutions. We also offer services that enhance knowledge and decision-making for management practices and welfare standards. This comprehensive set of products and services helps our customers mitigate diseases that directly impact animal health and welfare by controlling zoonotic bacteria that is important for public health and food safety.

A vital component of antimicrobial stewardship includes working to prevent the development of disease in the first place. As an example of our efforts, Elanco is a leader in the prevention of salmonella in poultry through our suite of vaccines. This vaccine helps reduce transfer of the disease to humans, where it would be treated with an antibiotic. Preventing the issue reduces the potential need for antibiotic use in humans.



We recognize every farm operation is different. Most importantly, every animal is different. Advances in animal science, farming innovation and veterinary diagnostics allow practitioners to tailor health programs with a focus on preventing disease through better animal care practices, vaccination programs, nutrition and biosecurity. By understanding the needs of veterinarians and farmers and closely partnering with them, we can minimize and target how the antibiotic is used.

### **Antibiotic Resistance Monitoring**

Antibiotic resistance monitoring is an essential component of responsible antibiotics use.

Elanco has been part of the [Centre Européen d'Etudes pour la Santé Animale](#) (CEESA) antibiotic resistance monitoring program in the EU since its inception in 1998 and continues to take an active role in the organization's internationally recognized programs which monitor for trends in resistance that may impact the efficacy of treatments or the safety of food and gives early indications if any upward trends emerge. Elanco's Chief Medical Officer has been an active member of this CEESA program since 2004 and chaired the group's VetPath program for five years.

CEESA's AMR programs monitor the emergence of antibiotic resistance in foodborne pathogens as well as in pathogens that cause infections in farm and pet animals. Data from the program is used for risk assessments across the EU as well as in other geographies around the world. The programs also provide continued data on the efficacy of Elanco antibiotics, which can be used as an early indicator of emerging resistance profiles so usage patterns can be modified.

Over 20 years of CEESA data supports the findings that resistance in food-borne pathogens, as well as disease causing organisms, has remained low and stable across the EU. Elanco continues to work with the CEESA group making the data publicly available in a timely manner via peer reviewed publications as well as at international conferences in the form of oral publications and poster presentations.

In the United States, the Centers for Disease Control and Prevention tracks 18 major antibiotic resistance threats. Only two, campylobacter and non-typhoidal salmonella, are associated with animals. While antibiotic resistance to the primary treatments associated with animal agriculture remains low, the industry is committed to continued evaluation and improvement.

### **Governance and Risk Management**

Our antimicrobial stewardship efforts are led by the joint efforts of our Executive Vice President of Innovation and Regulatory Affairs, as well as our Chief Medical Officer, who report twice per year to the Innovation, Science and Technology Committee of the Board of Directors.

The Innovation, Science and Technology Committee reviews the Company's regulatory strategy and compliance programs, as well as the competitive landscape in terms of related external



scientific research, discoveries and commercial developments and potential future innovations in animal healthcare, as appropriate. The committee also assists the Board with oversight for enterprise risk management in areas affecting the Company's research and development efforts.

### **External Affiliations and Collaborations**

Together with approximately 200 other companies and 700,000 veterinarians worldwide, Elanco undersigned the Health for Animals 2017 publication "Commitments and Actions on Antibiotic Use," which outlines key principles for responsible antibiotic use in the animal medicines industry. [Health for Animals](#) publications are an excellent resource for research.

Following the World Health Organization 2015 Global Action Plan on Antimicrobial Resistance, countries around the world are requested to develop National Action Plans (NAPs) for reducing antimicrobial resistance. Elanco played an active role providing comments on draft NAPs as they were made available for public consultation.

Elanco also works with international institutions to conduct seminars and laboratory training on antibiotic resistance monitoring in compliance with current international standards. To date, Elanco has been involved in training across more than 20 countries and has trained over 500 laboratory and technical personnel.

We work closely with regulators and veterinarians to ensure, where appropriate, antibiotics are used under strict professional supervision and follow responsible use guidelines and principles. We also collaborate with key stakeholders across the value chain, including universities, global health organizations, veterinary medicine professionals, and farm animal producers' associations in markets where Elanco commercializes antimicrobials.

### **Clinical and Laboratory Standards Institute**

Elanco is a founding and active member of the [Clinical and Laboratory Standards Institute](#) (CLSI) Veterinary Antimicrobial Susceptibility Subcommittee. The CLSI is responsible for establishing methods for testing antibiotic susceptibility, and for setting interpretive criteria which allow veterinarians to select the most appropriate antibiotics for treating sick animals. Elanco's Chief Medical Officer served as a voting member for a decade on this committee, and as co-chair for five years.

### **Metrics and Targets**

By 2030, Elanco seeks to:

- Invest more than \$3.5B in innovation to pursue the discovery and development of products that improve the health and care of animals, including products that would reduce the need for medically important antibiotics.



- Expand the availability of vaccines, nutritional health products, and diagnostics in underserved markets that currently rely on medically important antibiotics.
- Increase access to innovation, knowledge, and partnerships for small-holder farmers by adapting the value-chain to ensure the responsible use of antibiotics.
- Communicate with veterinarians and stakeholders about pharmaceuticals, vaccines, and nutritional health products that potentially reduce the need for medically important antibiotics in animals.
- Expand engagement with stakeholders, solicit concerns and expectations of responsible antibiotic use and the responsible care of antibiotics.

With these commitments, Elanco continues to build on international guidelines laid out by the World Organisation for Animal Health and Codex Alimentarius. Elanco is confident that these actions can meaningfully limit the risk from antibiotic resistance and protect sustainable animal production and pet health well into the future.

### Metrics

Elanco has intentionally shifted our business away from medically important (shared-class) antibiotics and are focusing on non-medically important (animal-only) antibiotics, which do not pose a resistance risk to human health, as well as antibiotic-free solutions. When Elanco began this journey in 2015, shared class antibiotics were 16% of revenue.

Metrics on antimicrobial resistance monitoring

% of Total Company Revenue	2018	2019	2020*	2021	2022
Shared-class antibiotics (%)	12%	11%	12%	9%	8%
Animal-only antibiotics & ionophores (%)	25%	24%	17%*	14%	15%

\* In August 2020, Elanco completed the acquisition of the animal health business of Bayer, increasing the total revenue of the company. The additional revenue was primarily in pet health but included shared-class antibiotics as well. These dynamics are important to consider when comparing the metric annually over the five-year window.

The content of this brief is informed by the following ESG disclosure standards:

- *Policies and commitments to the material issue (GRI 3-3c)*
- *Impact Management of Resilience Issues (GRI 3-3d)*
- *Stakeholder engagement informing actions (GRI 3-3f)*



- *Describe targets related to the material issue (IFRS S1, GRI 3-3e)*
- *Disclose GRI 'topic-specific indicators' relevant to the material issue*
- *Describe processes used to track effectiveness and lessons learned (GRI 3-3e)*
- *Describe how stakeholder engagement has informed whether the actions have been effective (GRI 3-3f)*
- *Resilience and material issue action statements (IFRS S1)*
- *Mechanisms to integrate the material issue into strategy, decision-making and financial planning (IFRS S1)*
- *Describe the board and management responsibilities related to the material issue (IFRS S1, GRI 2-12, 2-13, 2-14)*
- *Describe any connections between the material issue and remuneration outcomes (IFRS S1, GRI 2-17, 2-18)*
- *Industry associations, other membership associations, and national or international advocacy organizations in which Elanco participates in a significant role (GRI 2-28)*

## Definitions

**Animal-only antibiotic:** An antibiotic that is prescribed for animal use only and does not have a human use.

**Antibiotic:** substance with a direct action on bacteria used for treatment or prevention of infections or infectious diseases (EPCEU. Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. 2019)

**Antibiotics resistance:** the ability of micro-organisms to survive or to grow in the presence of a concentration of an antibiotic agent which is usually sufficient to inhibit or kill micro-organisms of the same species (EPCEU. Antibiotic resistance occurs naturally in the environment, as part of the biological process for bacterial survival in defense against the drugs designed to kill them. The resistance process is complex and occurs over time. Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. 2019)

**Antimicrobials:** substance with a direct action on micro-organisms used for treatment or prevention of infections or infectious diseases, including antibiotics, antivirals, antifungals and anti-protozoal (EPCEU. Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. 2019)

**Antibiotic stewardship:** the actions taken individually and as a profession to preserve the effectiveness and availability of antibiotic drugs through oversight and educated medical decision making while at the same time safeguarding animal, human, and environmental health

**Antiparasitic:** substance that kills or interrupts the development of parasites, used for the purpose of treating or preventing an infection, infestation or disease caused or transmitted by parasites, including substances with a repelling activity (EPCEU. Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. 2019)

**Control/metaphylaxis:** administer an antibiotic agent to a group of animals containing sick animals and healthy animals (presumed to be infected), to minimize or resolve clinical signs and to prevent further spread of the disease ((<https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/>))

**Indication:** in medicine, a sign, symptom, or medical condition that leads to the recommendation of a treatment, test or procedure

**Medically important antibiotics:** Antibiotic classes used in human medicine

**Non-medically important antibiotics:** Antibiotic classes not used in human medicine

**One Health:** an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems – recognizing the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are intricately linked and interdependent.

**Prevention/prophylaxis:** administer an antibiotic agent to an individual or a group of animals at risk of acquiring a specific infection or in a specific situation where infectious disease is likely to occur if the drug is not administered (- (<https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/>))

**Resistance-transfer:** the transfer of antibiotic resistance to humans

**Shared-class Antibiotic:** An antibiotic which may be prescribed for both animals and humans.

**Treatment:** administer an antibiotic agent to an individual or a group of animals showing clinical signs of an infectious disease (<https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/>)

**Veterinarian:** A person who is registered or licensed by the relevant veterinary statutory body of a country to practice veterinary medicine/science in that country (<https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/>)

**Footnotes**

<sup>1</sup>Official Journal of the European Union, Directive C 299/20 (11.9.2015), Commission Notice – Guidelines for the Prudent Use of Antimicrobials in Veterinary Medicine, Section 6.1  
[https://health.ec.europa.eu/system/files/2016-11/2015\\_prudent\\_use\\_guidelines\\_en\\_0.pdf](https://health.ec.europa.eu/system/files/2016-11/2015_prudent_use_guidelines_en_0.pdf)

## Citations

### Talks

**Simjee S.** 2022. Global Progress on Antimicrobial Stewardship: Updates from The European Union. Animal Agriculture Alliance seminar on 'Emerging Issues Update: Responsible Antibiotic Use in Animal Agriculture. 28<sup>th</sup> March 2022.

**Simjee S.** 2022. The Urgent need to harmonise definition in the AMR space. Indian Association for the Advancement of Veterinary Research (IAAVR) 22<sup>nd</sup> Annual Conference. 9<sup>th</sup> April 2022. **(Invited Speaker)**

**S Simjee.** 2022. Updates from the EU on Antibiotic Policies. CONAFAB Conference. September 21-22, Guadalajara, Mexico.

**S Simjee.** 2022. Updates from the EU on Antibiotic Policies. Global Salmon Initiative. Madrid, Hyatt Centric Gran Via – Gran Vía, 31, Madrid, 28013, Spain

**S Simjee.** Coffee Chat on Antibiotic Resistance and development of Antibiotic Alternatives. 7<sup>th</sup> Annual Animal Health, Nutrition and Technology Innovation Asia. October 18-19 Bangkok, Thailand.

**Simjee S.** 2022. Responsible use of antibiotics in Veterinary Medicine. WAAW Jakarta Indonesia 22<sup>nd</sup> November 2022. **(Invited Speaker by WOA)**

**Simjee S.** 2022. Responsible use of antibiotics in Veterinary Medicine. WAAW South Africa 23<sup>rd</sup> November 2022. **(Invited Speaker by WOA)**

### Papers

**Simjee S,** Henninger M, Ippolito G and Atkinson J. 2022. Can we align antibiotic policies at an international level in the absence of harmonized definitions? *Journal of Antimicrobial Chemotherapy*, 77: 549–555. <https://doi.org/10.1093/jac/dkab465>

Trongjit S, Assavacheep P, Samngannim S, My TH, An VTT, **Simjee S** And Chuanchuen R. 2022. Plasmid-mediated colistin resistance and ESBL production in *Escherichia coli* from clinically healthy and sick pigs. *Nature Portfolio Scientific Reports* 12:2466. <https://doi.org/10.1038/s41598-022-06415-0>

De Jong A, El Garch F, Hocquet D, Prenger-Berninghoff E, Dewulf J, Migura-Garcia L, Perrin-Guyomard A, Veldman KT, Janosi S, Skarzynska M, **Simjee S**, Moyaert H and Rose M. 2022. European-wide antimicrobial resistance monitoring in commensal *Escherichia coli* isolated from healthy food animals between 2004 and 2018. *Journal of Antimicrobial Chemotherapy*.

**Simjee S**, and Ippolito G. 2022. European regulations on prevention use of antimicrobials from January 2022. *Brazilian Journal of Veterinary Medicine*, 44, e000822. <https://doi.org/10.29374/2527-2179.bjvm000822>

### Posters

Parent E, Gould G, Farran J, Maduro L, Boulianne M and Simjee S. 2022. Minimal inhibitory concentrations of avilamycin to *Clostridium perfringens* isolates from broiler chicken farms before and after the approval of Surmax® Premix (Avilamycin) in Canada. American Veterinary Medical Association (AVMA)/American Association of Avian Pathology (AAAP) conference. Philadelphia, July 29-August 2, 2022

**Simjee S**, Power, W. 2022. Efficacy of florfenicol against *Staphylococcus pseudintermedius* recovered from dogs with otitis externa across the EU between 2017-2018. British Small Animal Veterinary Association Annual Conference. March 24-26, Manchester, UK.