

Industry perspective on the registration of alternatives to antibiotics

ATA2019

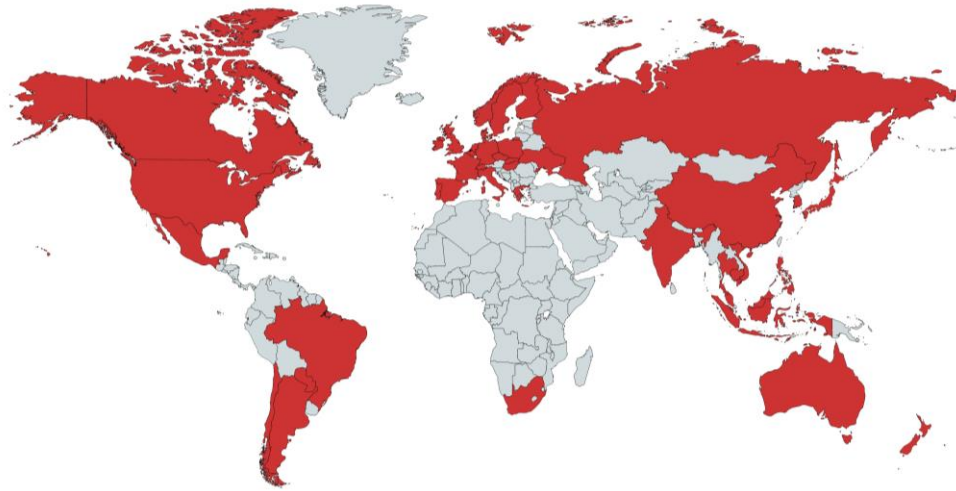
Bangkok, December 2019

On Behalf of HealthforAnimals

prof dr Erik De Ridder



29 Regional & National Associations



vaccines, antibiotics, parasiticides,
nutrition and other products

85% of global animal medicines sector

Ten Largest Animal Health Companies Working in 100+ countries

zoetis

Elanco

Boehringer
Ingelheim

vetoquinol
ACHIEVE MORE TOGETHER

ceva

MERCK
Animal Health

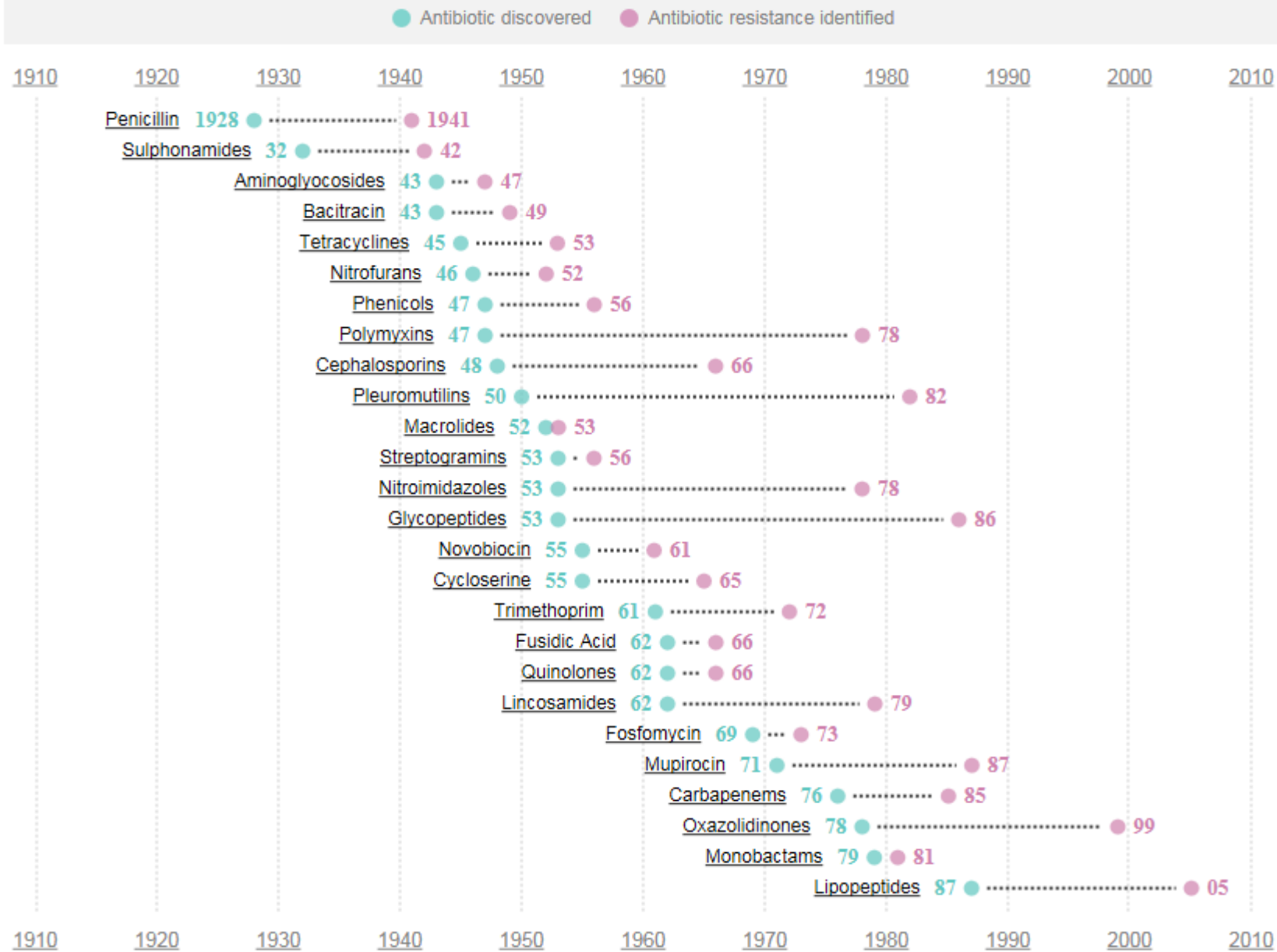
B
A
Y
E
R

Virbac

Phibro
ANIMAL HEALTH CORPORATION

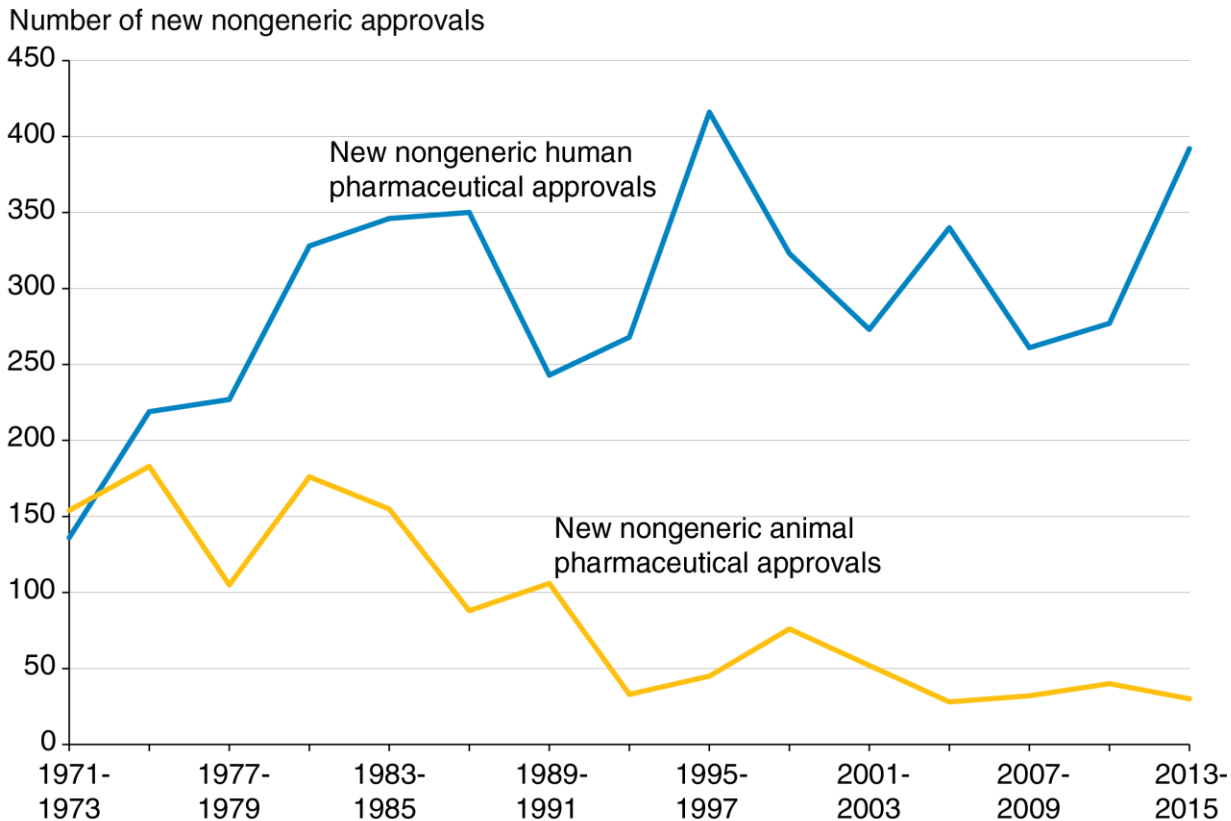
ZENOAQ

A HISTORY OF RESISTANCE



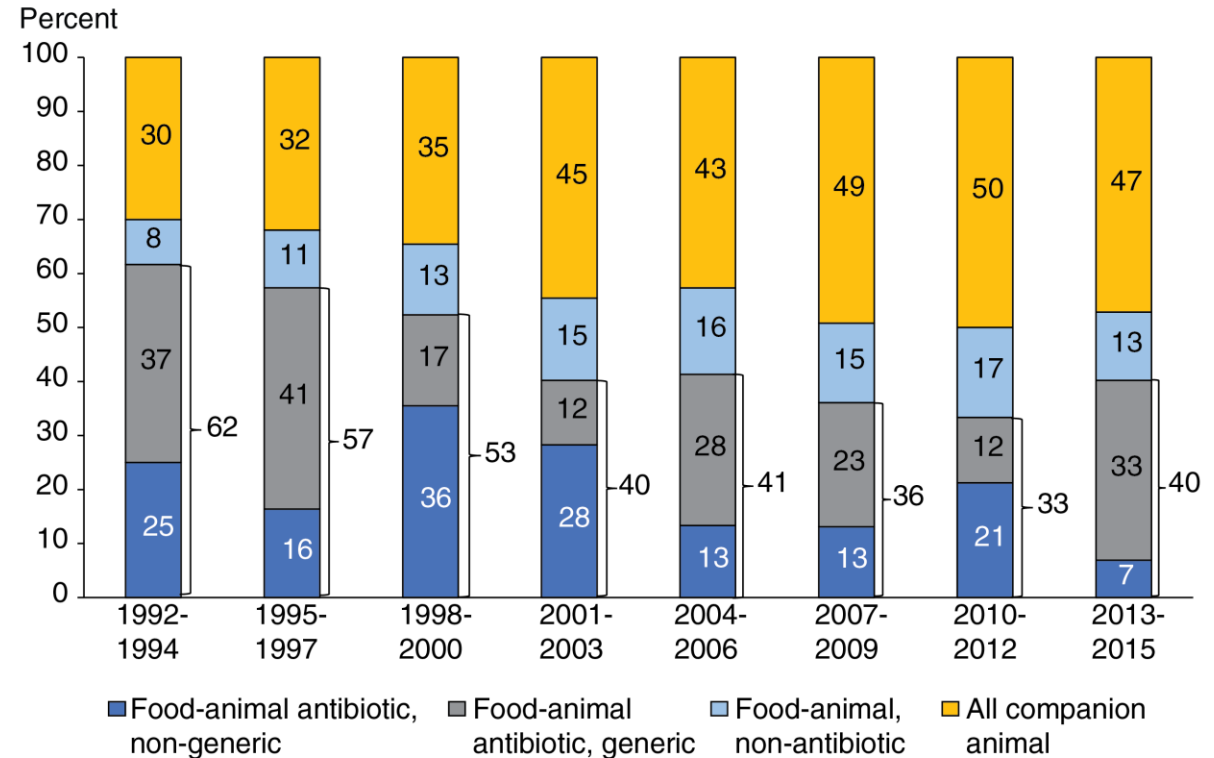
Nil novi sub sole?

New nongeneric human drug approvals increased while new animal drug approvals declined between 1971 and 2015



Note: Medical gases approved for use in animals not included.
Source: USDA, Economic Research Service calculations from Food and Drug Administration Center for Veterinary Medicine Green Book (FDA-CVM Green Book) reports of veterinary product approvals and Food and Drug Administration Center for Drug Evaluation and Research data on human drug approvals.

Approvals of food-animal antibiotics have declined as a share of new approvals for animal pharmaceuticals between 1992 and 2015



Note: Bars may not sum up to 100 due to rounding. Data do not include approvals of products for minor species or products without a species listed. Combined, these excluded products account for 2.5 percent of approved products between 1992 and 2015. The “food animal” categories include the few products approved for both companion or food animals. Medical gases approved for use in animals not included.
Source: USDA, Economic Research Service analysis of Food and Drug Administration Center for Veterinary Medicine Green Book (FDA-CVM Green Book) reports of animal pharmaceutical product approvals.

Fighting AMR (development): a common need

- **Not a surprise:**
 - common need for all “one health” stakeholders
 - to fight antimicrobial resistance and the development of antimicrobial resistance
 - to keep antibiotics working
 - to reduce the need for antibiotics
- **Reducing the need for antibiotics: a HealthforAnimals commitment**
 - Via better prevention
 - Tools to improve vaccination, biosecurity, health and wellbeing
 - Via better detection
 - Tools for improved monitoring and diagnostics
 - Via better treatment
 - Responsible Antibiotic Use
- **Active development of alternatives to antibiotics**

What are ATAm?

- What is antimicrobial and antibiotic?
 - International alignment
- But what is an “Alternative to antibiotics”?
- Globally agencies and academia reflect...
 - “Alternatives to overcoming bacterial resistances” (Rios, 2015)
 - “Technologies to address AMR” (Baker, 2018)
 - CVMP (EU)
 - Proposes “a veterinary medicinal product the use of which provides an alternative approach to the use of antimicrobials in animals or that reduces the need for their use”
 - Veterinary drugs, feed additives, biocides or... depending on presentation, intended use and claims...
 - CVMP listed 17 very diverse examples (2019)

ATAm examples listed by CVMP (2019)

FEED ADDITIVES ("EU")

Organic acids

Herbals/Botanicals

Prebiotics

Minerals (e.g. ZnO)

Toxin binding products

Competitive exclusion product

Bacteriophages

Symbiotics

In-feed antibodies

CRISPR-Cas9
(gene editing derived products)

Immunostimulators
(non-specific)

"BORDERLINE"

VETERINARY DRUGS ("EU")

Vaccines

Antimicrobial peptides

Phytochemicals

Physical devices
(e.g. teat sealants)

HealthforAnimals proposes to work with 3 categories of ATAm

- **Anti-bacterial products**

- **New antibacterials** with new mechanisms. (→?alternatives?)
- **Susceptibility enhancing products**
 - target pathogens to be more susceptible to therapy, or overcoming resistance mechanisms.
 - virulence modifier or adjuvant to maximize benefit of antimicrobial therapy and/or minimize risk of resistance development.

- **Infection prevention products**

- **Infection prevention products**, essentially vaccines,
- **Supportive products**,
 - Help prevent conditions that lead to bacterial infections, for instance ...
 - impacting microbiome or intestinal health
 - protecting integrity of immune system or stimulate immune response to target key pathogens
 - Not directly antimicrobial, but enable animal to respond more effectively to *possible* infections.

- **Infection prevention approaches**

- For instance better bio-security, animal husbandry, stress mitigation, teat sealants, and genetic selection for reduced disease susceptibility
- Approaches that help animals avoid or cope with bacterial infections as an alternative to antibiotic use

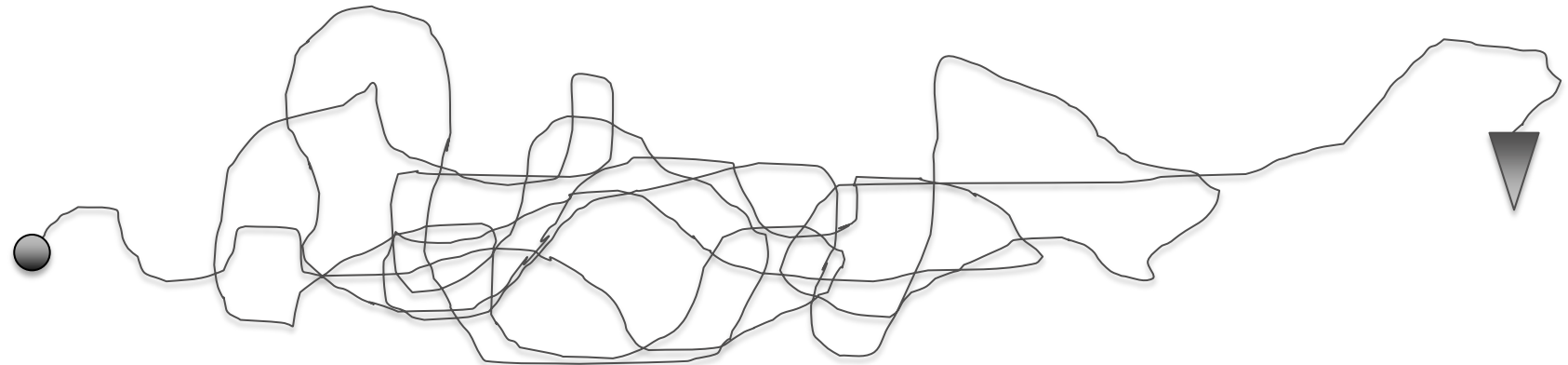
Challenges associated with ATAm?

- Purely regulatory as well as more political/societal issues
- Five themes
 - Lack of definition and clear classification, allowing for new technologies
 - Unclear regulatory pathway and objectives (procedure and claims)
 - Lack of regulatory convergence adding to risk and cost
 - Need for public and consumer acceptance
 - Need regulatory environment with appropriate data protection that really fosters/stimulates radical innovation



Hurdle 1: Lack of definition and clear classification, allowing for new technologies

- Semantic issue linked to functional definition of antibiotic/antimicrobial
- “A veterinary medicinal product the use of which provides an alternative approach to the use of antimicrobials in animals or that reduces the need for their use”?
 - Only veterinary products?
 - Need definition / classification that allows for new technologies



Hurdle 2:

Unclear regulatory pathway and objectives

- Unclear definition leads to unclear regulatory pathway
- Current regulatory paradigms based upon clear definition of product-claim combinations
 - Either VMP or feed additive (EU)
 - Either Pharma or Immunological product
 - Either CVM, or USDA or EPA (US)
- Need more flexible regulatory approaches
 - Type of product
 - Type of claim
 - Move away from therapeutic efficacy
 - Enable claims such as “reduction of need of treatment with medically important antibiotics”



Hurdle 3: Lack of regulatory convergence adding to risk and cost

- Positive: VICH exists since 1996
 - Almost 60 guidelines on technical requirements
 - Including GLs on antibiotics
 - GL 27 Guidance on pre-approval information for registration of new veterinary medicinal products for food producing animals with respect to antimicrobial resistance
 - GL 36: Studies to evaluate the safety of residues of veterinary drugs in human food: general approach to establish a microbiological ADI
- Convergence of all aspects of regulatory systems needed to create more space for paradigm shifting innovation, including
 - More recognition, more joint assessments
 - Shorter and standardized timelines for reviews
 - ...
- Need support from HealthforAnimals and all stakeholders for OIE initiatives
 - To obtain better, modern and flexible regulatory veterinary systems
 - To control illegal and falsified medicines



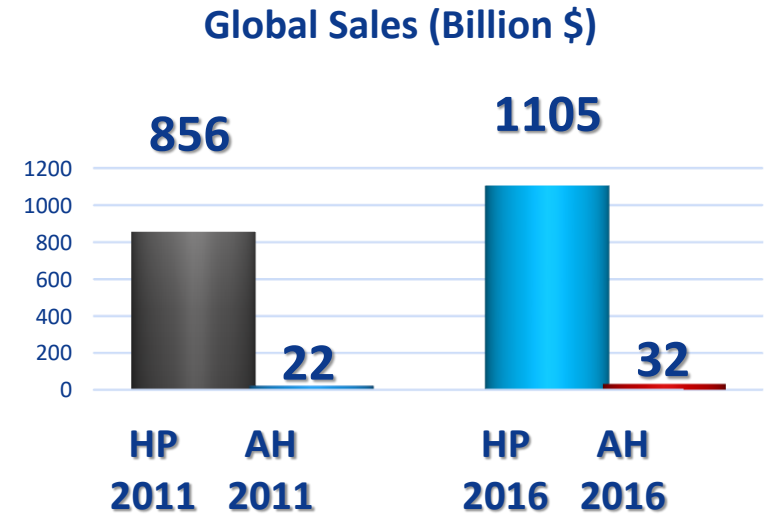
Hurdle 4:

Need for public and consumer acceptance

- New technologies will require public and consumer acceptance
 - Track record from “Dolly” to genetically modified organisms is not great
- Need for collaborative effort from all stakeholders
- Need proactive communication strategy



Hurdle 5: Need regulatory environment with appropriate data protection



- Small
 - Animal health market is small
 - With small margins and little time to get return on investment
- Need regulatory environment with appropriate data protection that really fosters/stimulates radical innovation
 - Main driver is protection of data in a more efficient way
 - Negative impact of increasing “open” data in animal health

- Being accountable and responsible about antimicrobial resistance in a One Health environment...
 - Antibiotics are a cornerstone of modern medicine and public health
 - Antibiotics are the only way to treat a bacterial disease. There is currently no alternative.
 - However, we can exploit the full spectrum of animal health tools to reduce the need for medically important antibiotics
 - Using these tools can improve the prevention, detection and treatment of animal disease.
- The animal health sector is committed to the fight:
 - In 2017, we launched our 'Antibiotics Commitment', and
 - In 2019, we built upon this with our Roadmap to Reducing the Need for Antibiotics.
 - <https://healthforanimals.org/roadmap/activities.html>



Antibiotics are key to treating infections in humans and animals - there are no alternatives to treating life-threatening bacterial infections. The world has recognized that antimicrobial resistance (AMR) is a challenge that costs lives. Our vision is a world where veterinary antibiotics are used responsibly to protect and treat animals, and where they maintain their value as a therapeutic tool. An equally important challenge is maintaining and increasing food safety and security. To address these interconnected challenges, companies and organizations commit to five principles and practical actions, and will proactively encourage others to embrace them.



Principle 1: Protect animal health and welfare in a unified One Health approach.

Actions: We will meet the ethical requirement of protecting animals by providing animal health products of the same high quality as products developed for people. In addressing antimicrobial resistance, we will take a One Health approach to cooperation, equally considering human and animal health, and environmental impact. To address AMR, we will strengthen partnerships between animal health companies, farmers, veterinarians, retailers, authorities and associations. We will reach out to seek new solutions and ideas and are open to explore joint actions with others.



Principle 2: Use antibiotics judiciously and responsibly.

Actions: We promote the use of antibiotics for therapeutic reasons. Under the adage "as little as possible, as much as necessary", we will continue to promote responsible/judicious use by providing clear labels and good technical advice. We recommend antibiotics be used under veterinary supervision where available. In countries that lack veterinary capabilities, imposing this requirement before addressing the shortage of veterinarians condemns animals to unnecessary suffering. We will increase our efforts to encourage investment in better access to veterinary care. We actively contribute to the promotion of responsible use principles and practices in national responsible use coalitions.



Principle 3: Promote disease prevention and increased access to products and expertise.

Actions: We promote animal husbandry techniques that contribute to disease prevention by sharing our knowledge with producers. We commit to continuing to improve availability of vaccination. We will seek maximum access and affordability of legitimate products to counter the use of illegal, low quality and fake products in some markets, and contribute to education and training on the dangers of their use. We will advocate for programs to increase the number of veterinarians in developing countries.



Principle 4: Invest in development of products for prevention and treatment.

Actions: We will invest in new products that reduce reliance on antibiotics. As animal health companies we will invest between 6%-9% of our annual turnover in the development of new products, diagnostics, genomics and life-cycle management of existing products. Global annual animal health sector revenues are estimated at US\$30 billion. Assuming companies not part of HealthforAnimals also invest a similar percentage, this equates to an annual investment of US\$1.8 - 2.7 billion for prevention and treatment options for food and companion animals. Investment at these levels for new solutions is commercially viable only if rising cost factors like regulatory cost are reduced. We encourage governments to: increase incentives for new technological advances, facilitate regulatory pathways for all types of products, encourage increased uptake of vaccination, and support availability and access to veterinarians.



Principle 5: Increase knowledge, transparency and communication.

Actions: We support science and evidence-based solutions. Many animal health companies undertake scientific research into AMR pathways, and we support other groups in their research. We will continue to contribute to the collection of national and international antibiotic use data. We will encourage producers and retailers to be transparent about animal health and welfare impacts resulting from antibiotic-free production practices. We will increase our communications efforts about responsible use, vaccination and other prevention methods, while continuing to provide data and advice to our customers on managing diseases.

This Commitment is managed by HealthforAnimals, the global animal medicines association, and our Members. Other organizations or companies are encouraged to join us in affirming these principles.

Contact info@HealthforAnimals.org to learn how to join the Commitment and become a signatory.

View full Commitment and 'Principles in Action' at www.HealthforAnimals.org/OurCommitment






Roadmap to reducing the need for antibiotics (HealthforAnimals, 2019)

- 2017: HealthforAnimals Antibiotics Commitment for 2025

An industry wide Commitment

- Supported by organizations representing 200+ animal health companies and 700,000 veterinarians
- Underpinned by **concrete actions**
 - Responsible use partnerships
 - New vaccine and diagnostic R&D
 - Research and monitoring
 - Veterinary support

www.HealthforAnimals.org/OurCommitment

 Principle 1:	Protect animal health and welfare in a unified One Health approach
 Principle 2:	Use antibiotics judiciously and responsibly
 Principle 3:	Promote disease prevention and increased access to products and expertise
 Principle 4:	Invest in development of products for prevention and treatment
 Principle 5:	Increase knowledge, transparency and communication

- 2019 Roadmap to reducing the need for antibiotics

- Reporting first results (summer 2019)

Roadmap to Reducing the Need for Antibiotics

Our Vision

Specifics on: Prevention, Detection, Treatment

Our Contribution

Actions (+metrics) we pledge to undertake by 2025

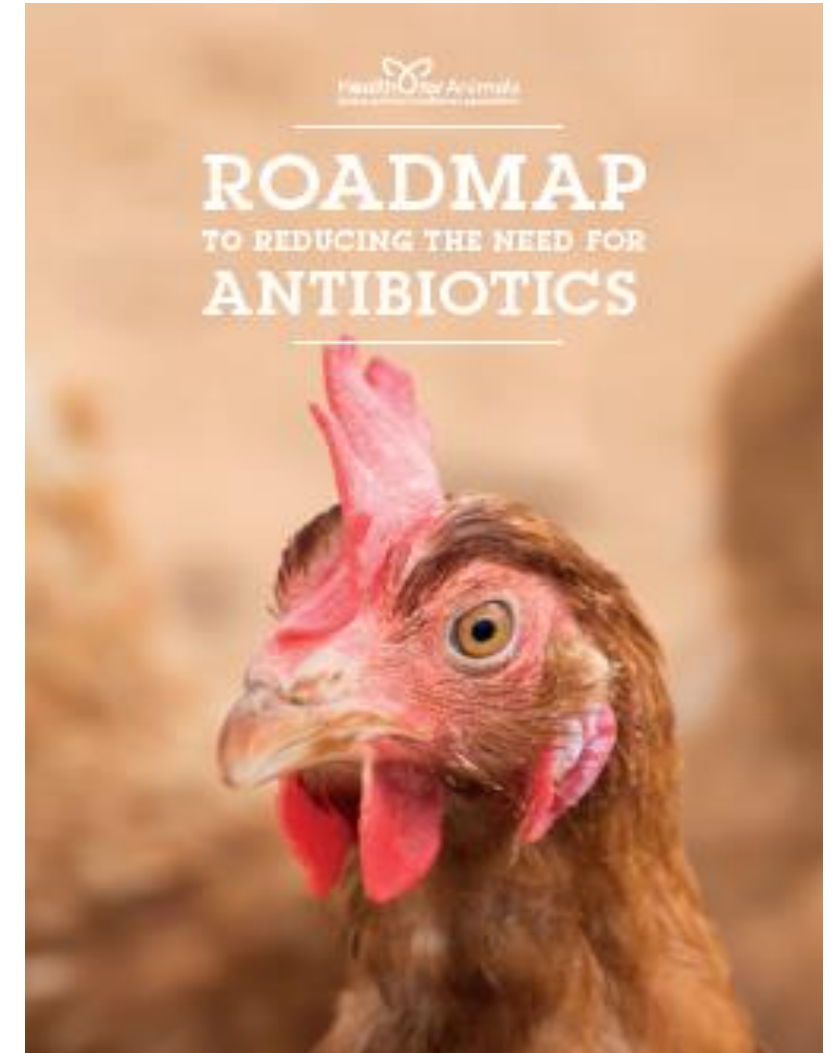
Our Actions

50 detailed actions we are taking to address AMR

Call to Action

Specific steps policymakers and IGOs can take

<https://healthforanimals.org/roadmap/activities.html>



- HealthforAnimals Members, representing more than 85 percent of the animal medicines industry, pledge to collaboratively undertake clear, measurable actions by 2025
 - To improve the three areas of our vision: prevention, detection and treatment
 - Actions are done and reported in six domains
 - ... Cooperations
 - ... Knowledge
 - ... One Health
 - ... Communication
 - ... Veterinary training & access to knowledge on responsible use
 - ... Research and development

Practical examples of action by industry (1)

- **Cooperation**

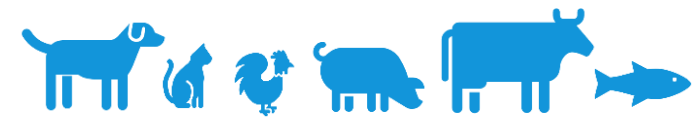
- We build partnerships and work across disciplines to reduce the need for medically important antibiotics. To do this, we will amongst others:
 - Participate in responsible use coalitions in major markets
 - 5 new partnerships that deliver products to help to reduce the need for antibiotics in underserved markets
 - Encourage medicine users to submit efficacy reports into pharmacovigilance monitoring systems

- **Knowledge**

- Addressing AMR requires greater knowledge and understanding. To support this, we will amongst others:
 - Provide research grants of at least \$1 million
 - Provide data and support to help improve disease tracking to organizations such as the World Organisation for Animal Health (OIE)

- **One Health**

- AMR affects animals, people and the planet, and can only be addressed through working across disciplines. To help achieve this, we will:
 - Deliver new tools that reduce the likelihood of human exposure to a resistant pathogen such as *Salmonella*, *Campylobacter*, or *E. coli*
 - Conduct an AMR risk analysis for every new antibiotic brought to market



Practical examples of action by industry (2)

- **Communications: we will amongst others...**
 - Participate in forums and public dialogues to help build understanding of risks, benefits, and actions that different stakeholders can take to improve public health outcomes in the fight against AMR
 - Issue Roadmap Updates in 2021 and 2023
- **Veterinary training & access to knowledge on responsible use: we will amongst others...**
 - Provide clear labels on every, single product
 - Make technical guidance available to all product users
 - Train more than 100,000 veterinarians in responsible use of medicines
 - Invest at least \$5 million in veterinary education scholarships and grants
- **Research & development: we will amongst others...**
 - Invest at least \$10 billion in research and development
 - Deliver at least 100 new vaccines
 - Deliver at least 20 new diagnostics tools
 - Deliver at least 20 new nutritional enhancement products
 - Deliver at least 30 other products that can reduce the need for an antimicrobial by reducing animal stress or boosting the natural immune system (ex. parasiticides, immunostimulants, anthelmintic, etc.)



And yes: a call to action...

- The animal medicines industry cannot reduce the need for antibiotics alone.
- Need the public sector and international organisations to (keep) join(ing) us in this effort to reduce the need for antibiotics by improving prevention, detection and treatment of animal disease.
- Supportive public policies can drastically change farmer access to new treatments, preventative tools and veterinary expertise, which will allow them to improve animal health and reduce the need for antibiotics.
- This will require decisive policy action across the following four areas

Regulation 	Consumer acceptance 
Funding for livestock 	Access to veterinary expertise 

More information:

www.healthforanimals.org
www.animalhealthmatters.org

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