



Antimicrobial stewardship and its role in sustainable poultry farming and egg production

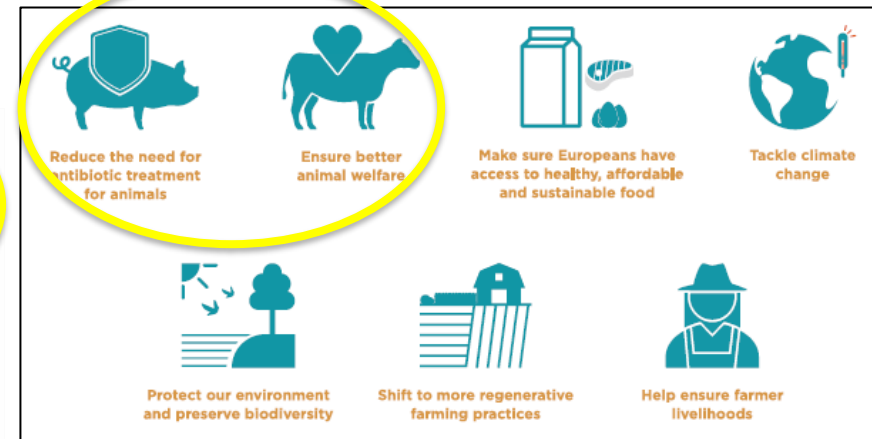
Marcon Tigges BSc, DVM, MBA

Topics

1. Why sustainability and antibiotic stewardship matter
2. Antibiotic classifications and the link to the future
3. The European example
4. The significance for SE Asia and the poultry industry

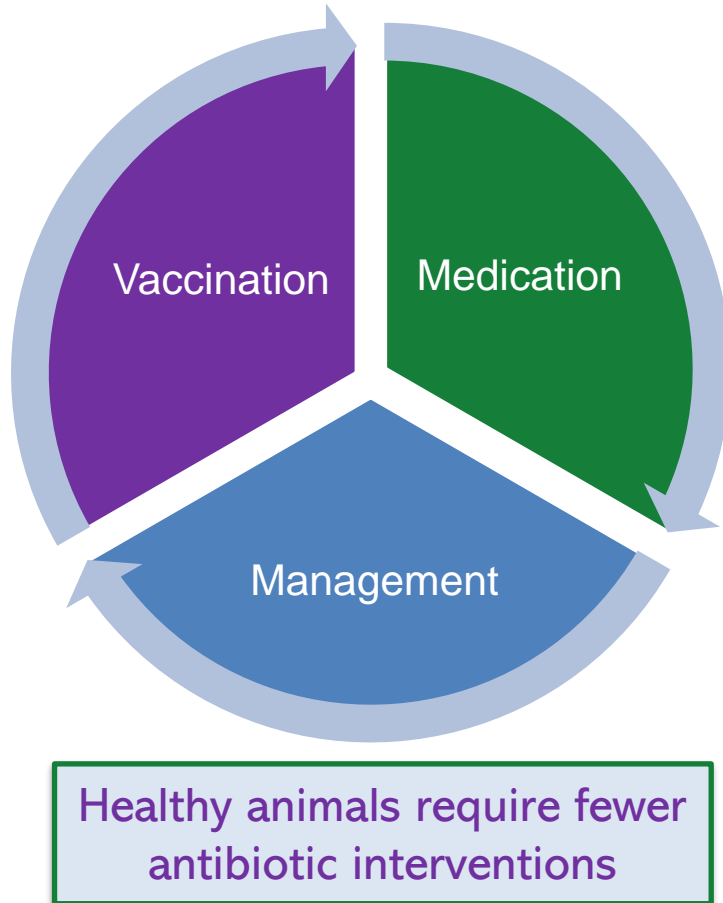
Sustainability and animal health

- The UN Sustainable Development Goals (SDGs) as a blueprint for a better and more sustainable future
- Better animal health contributes to at least 10 of these SDGs¹
- Reduce the need for antibiotics and ensure better animal welfare



1. Animal Health Europe. Healthy animals, healthier people and a healthier planet: the European animal health industry's sustainability focus

Better animal health requires a holistic approach



RESPONSIBLE USE OF MEDICINES IN AGRICULTURE ALLIANCE

ruma

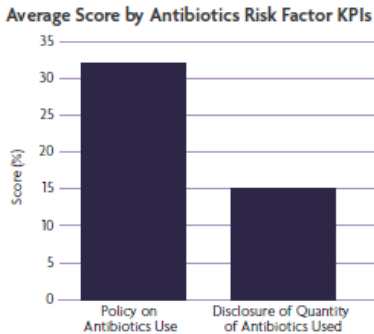
‘All medicines on farm should be used as little as possible and as much as necessary’



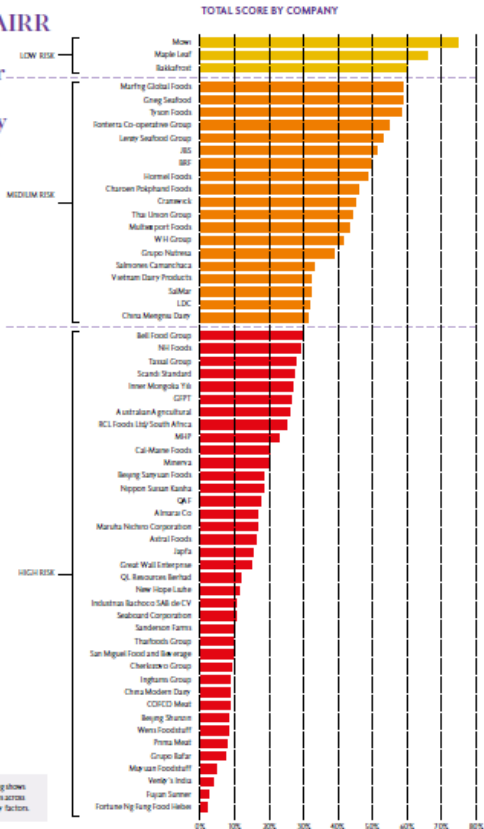
NGO, consumer and investor *awareness* of sustainability and AMR



COMPASSION
in world farming



Collier FAIRR
Protein
Producer
Index:
Company
Ranking



‘70% of Index companies, totalling \$243.8bn in market capital, and 89% of companies in Asia rank as HIGH RISK for Antibiotics.

Perception rather than science for the AMR component?



Growing demand for animal-sourced protein in Asia

- Global population predicted to grow by 1/3 (2015 to 2050) to reach 9.7 bn¹
- Growing demand for animal-sourced protein in low-income countries as incomes rises

Asia's growth is predicted to outperform the rest of the world's²

Predicted Growth (%) ²		
	Asia	World
2021	7.5	6.0
2022	6.4	4.9

- Food scares, health perceptions, welfare and sustainability leading to interest in plant-based or meat alternatives

Animal-based protein contribution to AMR

WHO '10 Threats to Global Health in 2019',
the start of the next 5-year strategic plan

1. Air pollution and climate change
2. Noncommunicable diseases
3. Global influenza pandemic
4. Fragile and vulnerable settings
- 5. Antimicrobial resistance**
6. Ebola and other high-threat pathogens
7. Weak primary health care
8. Vaccine hesitancy
9. Dengue
10. HIV

‘Drug resistance is driven by the overuse of antimicrobials in people, but also in animals, especially those used for food production, as well as in the environment. WHO is working with these sectors to implement a global action plan to tackle antimicrobial resistance by increasing awareness and knowledge, reducing infection, and encouraging prudent use of antimicrobials. ‘



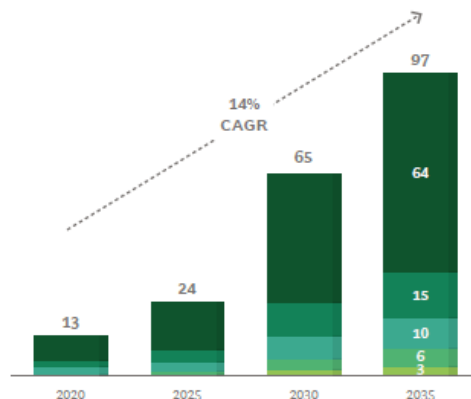
Opportunity for alternative proteins?

- 11-22% of global animal-based protein is “very likely” to be alternative by 2035²

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Asia-Pacific, the largest market for alternative proteins, will continue to grow the fastest

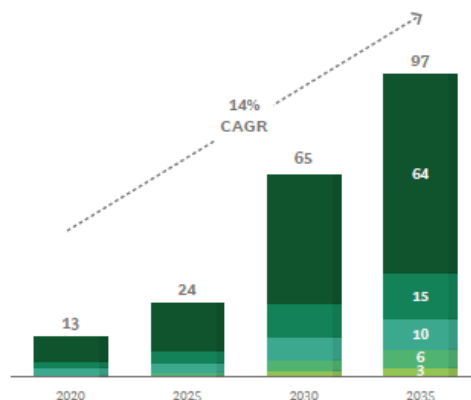


- Asia-Pacific
- Europe
- North America
- Latin America
- Rest of the World

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- Asia-Pacific
- Europe
- North America
- Latin America
- Rest of the World



The macroenvironment for sustainable livestock farming

- Protein demand will increase
- Healthy animals contribute to sustainability
- Pressure placed on livestock protein-sector from NGOs and consumers around sustainability, welfare, healthy diets, food safety, AMR
- There could be an increased interest in alternative over animal-based in the future
- Sustainable livestock protein production into the future will depend on meeting stakeholder demands

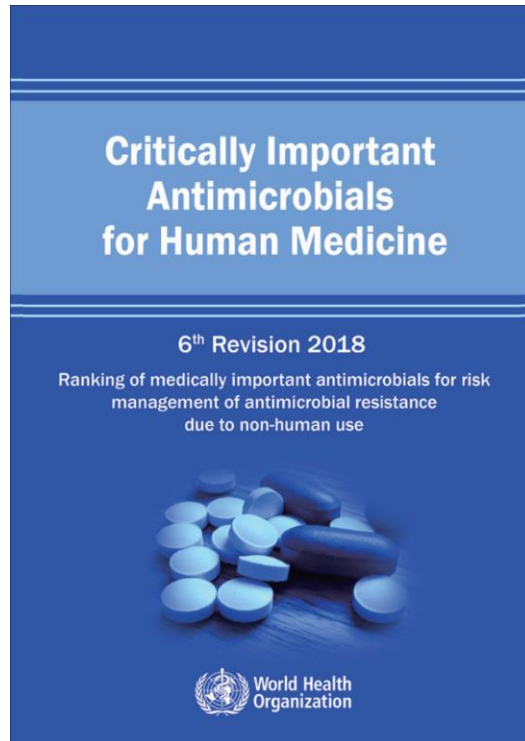
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- 2. Antibiotic classifications and the link to the future**
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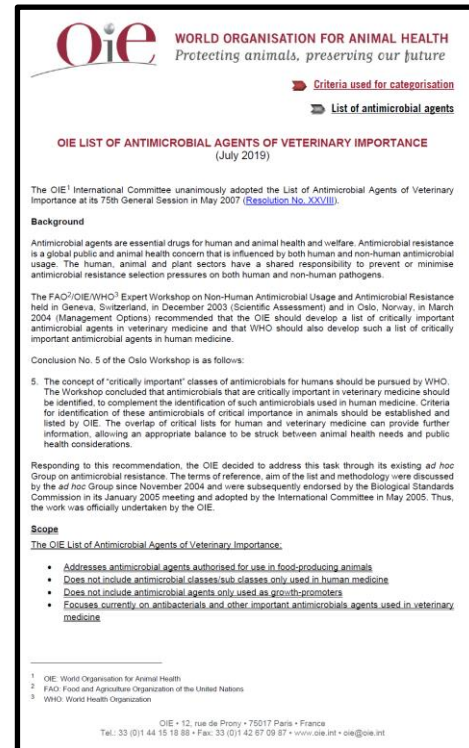
WHO, FAO and OIE – the antimicrobial stewardship ‘triumvirate’

WHO and OIE categorised antibiotics for human and vet medicine, respectively

World Health Organisation
(WHO) 6th Revision 2018



World Organisation for
Animal Health (OIE)
July 2019



WHO classification in CIA, Highly Important & Important

Antimicrobial classes used in human medicine categorized based on 2 criteria

C1: The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people

C2: The antimicrobial class is used to treat infections in people caused by either (1) bacteria that may be transmitted to humans from non-human sources, or (2) bacteria that may acquire resistance genes from non-human sources

Critically Important

Both C1 & C2 met

Highly Important

C1 or C2 met

Important

Neither C1 nor C2 met

WHO classification in CIA, Highly Important & Important

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Highly Important

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Neither C1 nor C2 met

Highest Priority CIAs

All P factors met

High Priority CIAs

Not all P factors met

CIAs further prioritized according to 3 factors

P1: Used to treat a large number of people with infections for which limited antimicrobials are available

P2: Used with high frequency in human medicine or in certain high-risk groups

P3: Used to treat human infections for which an extensive evidence exists on the transmission of resistant-bacteria or genes from non-human sources

World Organisation for Animal Health (OIE) List of Antimicrobial Agents of Veterinary Importance (2019)

3 Categories based on 2 Criterion

C1: Response rate to the questionnaire regarding Veterinary Important Antimicrobial Agents. Met when a majority of the respondents (more than 50%) identified the importance of the antimicrobial class in their response to the questionnaire.

C2: Treatment of serious animal disease and availability of alternative antimicrobial agents. Met when compounds within the class were identified as essential against specific infections and there was a lack of sufficient therapeutic alternatives.

Vet Critically Important (VCIA)

Both C1 & C2 met

Vet Highly Important (VHIA)

C1 or C2 met

Vet Important (VIA)

Neither C1 nor C2 met

OIE Recommendations*

Fluoroquinolones, 3rd & 4th generation Cephalosporins and Colistin:

1. Not to be used orally as preventive treatment in the absence of clinical signs in the animal(s) to be treated
 2. Not to be used as a first line treatment unless justified; when used as a second line treatment, it should ideally be based on the results of bacteriological tests
 3. Extra-label/off label use should be limited and reserved for instances where no alternatives are available. Such use should be in agreement with the national legislation in force
 4. Urgently prohibit their use as growth promoters
- The classes in the WHO category of Highest Priority Critically Important Antimicrobials should be the highest priorities for countries in phasing out use of antimicrobial agents as growth promoters

WHO and OIE lists comparison

WHO classification (6th revision, 2018)

Critically Important (CIA)
Highest Priority
Cephalosporins (3rd, 4th & 5th gen)
Glycopeptides
Macrolides & Ketolides
Polymyxins
Quinolones
High Priority
Aminoglycosides
Ansamycins
Carbapenems & other penems
Glycylcyclines
Lipopeptides
Monobactams
Oxazolidinones
Certain Penicillins
Phosphonic acid derivatives
Drugs for TB, mycobacterial dis

Highly Important
Amphenicols
Cephalosporins (1st & 2nd gen)
Lincosamides
Certain Penicillins Pseudomonic acids
Riminofenazines
Steroid antibacterials
Streptogramins
Sulfonamides, combos, etc
Sulfones
Tetracyclines

Important
Aminocyclitols
Cyclic polypeptides
Nitrofurans derivatives
Nitroimidazoles
Pleuromutilins

OIE List of Antimicrobial Agents of Veterinary Importance (2019)

Vet Critically Important
Aminoglycosides
Amphenicols
Cephalosporins (3rd & 4th Gen)
Macrolides
Penicillins
Quinolones (2nd gen - FQs), Sulfonamides & Diaminopyrimidines
Tetracyclines

Vet Highly Important
Ansamycin - Rifamycins
Cephalosporins (1st & 2nd Gen)
Ionophores
Lincosamides
Phosphonic Acid Derivatives
Pleuromutilins
Polypeptides & Polymyxins
Quinolones (1st Gen)

Vet Important
Aminocoumarin
Arsenical
Bicyclomycin
Fusidane
Orthosomomycins
Quinoxalines
Streptogramins
Thiostrepton



WHO and OIE lists comparison

WHO classification (6th revision, 2018)

Critically Important (CIA) Highest Priority
Cephalosporins (3rd, 4th & 5th gen) Glycopeptides Macrolides & Ketolides Polymyxins Quinolones
High Priority
Aminoglycosides Ansamycins Carbapenems & other penems Glycylcyclines Lipopeptides Monobactams Oxazolidinones Certain Penicillins Phosphonic acid derivatives Drugs for TB, mycobacterial dis
Highly Important
Amphenicols Cephalosporins (1st & 2nd gen) Lincosamides Certain Penicillins Pseudomonic acids Riminofenazines Steroid antibacterials Streptogramins Sulfonamides, combos, etc Sulfones Tetracyclines
Important
Aminocyclitols Cyclic polypeptides Nitrofurans derivatives Nitroimidazoles Pleuromutilins

OIE List of Antimicrobial Agents of Veterinary Importance (2019)

Vet Critically Important
Aminoglycosides Amphenicols Cephalosporins (3rd & 4th Gen) Macrolides Penicillins Quinolones (2nd gen - FQs), Sulfonamides & Diaminopyrimidines Tetracyclines
Vet Highly Important
Ansamycin - Rifamycins Cephalosporins (1st & 2nd Gen) Ionophores Lincosamides Phosphonic Acid Derivatives Pleuromutilins Polypeptides & Polymyxins Quinolones (1st Gen)
Vet Important
Aminocoumarin Arsenical Bicyclomycin Fusidane Orthosomomycins Quinoxalines Streptogramins Thiostrepton

WHO & OIE lists should form the basis for national and regional planning

National Action Plans (NAPs) and local lists should reflect the market situation



Some factors that can influence local antimicrobial use (AMU) guidelines

Definitions and categorisation of antibiotics e.g. CIAs

Antibiotic Growth Promotion (AGP) use allowed?

Vet prescription needed?

Animals/products are exported to Europe, what does this mean?

Are antibiotics allowed for disease prevention?

Buyer/retailer with restrictions on antibiotic use?

Requirement to reduce use of antibiotics



Topics

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The EU example

- European Commission (EC) requested of the EMA answers on:

- the impact of the use of antibiotics in animals on public and animal health
- measures to manage the possible risk to humans

- Report prepared by the Antimicrobial Advice ad hoc Expert Group (AMEG)

Categorisation of antibiotic classes for veterinary use (with examples of substances authorised for human or veterinary use in the EU)				
A	Amidoglycosides neomycin framycetin	Carbapenems meropenem durlobactam	Drugs used solely to treat tuberculosis or other mycobacterial diseases isoniazid ethambutol pyrazinamide ethionamide	Glycopeptides vancomycin
	Ketoles salicylic acid	Lipopeptides dalacin		Glycylcyclines tigecycline
	Monobactams aztreonam	Oxazolidinones linezolid		Phosphonic acid derivatives fosfomicin
	Rifamycins (except rifaximin) rifampicin	Streptogramins dalfuprime dalacin	Other cephalosporins and penicillins (ATC code J01C), including combinations of 3rd generation cephalosporins with beta-lactamase inhibitors ceftriaxone cefepime cefazolin cefuroxime cefepime cefepime	Pseudomonic acids mupirocin
B	Carbapenems and oxazolidinones, including combinations with beta-lactamase inhibitors meropenem dalacin	Streptogramins dalfuprime dalacin		Substances newly authorised in human medicines following notification of the AMEG categorisation to be determined
	Cephalosporins, 3rd- and 4th-generation, with the exception of combinations with beta-lactamase inhibitors cefuroxime cefepime cefazolin cefuroxime cefepime	Polymyxins colistin polymyxin B	Quinolones: fluoroquinolones and other quinolones ciprofloxacin levofloxacin moxifloxacin gatifloxacin flumequine difloxacin	RESTRICT
	Amidoglycosides (except spectinomycin) amikacin gentamicin paromomycin netilmicin streptomycin spectinomycin tobramycin	Amidoglycosides, in combination with beta-lactamase inhibitors amikacin + clavulanic acid amikacin + sulbactam	Amphotericins chitosan chitosan chitosan	Macrolides erythromycin clarithromycin azithromycin midecamycin telithromycin telithromycin telithromycin
	Amidoglycosides, without beta-lactamase inhibitors amikacin gentamicin paromomycin netilmicin streptomycin spectinomycin tobramycin	Amidoglycosides, 3rd- and 4th-generation, and cephalosporins amikacin gentamicin paromomycin netilmicin streptomycin spectinomycin tobramycin	Lincosamides clindamycin lincosamine lincosamine	Fluorethyls lanolin vitamin
C	Amidoglycosides, without beta-lactamase inhibitors amikacin gentamicin paromomycin netilmicin streptomycin spectinomycin tobramycin	Amidoglycosides, 3rd- and 4th-generation, and cephalosporins amikacin gentamicin paromomycin netilmicin streptomycin spectinomycin tobramycin	Fluorethyls lanolin vitamin	Fluorethyls lanolin vitamin
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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

4 February 2019
EMA/CVMP/CHMP/VS/2195/2017
Committee for Medicinal Products for Veterinary Use (CVMP)
Committee for Medicinal Products for Human Use (CHMP)

5 Answer to the request from the European Commission for
6 updating the scientific advice on the impact on public
7 health and animal health of the use of antibiotics in
8 animals - Categorisation of antimicrobials
9 Draft

Agreed by the Antimicrobial Advice ad hoc Expert Group (AMEG)	29 October 2018
Adopted by the CVMP for release for consultation	24 January 2019
Adopted by the CHMP for release for consultation	31 January 2019
Start of public consultation	5 February 2019
End of consultation (deadline for comments)	30 April 2019

10 Comments should be provided using this [template](#). The completed comments form should be sent to
11 vet-guidelines@ema.europa.eu

12 Keywords antimicrobials, antimicrobial resistance, categorisation

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2nd EMA/AMEG report

Category A 'Avoid'

- Not authorised as medicines in the EU
- Don't use for livestock
- Only in exceptional circumstances may be used in companion animals

Category B 'Restrict'

- Critically important in human medicine
 - Only consider if no antibiotic in Categories C or D may be effective and only with antimicrobial susceptibility testing if possible
- 3rd/4th generation cephalosporins, FQs & polymixins (colistin)**

Category C 'Caution'

- In this group, there are alternatives in human medicine
- For some vet indications, there are no alternatives in Category D
- Should be considered only when there are no alternatives in Category D that could be clinically effective

Aminoglycosides, some Aminopenicillins, Amphenicols, Cephalosporins (1st&2nd gen) and cephameycins, Lincosamides, Macrolides, Pleuromutilins, Rifamycins (rifaximin only)

Category D 'Prudence'

- Should be used 1st-line whenever possible
 - Use prudently only when medically needed
- Aminoglycosides (spectinomycin only), some Aminopenicillins, Cyclic polypeptides, Nitrofurantoin derivatives, Nitroimidazoles, Penicillins (some), Steroid antibacterials, Sulfonamides, dihydrofolate reductase inhibitors and combinations, Tetracyclines**

Comparison of the reports

	WHO 6 th Report (2018)	OIE (2019)	EMA/AMEG 2 nd Report (2019)
Antibiotics included	All used in humans	All used in food producing animals	All WHO antibiotics
Categories	Critically Important Highly Important Important	Vet Critically Important Vet Highly Important Vet Important	A: Avoid B: Restrict C: Caution D: Prudence
Macrolide Categorisation	Critically Important	Vet Critically Important	Category C ('Caution')
Pleuromutilins	Important	Vet Highly Important	Category C ('Caution')
Commentary around macrolides	Important in treatment of Campylobacter (which can also develop resistance)	The wide range of applications and the nature of the diseases treated make macrolides extremely important for vet medicine. Macrolides are used to treat Mycoplasma infections in pigs & poultry, haemorrhagic digestive disease in pigs (<i>L. intracellularis</i>) and liver abscesses (<i>F. necrophorum</i>) in cattle, where they have very few alternatives. This class is also used for respiratory infections in cattle.	Important for treatment of mycoplasma infections in pigs and poultry . Newer macrolides are among few alternatives for treatment of respiratory tract infections caused by bacteria that are resistant to alternatives in Category D. Some alternatives are Category B.

EU farming strategy and sustainability

- 'Farm to Fork Strategy' adopted 2020
- Will help to enable EU sustainable food systems
- Includes an objective to reduce total EU sales of antimicrobials in livestock (and aquaculture) by 50% by 2030¹



2006:

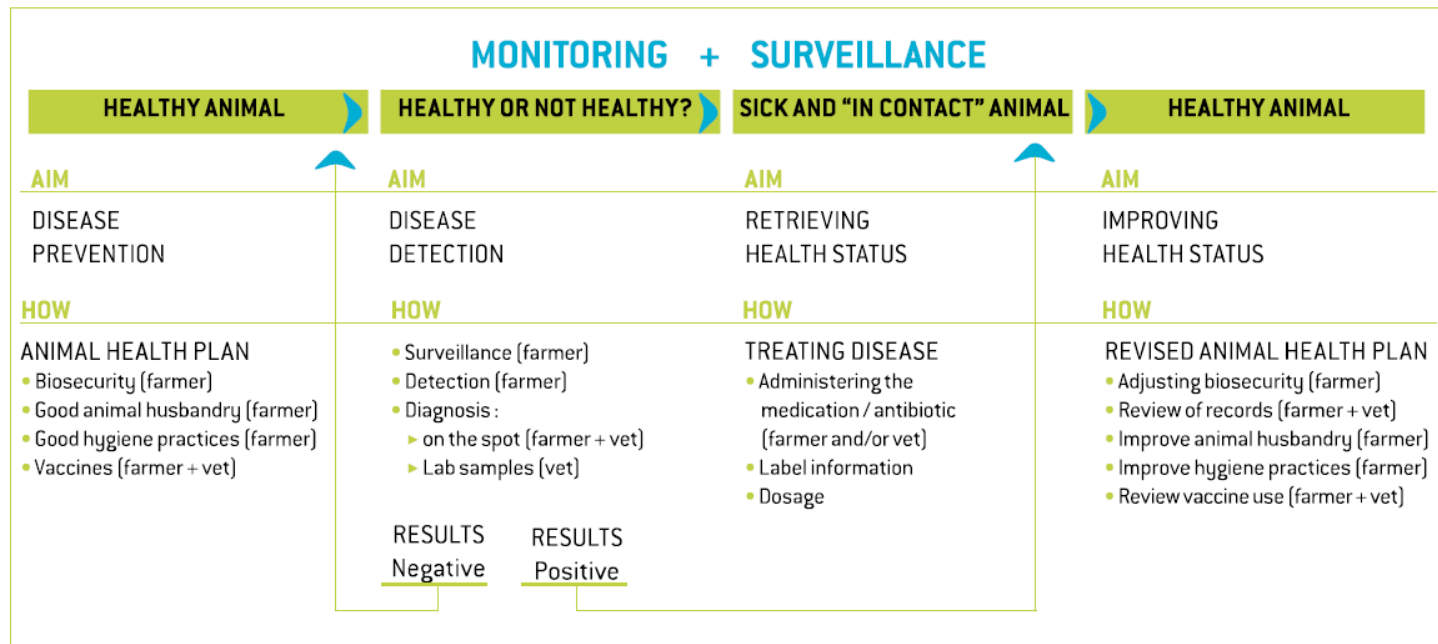
- Antibiotic use for growth promotion banned in Europe

2022 (January):

- Ban on prophylactic use of antibiotics in livestock¹
- Updated EU Regulations on Veterinary Medicinal Products (VMPs)

Improving health to reduce antimicrobial use

- Link between Antimicrobial Use (AMU) and Antimicrobial Resistance (AMR)
- Ensuring health of animals through management and vaccines can reduce the need for antibiotics¹



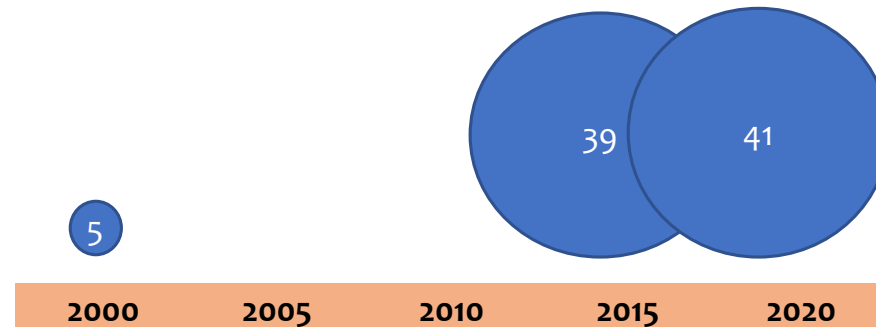
Livestock antimicrobials surveillance programmes

- Surveillance networks for AMU* and AMR* created over past 20 years, but mainly in high income countries¹

Country	Start	Name	Data Type
Denmark	1996	DANMAP	Sales
Japan	2000*	JVARM	
Canada	2008	CIPARS	Sales
EU	2011	ESVAC	Sales

*1st year of data collection, not when report was 1st published; 1st country in Asia to start reporting

Number of countries reporting antimicrobial sales



***AMU**: Antimicrobial Use ***AMR**: Antimicrobial Resistance

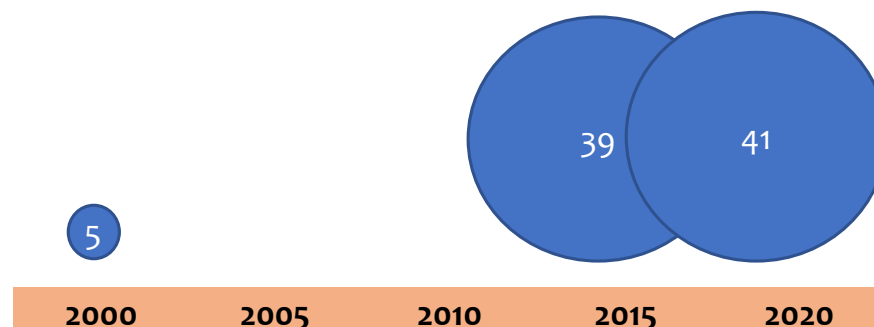
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Number of countries reporting antimicrobial sales



- AMU data can assist policy makers in regulating livestock product imports from different countries & also to restrict imports from countries using antibiotic classes or quantities different from their own¹

***AMU**: Antimicrobial Use ***AMR**: Antimicrobial Resistance

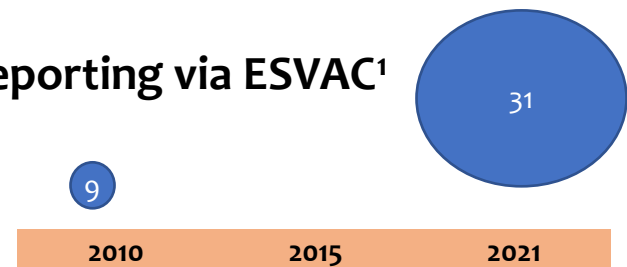
EU ESVAC and AMU information

- EC requested a harmonised approach for collection and reporting of AMU data in animals
- EMA developed ESVAC:
 - collects information on how antimicrobial medicines are used in animals across the EU, helping to identify possible risk factors leading to the development and spread of AMR in animals

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Number of EU countries reporting via ESVAC¹



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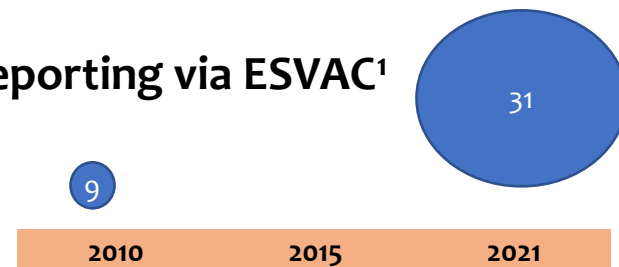


Figure 1 - Antibiotic reduction in The Netherlands.

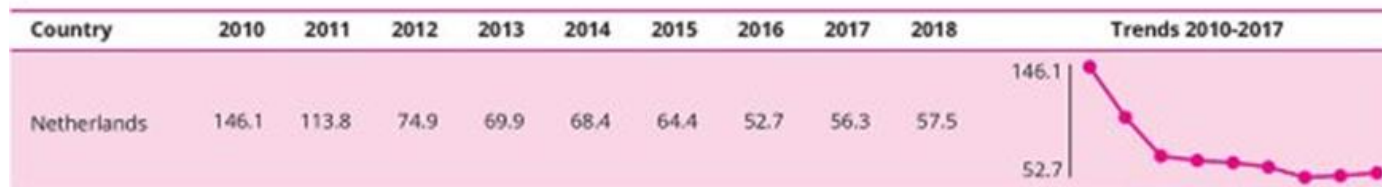
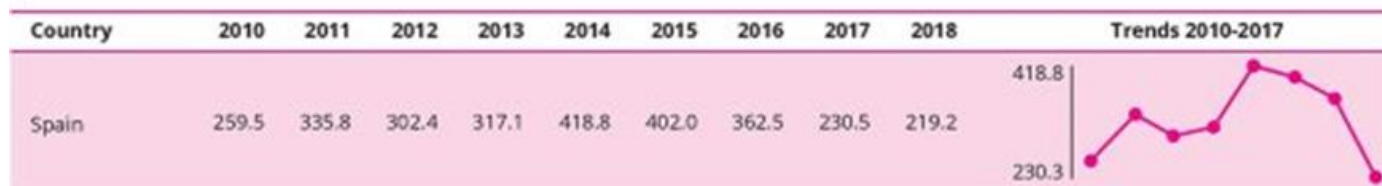
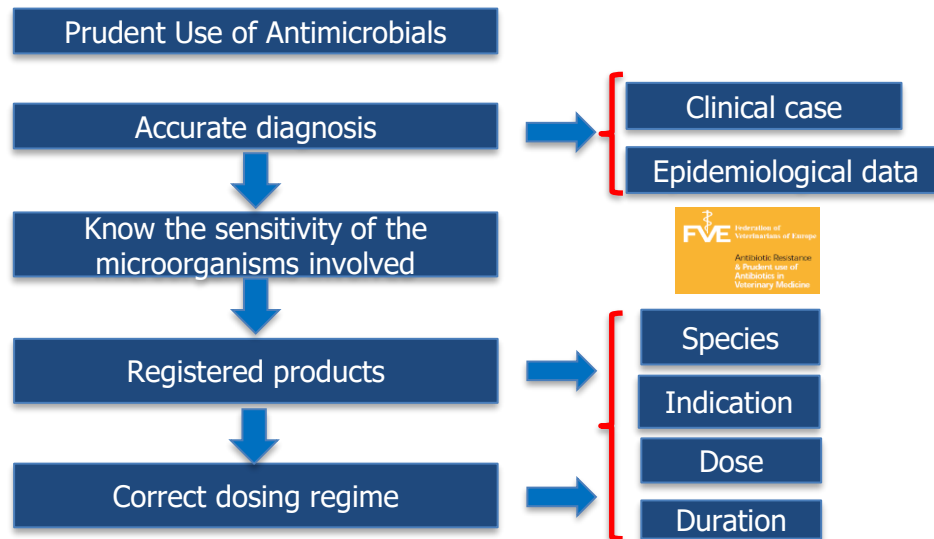


Figure 2 - Antibiotic reduction in Spain.



The Spanish example – prudent use of antimicrobials¹

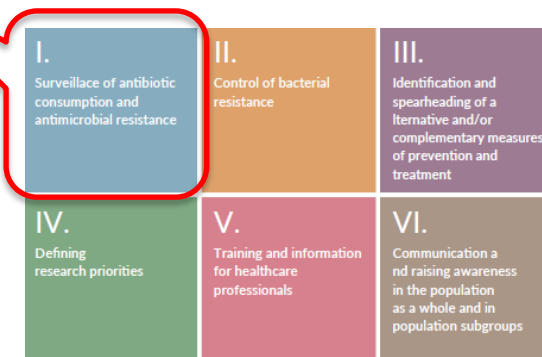
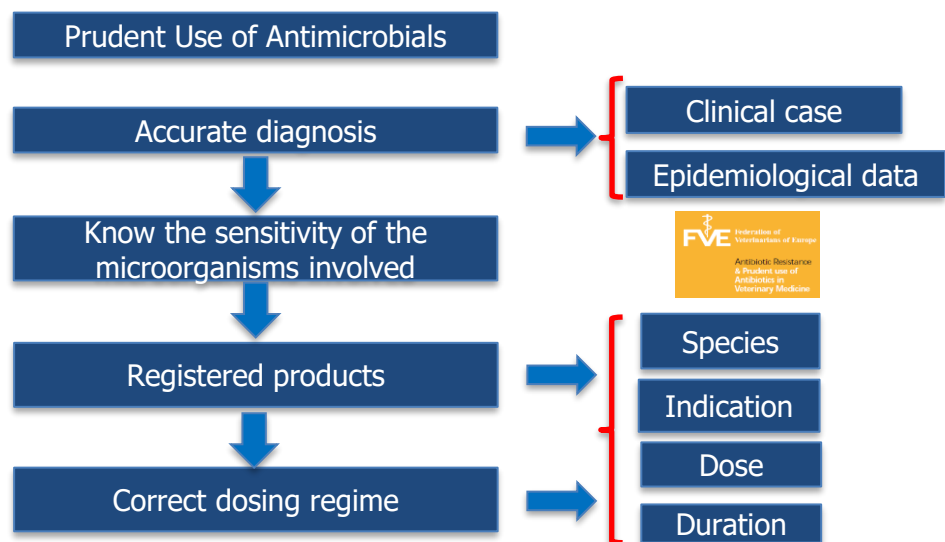
- Principles for prudent use is a guide for optimal use of antimicrobials.



The Spanish example – prudent use of antimicrobials¹

- Principles for prudent use is a guide for optimal use of antimicrobials.
- Six-part Strategic Action Plan to reduce risk of selection and dissemination of AMR

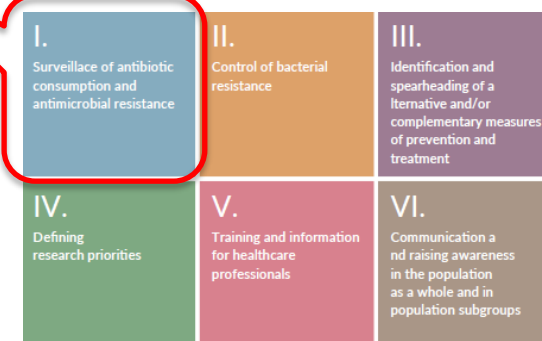
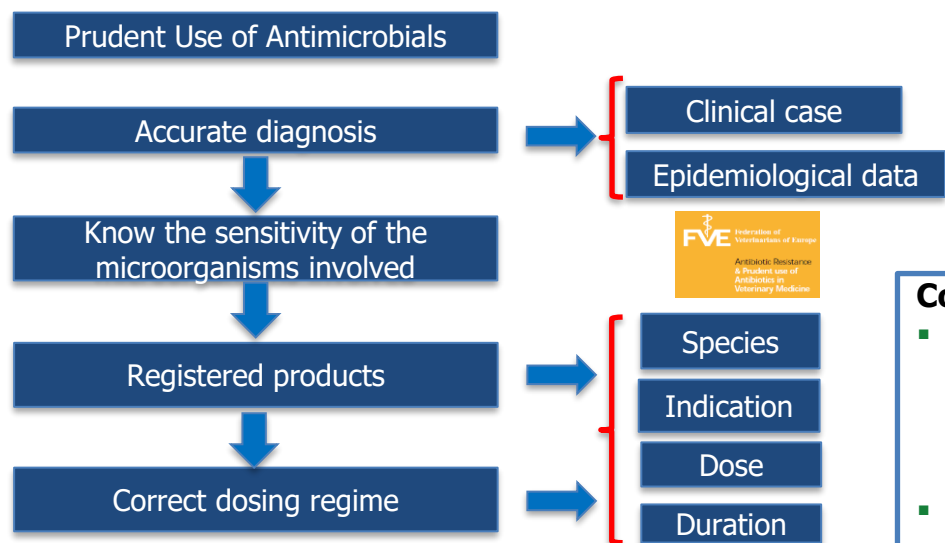
Part 1: Surveillance of antibiotic consumption and AMR



The Spanish example – prudent use of antimicrobials¹

- Principles for prudent use is a guide for optimal use of antimicrobials.
- Six-part Strategic Action Plan to reduce risk of selection and dissemination of AMR

Part 1: Surveillance of antibiotic consumption and AMR



Conclusions:

- The antimicrobial sensitivity of clinical pathogens needs to be monitored:
 - Isolating and diagnosis
 - Determination of antimicrobial susceptibility (pharmacodynamics)
- Prudent use of antimicrobials is possible under field conditions.
- We need to explain and accept the epidemiological criteria when selecting antimicrobials in livestock. It must be known and accepted by:
 - National authorities
 - Veterinarians

Topics

1. Why sustainability and AMR matter
2. Antibiotic classifications and the link to the future
3. The European example
- 4. The significance for SE Asia and the poultry industry**

SE Asia is also responding

- Transition by some producers to cage-free eggs in Thailand, Malaysia and Vietnam
- Tesco UK planning for 100% cage-free egg production by 2025 and in Thailand's Tesco Lotus by 2028 – have already begun



'Consumers' concern regarding animal welfare is increasing'
July '21 Vietnam

Thailand's National Strategic Plan on AMR 2017-2021: Goals - By the year 2021:

1. 50% reduction in AMR morbidity
2. 20% reduction in antimicrobial consumption in humans
3. **30% reduction in antimicrobial consumption in animals**
4. 20% increase of public knowledge on AMR and awareness of appropriate use of antimicrobials
5. Capacity of the national AMR management system is improved to level 4

Thailand's National Strategic Plan
on Antimicrobial Resistance
2017-2021



Delivery by 5 Strategies

1. AMR surveillance system using One Health approach

2. Regulation of antimicrobial distribution

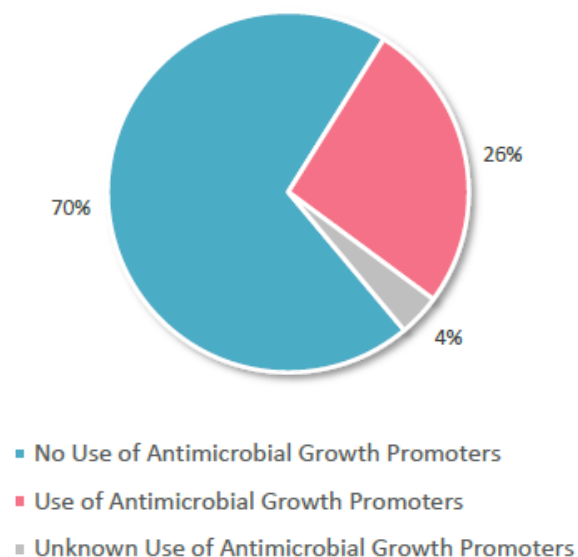
3. Infection prevention and control and antimicrobial stewardship in humans

4. AMR prevention and control and antimicrobial stewardship in agriculture and animals

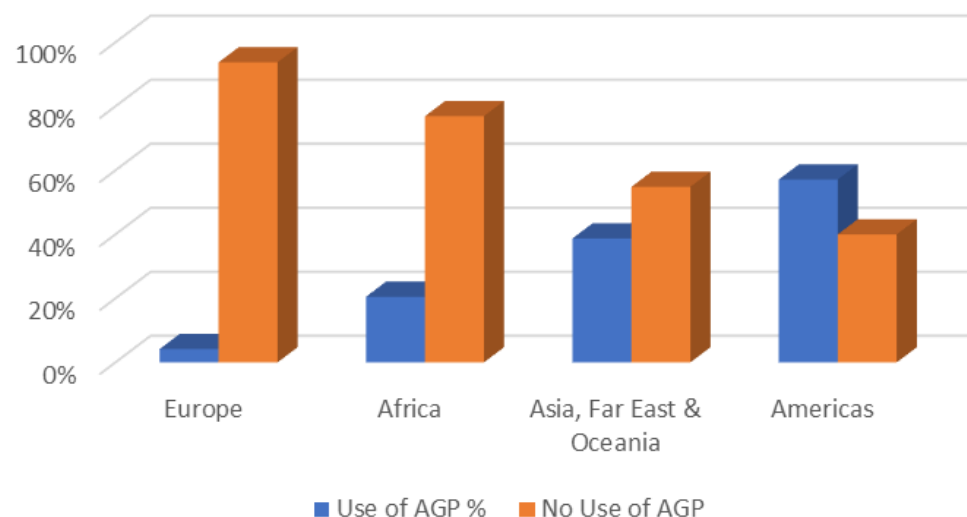
5. Public knowledge on AMR and awareness of appropriate use of antimicrobials

SE Asia is responding rapidly to consumer demand

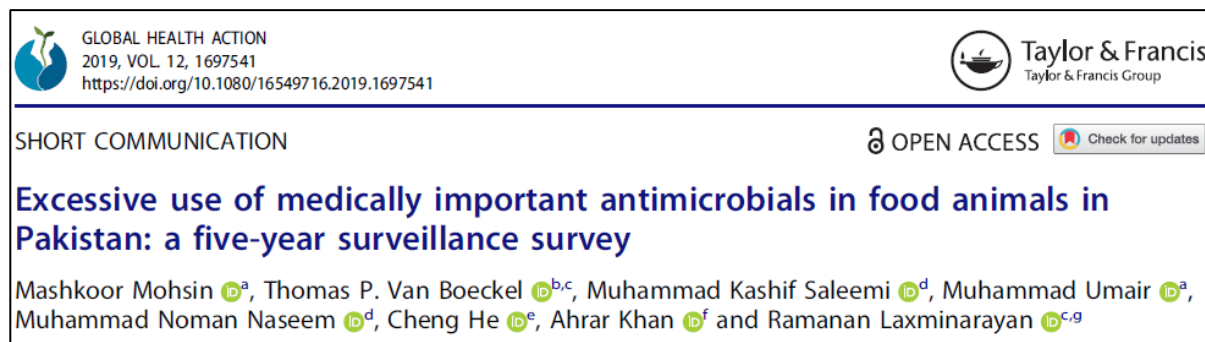
Use of AGPs in 160 Countries in 2019¹



Use of Antibiotic Growth Promoters (2019)¹



Pakistan could reduce AMU and should phase out CIAs¹



Monitored AMU in 30 flocks from a commercial broiler farm in Punjab between 2013 and 2017 then extrapolated to the national flock

- 'expansion of large commercial (broiler chicken) farms where antimicrobials are used as surrogates for hygiene (and) good nutrition'
- Consumption estimated at 250.84 mg API/kg final flock weight – 2nd highest use after China
- Most frequently used were colistin, tylocin, doxycycline and enrofloxacin
- 'Our findings call for immediate actions to reduce AMU in Pakistan and countries with comparable farming practices' and to phase out use of CIAs

Challenges and a National Strategy in Bangladesh¹



- Growth of commercial chicken and aquaculture industries to meet protein requirements
- Increased use and misuse of antibiotics in livestock sectors
- Not all farmers aware of the negative impact of ‘excessive, irrational, and prophylaxis use of antibiotics in animals’
- ‘... inadequate vet facilities, insufficient monitoring ... of AMU, high occurrence of disease and poor practices by unqualified veterinary healthcare providers (quack, drug sellers, and animal feed dealers)

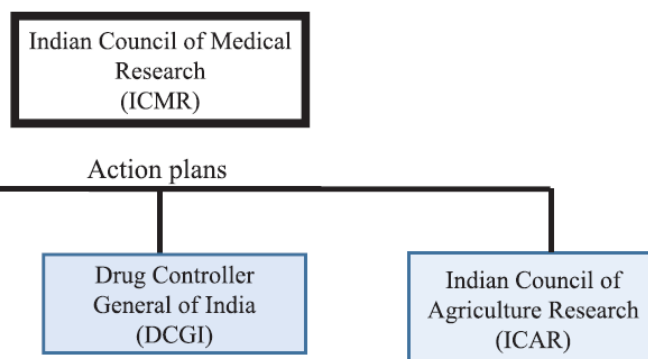
Challenges and a National Strategy in Bangladesh¹

National Strategy for AMR Containment 2017–2021 Objectives:

1. establish a multi–sectoral One Health approach to plan, coordinate, and implement ARC containment activities
2. ensure rational use of antimicrobial agents in humans and animals
3. strengthen infection prevention and control measures
4. strengthen bio-safety and bio-security practices
5. strengthen the surveillance system for AMR and promote operational research
6. strengthen regulatory provisions
7. establish advocacy, communication, and social mobilization

Increased AMU and Action Plans in India

- AMU in livestock expected to double by 2030 (and to triple in poultry), making regulation vital¹
- One Health initiative for regulation of AMU to be launched¹
- National livestock vaccination programme to improve health
- Colistin banned for use in livestock² in 2019



Action Plans include:3

- Ban premix feed
- Proper labelling of medicine containers
- Fix MRLs
- Ban use of loose powder premixes
- Education and awareness

- Guidelines on prophylactic, metaphylactic or therapeutic uses of antimicrobials
- Ban of premix feed
- To improve awareness and educate farmers, veterinarians, and consumers
- Proper labelling of medicine containers for treatment
- Fix the maximum residue limits for antibiotic residue

- Ban the use of loose powder of antibiotics
- Ban of premix feed
- Proper labelling of medicine containers for treatment
- to ensure compliance for drugs exclusively for human use

- To improve awareness and educate farmers, veterinarians and consumers
- Fix the maximum residue limits for antibiotic residue

In conclusion

- Livestock protein production and consumption will continue to grow in South-East Asia
- Alignment with local and global consumers and international bodies for continually improving antimicrobial stewardship platforms
- Harnessing the increasing demand for protein and ensuring that egg and poultry protein remains at the forefront, meeting evolving demands





Thank you

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