# Non-therapeutic antibiotic use and use of critically important antimicrobials in food-animals

**National Workshop on Development and Implementation of State Action Plan on Antimicrobial Resistance**

**June 10-11, 2019**

**Thiruvananthapuram, Kerala**

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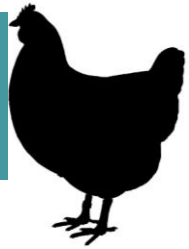
# Key points emerging out of deliberations on day 1

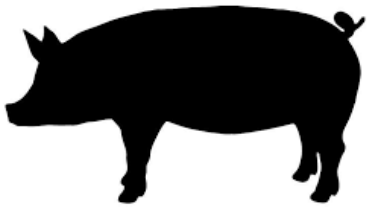
- Non-therapeutic antibiotic use in food-animals , i.e., routine use of antibiotics without veterinary supervision, needs to be addressed collectively
- Use of all HPCIAs in food animals should be done away with, not just colistin. May expand to other CIAs in long term
- With use of better alternatives such as vaccines, prebiotics, probiotics, better farm and waste management practices, better biosecurity, sanitation and hygiene- a lot of the antibiotic use at farm level can be brought down

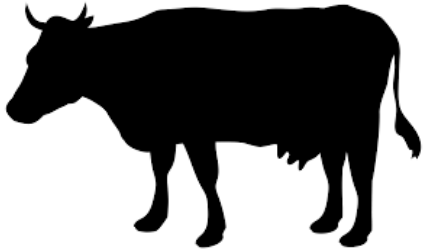
# Food from animals contribute about 40% of protein and 18% of calorie intake worldwide

**Major food producing animals:**

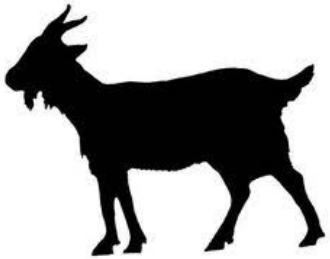
**Highest contributor**

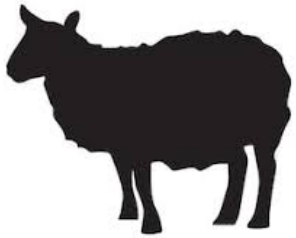


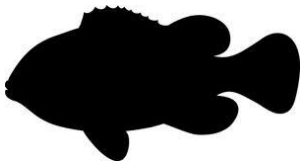




| | | | |
|---|---|---|---|
| **Animal/Bird** | **Chicken** | **Pig** | **Cattle and Buffalo** |
| **Food Produce** | **Meat (Poultry), Egg** | **Meat (Pork)** | **Meat (Cattle-Beef), milk** |







| | | | |
|---|---|---|---|
| **Animal** | **Goat** | **Sheep** | **Fish** |
| **Food Produce** | **Meat, milk** | **Meat, milk** | **Meat** |

# India is a leading producer of food from animals in the world

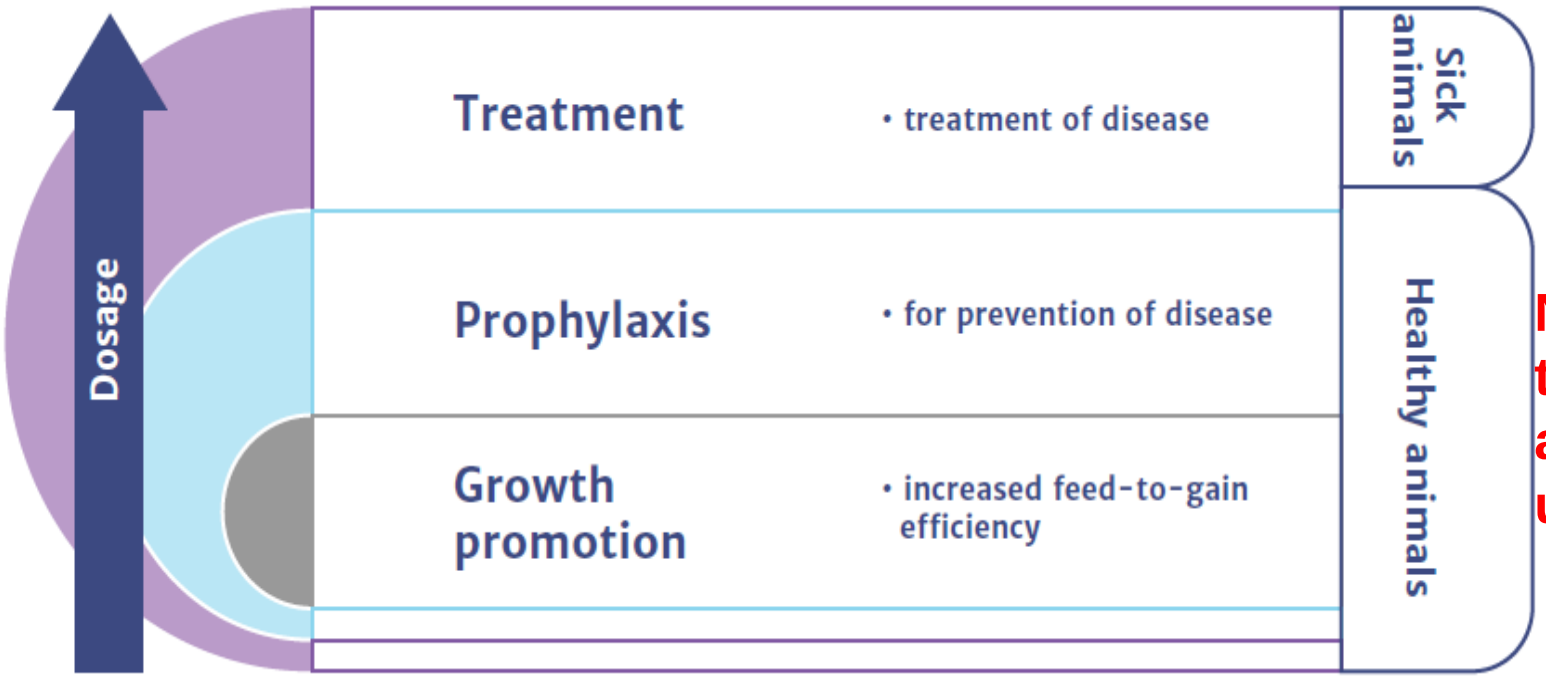
| Meat | Egg | Milk | Fish |
|---|---|---|---|
| China | China | India | China |
| European Union | United States | European Union | India |
| United States | India | United States | Indonesia |
| Brazil | Mexico | Pakistan | Vietnam |
| Russian Fed | Brazil | Brazil | Egypt |
| India | Japan | Russian Fed | European Union |

*2017-18*

**States producing high quantity of food from animals in India (examples)**

- Andhra Pradesh
- Tamil Nadu
- Uttar Pradesh
- Haryana
- West Bengal
- Rajasthan
- Maharashtra

# Antibiotic use in animals>> humans; Non-therapeutic use a big contributor



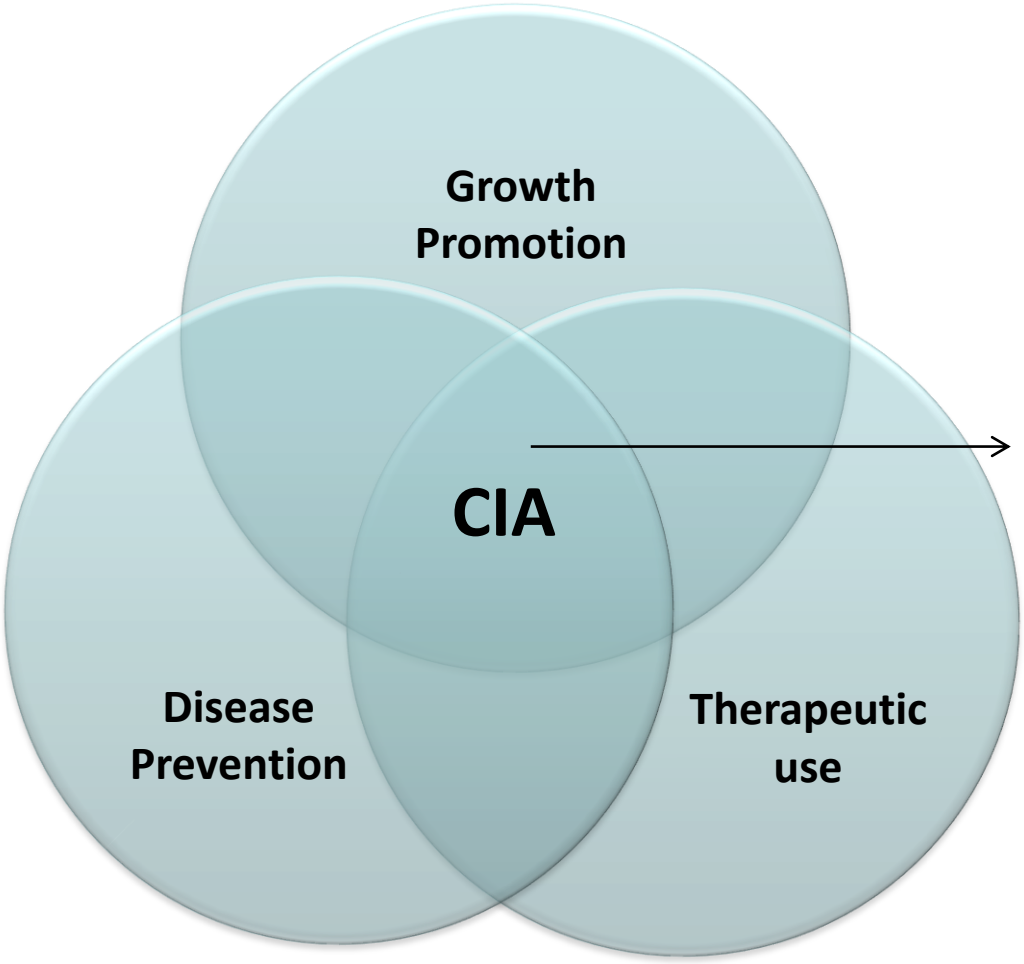

**Non-therapeutic antibiotic use**

# All non-therapeutic use needs to be addressed collectively …

- Routine/intermittent use
- Low/sub-therapeutic dose which can fuel greater resistance
- Mass administration to those with no signs of disease
- Largely through feed and water

- **Antibiotics in feed play a dual role (growth promoter and disease prevention)**
- **No fine line – segregating where one role stops and other begins**
- **Only collective action on both would solve the purpose**
- **Learnings from Denmark and others also suggest collective action will work best**

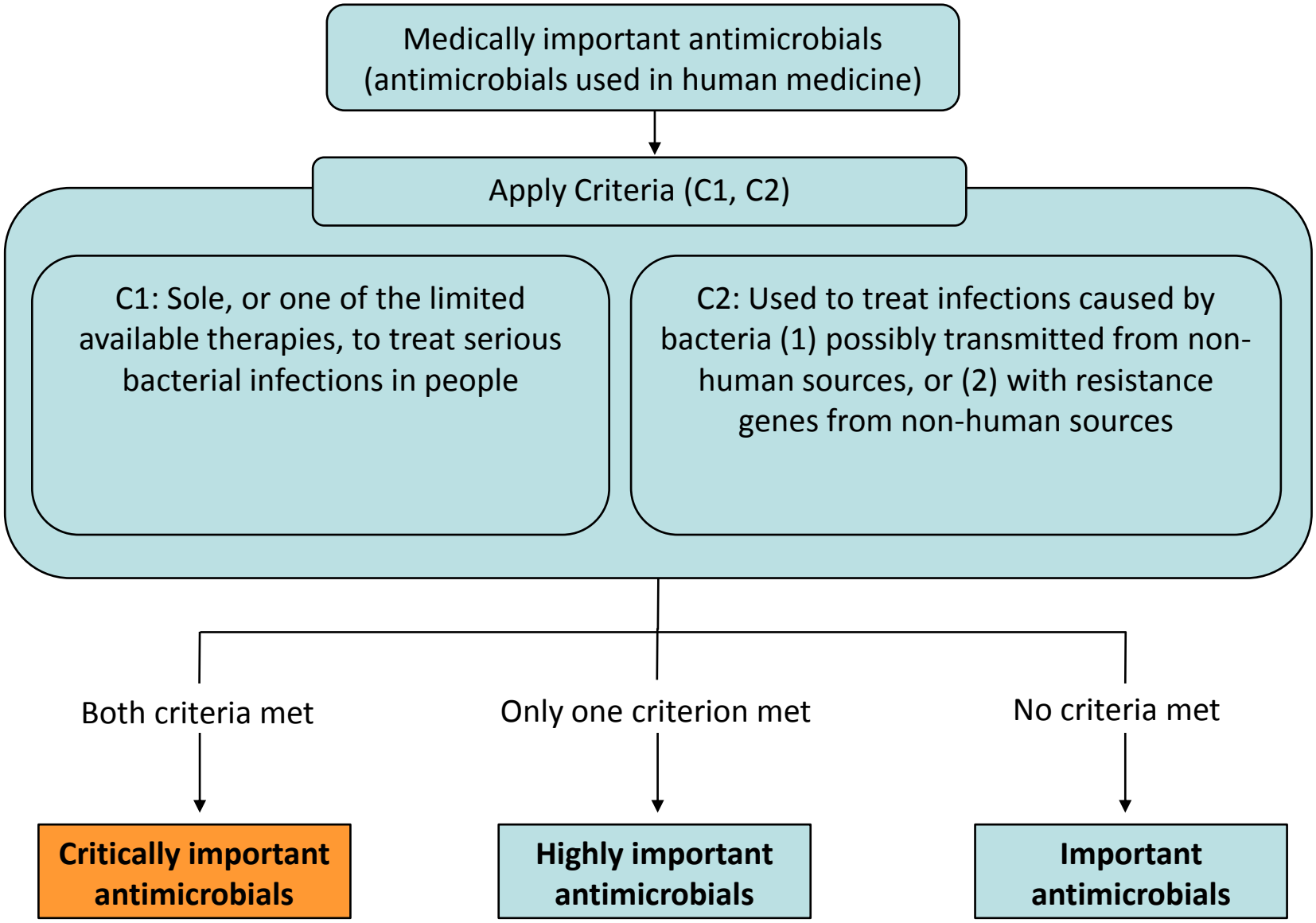
# Antibiotics which are critically important for humans (CIAs) are used for both therapeutic and non-therapeutic purpose; some like colistin are a last-resort for humans



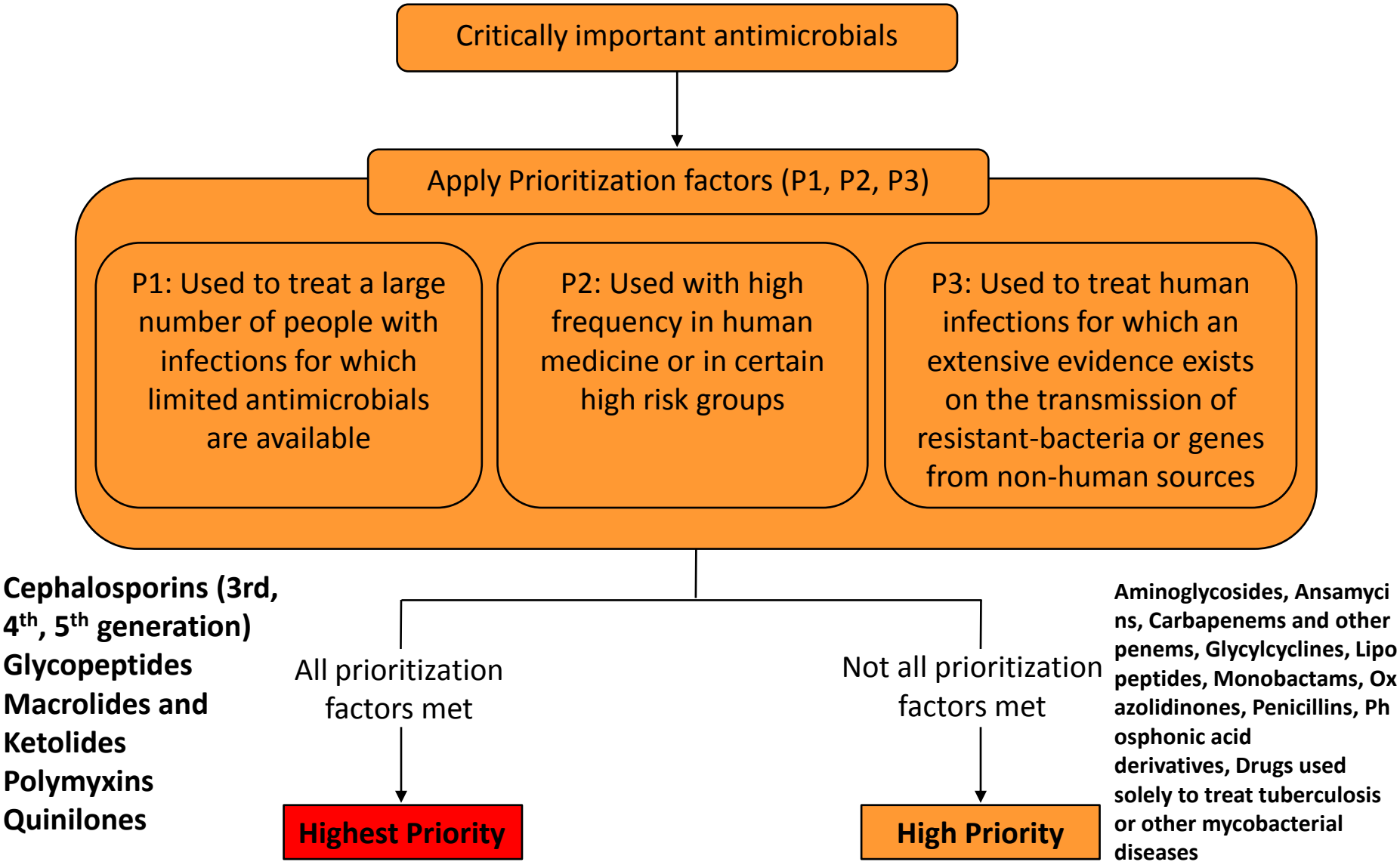

| | | |
|---|---|---|
| Highest Priority | Colistin | Roxithromycin |
| | Tylosin | Erythromycin |
| | Tilmicosin | Azithromycin |
| | Norfloxacin | Kitasamycin |
| | Enrofloxacin | Josamycin |
| | Levofloxacin | |
| | Ciprofloxacin | |

| | |
|---|---|
| High Priority | Fosfomycin |
| | Apramycin |
| | Kanamycin |
| | Streptomycin |
| | Neomycin |
| | Amikacin |
| | Ampicillin |
| | Amoxicillin |

# What are Critically Important Antimicrobials?



# Prioritization of Critically Important Antimicrobials



# Global guidance and initiatives

# Global guidance has shaped up to phase out non-therapeutic use and CIA use

- **Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals, 2017**
  Complete restriction of antimicrobial use as growth promoters and prophylaxis. HPCIAs should not be used for treating diseased animals
- **IACG Report, 2019**
  Use of antibiotics as growth promoters in animals should be phased out starting with an immediate end to the use of HPCIAs

**UK Swann Report, 1969**
Antimicrobial use in food animals leads to AMR; growth promoter use should be prohibited

- **WHA resolution, 1998**
  Use of antimicrobials in food-producing animals should be reduced
- **Global Principles for the Containment of AMR in Animals Intended for Food, 2000**
  CIA use for growth promotion should be terminated; their use for disease prevention should not be a substitute for good animal health management
- **Code of Practice to Minimize and Contain AMR, 2005**
  Responsible use of veterinary antimicrobial drugs in food-producing animals does not include their use for growth promotion; off-label use of antimicrobial growth promoters should not be permitted
- **Global Action Plan on AMR, 2015**
  Called on Member States to develop policies on use of antimicrobials in food-producing animals; phase out their non-therapeutic animal use
- **FAO Action Plan on AMR, 2016**
  Focuses on prudent use of antimicrobials and its monitoring in food and agricultural systems, improvement of awareness and promotion of good practices in food and agriculture

# Country-level initiatives to limit non-therapeutic antimicrobial use – feed first for growth promotion and then disease prevention !

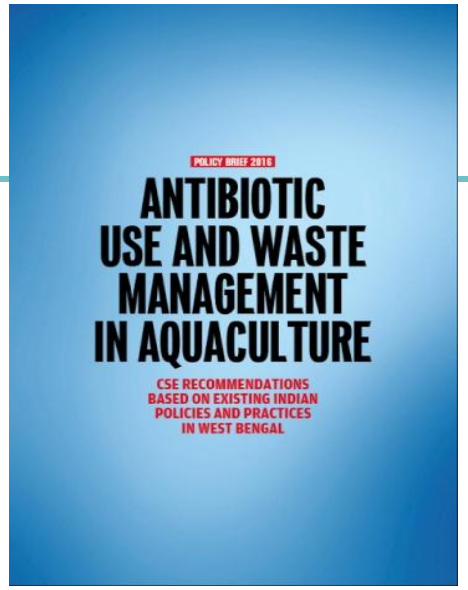
| Country | Year | Action |
|---|---|---|
| **EU countries** | 2006 | Ban on all growth promoter use in food animals, ban on preventive mass medication in animals to come into enforcement from 2022 |
| **China** | 2015 | Ban on use of select antibiotics in food animals,<br>Ban on colistin as feed additive for animals |
| **Bangladesh** | 2013 | All kinds of antibiotics are banned in animal feeds as growth promoter |
| **Malaysia** | 2013 | Prohibition of select antibiotics in feed and feed additives for the purposes of treatment, prevention and growth promotion in food-producing animals, colistin banned starting January 2019 |
| **Thailand** | 2015 | Ban on antimicrobial growth promoters, no registration of any antimicrobial/premix to be used as growth promoter, prohibition of medicated feed in aquaculture |
| **Indonesia** | 2018 | Ban on antimicrobial growth promoters in animal feed |
| **Vietnam** | 2018 | Ban on use of antimicrobials for use in animal feed as growth promoter |
| **Sri Lanka** | 2018 | Ban on antimicrobial growth promoters in animal feed |
| **Singapore** | - | Prohibition on use of antimicrobials as growth promoters in feed |

# India scenario (policy and practice)

# CSE studies

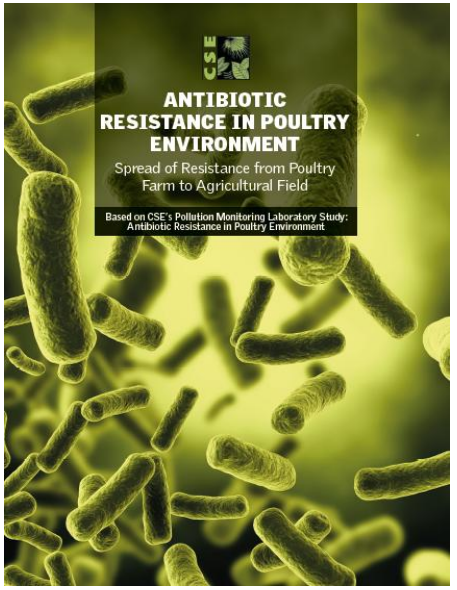

2010


2014




2016


2017




2017

# Evidence consolidating through numerous studies...(few examples)

- Multidrug resistance in *Salmonella* isolates from poultry samples in Mumbai that showed **100% resistant against three CIAs** - **Azithromycin, Erythromycin, Amoxicillin** *(Bandyopadhyay 2019)*

- **Colistin resistant bacteria** were found in food samples including meat, mutton, fish, fruits and vegetables collected from food outlets in Chennai *(Ghafur et al, 2018)*

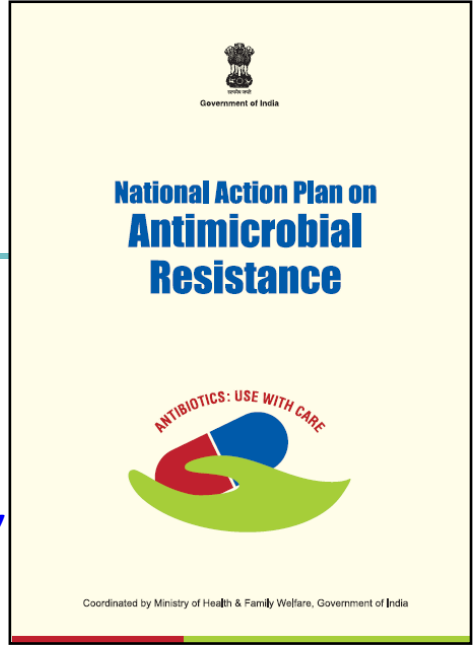
- Another study in Punjab shed light on the difference in resistance profiles between layer and broiler farms; **broiler farms more likely to harbor resistant strains**. The resistance was more in farms which used antibiotic growth promoters *(Brower et al, 2017)*

- A Bureau of Investigative Journalism study highlighted the **indiscriminate use of colistin for growth promotion and disease prevention** in chicken *(Bureau of Investigative Journalism, 2018)*

# Antibiotic laden feed easily available online; labelled for growth promotion; includes CIAs/HPCIAs (examples)

| Company | Brand name | Antibiotic(s) | Information on label |
|---|---|---|---|
| Venky's | Tylomix | **Tylosin** | **Increases the egg production**, hatchability and reduces the feed consumption per hatching egg |
| Vetline | Coligro 100 | **Colistin** sulphate | **For prevention and treatment** of bacterial infections |
| | Progro-Vet | **Colistin** sulphate, Doxycycline | Antibiotic **growth promoter** - Better feed conversion and hence increased weight gain in broilers |
| Vetneeds Labs | Zincstin | **Colistin**, colistin sulphate, Bacitracin | Antimicrobial **growth promoter** feed premix |
| | Doxicol | **Colistin** sulphate, Doxycycline | Antimicrobial performance promoter feed premix – **improves weight gain and egg production** |
| | Ceprostin plus | **Ciprofloxacin**, **Enrofloxacin** HCl, **Colistin** sulphate | Poultry feed supplement – **for prevention from infections** |
| Aadya Biological | K-Roxser | **Roxithromycin** | **Poultry feed supplement**, recommended for routine administration |
| Sinto Farm/ Lee Faris | Linco 11 | Lincomycin | For **increased weight gain and prevention** and treatment of necrotic enteritis |
| V S Chemical Industries | Neoxy-7 | **Neomycin**, Oxytetracyline | **Improves feed conversion** and overall performance, **prevents bacterial infections** |
| Vetcure Remedies | Colivet-100 | **Colistin** sulphate | **For prevention and treatment** of bacterial infections |
| | Levocol Plus | **Levofloxacin**, **Colistin** sulphate | For **enhanced growth and production**, reduced mortality |
| Biomir Venture LLP | CIPRO-MIR-FS | **Ciprofloxacin**, Metronidazole | **Growth promoter** and for **prevention of bacterial diseases** |

# NAP-AMR calls for restricting non-therapeutic use through multiple approaches




*"Restrict and **phase-out non-therapeutic use of antimicrobials** such as their use as **growth promoters** and **disease prevention in animals**"*

*"Restrict and **gradually eliminate the use of restricted antibiotics,** which are **critically important for humans in non-human sectors especially food-producing animals**"*

*"Restrict antibiotics in **animal feed, feed premix**"*

*"Ensure registration and use of **registered products** only; regulate their **importation**, **direct distribution** and **online marketing**; ensure appropriate **labelling**"*

*"Ensure **prescription sale** of antibiotics and their use under supervision"*

*"Ensure **labelling** of food from animals produced with or without routine use of antibiotics"*

*"**Support small and mid-size** poultry, dairy and fish farmers to reduce use of antibiotics, avoid non-therapeutic use and move to **safer alternatives**"*

*"Foster development of antimicrobial policies and **evidence-based standard treatment guidelines** for food animals"*

Joint declaration
endorsed by 12 ministries

सत्यमेव जयते

Government of India

# Delhi Declaration on Antimicrobial Resistance

*– an inter-ministerial consensus*

We, the ministers and policy-makers from various Ministries under the Government of India, assembled at the Inter-Ministerial Consultation on Antimicrobial Resistance, pledge to adopt a holistic and collaborative approach towards prevention and containment of antimicrobial resistance (AMR) in India, and :

**Acknowledge** that resistance of microorganisms to antimicrobials is a matter of serious concern; and is mainly due to inappropriate use in human, animal, food and agriculture sectors. Within AMR, resistance to antibiotics is the greatest and most urgent risk that requires focussed and immediate attention;

**Recognize** that emergence and spread of AMR is negating many twentieth century achievements, particularly reduction in illness and death from infectious diseases; and note with concern that without effective One Health and other multisectoral cooperation and actions, AMR is projected to cause millions of deaths worldwide (and in India) with massive

**Acknowledge that resistance of microorganisms to antimicrobials is a matter of serious concern; and is mainly due to inappropriate use in human, animal, food and agricultural sectors.**

<u>Commits to:</u>

*"Taking steps to ensure that national and state action plans on AMR include the development and strengthening of appropriate and effective surveillance, monitoring and regulatory frameworks on the preservation, use and sales of antimicrobial medicines for humans and animals"*

# DADF Advisory of 2014 disallows antibiotic use in feed as growth promoters

No. 102-74/2014-Trade
Government of India
Ministry of Agriculture
Department of Animal Husbandry, Dairying and Fisheries
Krishi Bhawan New Delhi
Dated : 2nd December, 2014

To,

The Commissioner/ Director,
Department of Animal Husbandry,
All State Governments and Union Territories

Subject: Use of antibiotics in food producing animals

*"Antibiotics should **not be allowed in feed and feed supplements as growth promoters***

*The use of antibiotics for prophylactic, metaphylactic and therapeutic purpose may be based on **prescription of veterinarians** and/or under their supervision*

*Use of **alternative antibiotic-free growth promoters** such as prebiotics, probiotics and phytotherapeutics should be encouraged*

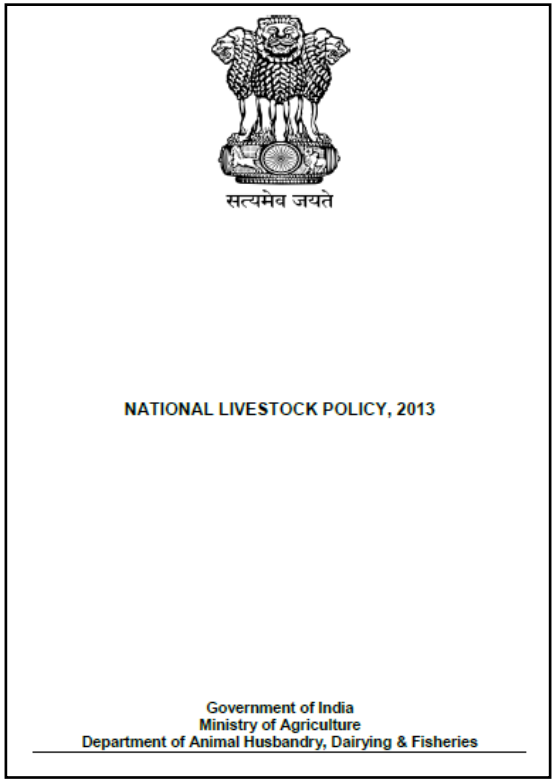
*A **licensed antibiotic** should reach a **registered user** through a registered distributor of veterinary medicine*

*The livestock and poultry farms should follow **good farm management practices** to control infection and stress among the flock. **Biosecurity** guidelines should be followed by making it available to all poultry farms*

*The State governments should **educate** their veterinarians, farmers and poultry entrepreneurs on the use of antibiotics, their withdrawal period, ill-effects of indiscriminate use of antibiotics and antimicrobial resistance"*

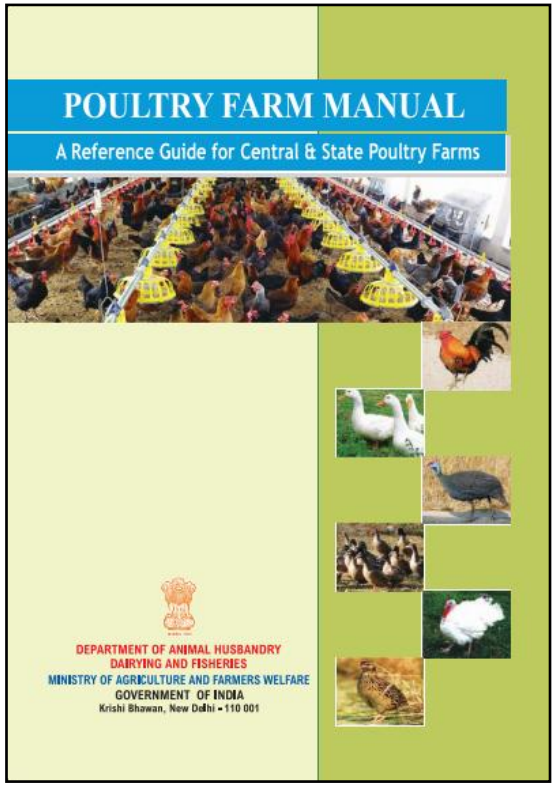
# DADF's livestock policy says no to residues; poultry farm manual recommends no antibiotics in feed

## National Livestock Policy, 2013




***"Livestock origin food and food products have to be free of*** *contaminants, toxins, pathogens, pesticides and* ***antibiotic residues****, harmful additives and adulterants"*

## Poultry Farm Manual, 2013




*"The use of* ***antibiotic growth promoters are NOT RECOMMENDED in poultry feed****. The most important reason being AMR due to antibiotic residues in animal tissues and products."*

# BIS also recommends no antibiotics in feed

- **Poultry feed standard** (IS 1374:2007) recommends:
  - Antibiotics with **systemic action** should not be used as growth promoters; these include chloramphenicol, doxycycline, tetracycline, nitrofuran, furazolidone
  - **Phase-out of gut-antibiotics**
- **Standards for fish feed** (IS 16150 : Part 1-4:2014):
  - Prohibit use of a set of antibiotics in fish-feed manufacturing units
  - The prohibited antibiotics include Nitrofurans (furaltadone, furazolidone, furylfuramide, nifuratel, nifuroxime, nifurprazine, nitrofurnatoin and nitrofurazone), Neomycin, Chloramphenicol, Nalidixic acid, Sulphamethoxazole, Dapsone, Sulfanoamide drugs (except approved sulfadimethoxine, sulfabromomethazine and sulfaethoxypyridazine), Fluoroquinolones, Glycopeptides

# Standards exist to monitor antibiotic residues in food from animals: eggs, fish, edible tissues and fat from animals

- In 2018, FSSAI has specified maximum permissible limits for **70+ antibiotics** in eggs, milk, edible animal tissues (including fish) and fat derived from animals. These include Colistin, Erythormycin, Neomycicn, Enrofloxacin
- Modified list of antibiotics not permitted to be used at any stage of **processing of meat and meat products, poultry and eggs, sea foods** including shrimps, prawns or any variety of fish and fishery products
  - Furaltadone, Furazolidone, Nitrofurnatoin, Nitrofurazone, Chloramphenicol Sulphamethoxazole, Metronidazole, **Glycopeptides**
- For four other antibiotics, separate tolerance limits are prescribed in **fish, fishery products and sea foods**. These are:
  - Tetracycline
  - Oxytetracycline
  - Trimethoprim
  - Oxolinic acid

# Coastal Aquaculture Authority (CAA) – regulates feed and antibiotics in coastal aquaculture

- CAA **registers antibiotic-free aquaculture inputs** categorized as chemical, disinfectant, drugs, feed additive, feed adult, feed larval, immunostimulant and probiotic; Shrimp hatchery operators and farmers can **use only the Registered Antibiotic-free Aquaculture Inputs**

- **CAA has banned** a list of antibiotics and other pharmacologically active substances for use in **shrimp aquaculture**. These are:
  Chloramphenicol, Nitrofurans including: Furaltadone, Furazolidone, Furylfuramide, Nifuratel, Nifuroxime, Nifurprazine, Nitrofurantoin, Nitrofurazone, **Neomycin**, Nalidixic acid, Sulphamethoxazole, Aristolochia spp and preparations thereof, Chloroform, Chlorpromazine, Colchicine, Dapsone, Dimetridazole, Metronidazole, Ronidazole, Ipronidazole, Other nitroimidazoles, Clenbuterol, Diethylstilbestrol (DES), Sulfonamide drugs (except approved Sulfadimethoxine, Sulfabromomethazine and Sulfaethoxypyridazine), **Fluroquinolones, Glycopeptides**

- The maximum residue limits for the above are specified as '**Nil**'

- Provides MRLs for four other antibiotics, the same as specified by FSSAI

# Antibiotics to be sold under prescription; withdrawal period specified and to be labelled for animal use

- **Schedule H1 to limit OTC sale of drugs, 2014 (D&C Act)**
  - H1 list includes **46 antibiotics**, such as third- and fourth-generation cephalosporins, carbapenems, antituberculosis drugs, and newer fluoroquinolones
  - Drugs covered by it to carry a prominent **Rx symbol in red and contain a box with red borders** with a printed warning on their packaging – ***Red line campaign***
  - Can only be sold with the prescription of a registered medical practitioner

- **Subrule 3A of Rule 97 in Drugs and Cosmetics Rules, 2012**
  - Specifies the **withdrawal period**, or the timeframe for poultry, livestock and marine products to be kept off antibiotics before they enter the food chain
  - The container of a medicine for treatment of food producing animals shall be **labeled with the withdrawal period of the drug** for the species on which it is intended to be used

# A 2011 case of Jharkhand – antibiotics in feed are drugs and not feed additive!

In a case related to use of antibiotic growth promoters in feed, the presence of antibiotic in feed was well recognized as drug and not feed additive.

***"If upon a drug or medicine, label is put that it is not a drug or medicine, it will not make that drug or medicine, something other than drug or a medicine."***

***"The question of whether commodity has been intended to be used as a drug or it has not been intended to be used as a drug, may not be relevant."***

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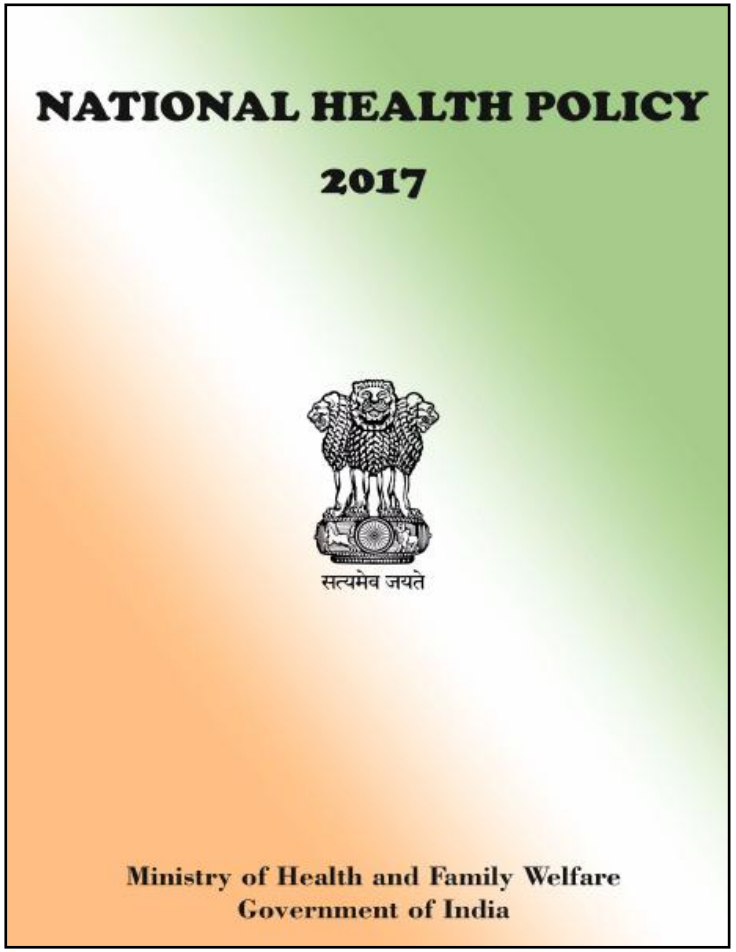
**In 2011,** the then Inspector of Drugs, Deoghar seized ***Ciproplus B WS feed supplement powder*** (manufactured by M/s-Intercorp Biotech limited, Delhi) as it contained Ciprofloxacin HCl and issued a letter to the manufacturer asking about the drug manufacturing licence

The manufacturer appealed in the various courts of India against the observation but it was **dismissed**.

# National Health Policy, 2017 also says no to growth promoters




- The problem of AMR calls for a rapid **standardization of guidelines regarding**:
  - Antibiotic use
  - Limiting the use of antibiotics as over-the-counter medication
  - **Banning or restricting the use of antibiotics as growth promoters in animal livestock**

# How can states go about it?

# Guidance framework: antibiotic use and AMR surviellance

| INTERVENTION AREAS |
|---|
| Policy/law/ regulations/ standards/ programmes |
| Implementation tools- Infrastructure/ capacity/systems/ resources |
| Advocacy/awarenes s and education/ training/curriculum |
| Record keeping/ database generation/ collation/ dissemination and research/survey |
| Review/monitoring /feedback |

## Responsible Antibiotic Use in Food Animals

| THEMATIC AREAS | | | | |
|---|---|---|---|---|
| Supply of antibiotics | Production Systems | | | Consumers |
| | Reduce need for antibiotics | Veterinarians and veterinary services | Farms and farmers | |

## Surveillance of Antibiotic Use, Residues and Resistance

| THEMATIC AREAS | | | |
|---|---|---|---|
| Antibiotic use in food animals | Antibiotic resistance in animals and food from animals | Antibiotic residues in food from animals | Environmental surveillance of residues and resistance |

## Environment Management to Contain Antimicrobial Resistance

| THEMATIC AREAS | | | |
|---|---|---|---|
| Registration/ licensing (based on environment risk assessment) | Biosecurity/sanitatio n and hygiene/good manufacturing Practices | Waste management | Research |

Short-term **(S)**: <1 yr; Medium-term **(M)**: 1-3 yrs;
Long term **(L)**: 3-5 yrs; Continues throughout: **(S-M-L)**

# Responsible antibiotic use in food animals

## Supply of antibiotics

**Policy/Law/ regulations/ standards/ programmes**

- Policy and regulatory framework on responsible antibiotic use with focus on **(S)**
  - Approval and authorisation of antibiotics for animals
  - Ban/phasing out of non-therapeutic use such as for **mass disease prevention and growth promotion**
  - Restricting use of critically important antibiotics for humans
  - Antibiotic use under supervision and prescription
  - Mitigating livelihood impact on small holder farmers

# Responsible antibiotic use in food animals

## Supply of antibiotics

**Policy/Law/ regulations/ standards/ programmes**

- Regulation to restrict antibiotics in animal feed and premix, registration of feed and premix, prescription and use of only registered products **(S)**
- Regulation on import of feed, feed premix and antibiotics for animal use **(S)**
- Labelling law for feed, premix **(S)**
- Labelling law for antibiotics for specie-specific use **(S)**
- Regulation on online marketing and direct distribution of antibiotics, premix, antibiotic feed or any other products with antibiotics **(S)**
- Law to ensure licensing of manufacturer, distributor and sellers of antibiotics, feed, premix and other inputs **(S)**
- Law to ensure prescription sale, including penalty for unauthorized sale **(S)**
- Plan to set reduction targets for antibiotic use by a certain date and with a review process **(S)**

**Necessary awareness creation, training, capacity building, monitoring in parallel**

**Implementation tools - infrastructure/ capacity/ systems/ resources**

- Authority for approving veterinary drugs and market authorization **(S)**
- Systems to enable data collection of antibiotic production, sale and import **(M)**
- Necessary enforcement systems through agencies, customs, infrastructure, human resource including those required for auditing/inspecting companies providing inputs (e.g. feed), ensuring prescription sale etc.**(M)**

# Responsible antibiotic use in food animals

## Reduce need for antibiotics

**Policy/Law/ regulations/ standards/ programmes**

- Develop guidelines for biosecurity **(S)**
  - Plan/programme for internal and external biosecurity and its enforcement
  - Programme to support small-holder farmers to implement biosecurity
- Programme to research, develop, promote access to alternatives such as vaccination, probiotics etc. **(S)**
- Plan for research and development of appropriate animal breeds. Which are, for example, resilient **(S)**

**Necessary awareness creation, training, capacity building, monitoring in parallel**

**Implementation tools - infrastructure/ capacity/ systems/ resources**

- Develop systems to ensure adoption and implementation of appropriate biosecurity measures at the farm level **(M)**
- Systems to register antibiotic free alternative products and their use **(S)**
- Support for programmes on development and adoption of vaccines **(M)**
- Investment and research in development of appropriate animal breeds with disease resilience **(M)**

# Responsible antibiotic use in food animals

## Veterinarians and veterinary services

**Policy/Law/ regulations/ standards/ programmes**

- Law for licensing/registration of veterinarians **(S)**
- Law to delink antibiotic prescription and incentives **(S)**
- Programme for accessible, affordable and quality diagnostic services to support judicious use of antibiotics **(S)**
- Programme for targeted, livestock specific veterinary services to provide free advisory services to farmers **(M)**

**Necessary awareness creation , training, capacity building, monitorin g in parallel**

**Implementation tools - infrastructure/ capacity/ systems/ resources**

- Set up licensing authority for veterinarians and those involved in fisheries **(S)**
- Develop capacity and infrastructure to ensure veterinary diagnostic services **(M)**
- Develop system to dis-incentivize antibiotic prescription by veterinarian **(S)**

# Thank you

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# Why ban colistin right away?

- **Resistance to colistin is rapidly spreading** around the world; emerging in India hospitals
- **7th most frequently used out of 35 antibiotics used for growth promotion** – OIE

- Inter-governmental organizations are pushing to ban the use of colistin for growth promotion (IACG, WHO) and also therapeutic use in animals (WHO).

- Countries have intitiated regulatory actions for use of colistin in food-producing animals. China, Argentina and Brazil have banned the use of colistin in animals.

- In India, colistin is rampantly used in food animals for growth promotion and disease prevention. Huge quantities of colistin are produced and imported in India and it is available over-the-counter without a prescription

# The global distribution and spread of the mobilized colistin resistance gene *mcr-1*