DEVELOPMENT AND IMPLEMENTATION OF STATE ACTION PLANS ON CONTAINMENT OF ANTIMICROBIAL RESISTANCE (SAPCAR)

Anil Agarwal Environment Training Institute (AAETI), Neemli, Rajasthan

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AMR pathways and containment options (Livestock and food)

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Sustainable food systems
CSE
Food production systems – key driver for AMR
Several sectors and sub-sectors are AMR pathways

Key sectors:
• Poultry farming for meat
• Aquaculture for fish meat
• Pig farming for meat
• Sheep farming for meat
• Beef cattle for meat
• Poultry farming for eggs
• Dairy farming for milk
• Bee-keeping for honey
• Crop agriculture (rice, fruits, vegetables, etc.)
• Farming for animal feed

Three AMR determinants (antibiotic residues, resistant bacteria, antibiotic resistance genes) travel across multiple sectors
Nature of waste and AMR determinants varies across sectors and local context
Key problem: Quantum of antibiotics use/misuse/overuse very high due to non-therapeutic purposes

Antibiotic use

Therapeutic
- Therapeutic doses
- Clinically diagnosed infectious disease

Non-therapeutic

Growth promotion
- Increase the rate of weight gain
- Increase efficiency of feed utilization
- Mass, routine use (largely through feed at sub-therapeutic doses)

Prevention (prophylaxis)
- Individual or group of animals
- With no clinical sign
- Often routine use

Prevention – (control/metaphylaxis)
- In a group of healthy animals (presumed to be infected/may have already been sub-clinically infected because they are at risk of infection), where one or more animal is already infected

Though non-therapeutic, now being positioned as therapeutic by some agencies
The problem becomes bigger because critically important antimicrobials (CIAs) are misused / overused – our report tells us from India

Partly due to incoherence in guidance from stakeholder agencies.

For example:
- **Overlap** in list of CIAs by WHO & OIE
- Need for coherence in **position on use** of CIAs in food-producing animals
- Need for **clarity and strong action** on use of antimicrobials for **disease prevention** in food-producing animals

However, starting this year Europe has banned use of antibiotic use for disease prevention.

But CODEX guidelines continue to support antibiotic use for disease prevention.
What are CIAs?

Medically important antimicrobials

Apply criteria (C1, C2)

C1: Sole, or one of the limited available therapies, to treat serious bacterial infections in people
C2: Used to treat infections caused by bacteria (1) possibly transmitted from non-human sources, or (2) with resistance genes from non-human sources

Both criteria met
Only one criterion (C1 or C2) met
No criteria met

Critically important antimicrobials
Highly important antimicrobials
Important antimicrobials

Apply prioritization factors (P1, P2, P3)

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

All prioritization factors met
Not all prioritization factors met

Highest priority critically important antimicrobials
High priority critically important antimicrobials
CIAs and HPCIAs used in all key food animal sectors

<table>
<thead>
<tr>
<th>Dairy</th>
<th>Poultry</th>
<th>Aquaculture</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 CIAs from 6 Classes</td>
<td>14 CIAs from 4 Classes</td>
<td>3 HPCIAs from 1 class</td>
</tr>
<tr>
<td>13 HPCIAs from 2 classes</td>
<td>8 HPCIAs from 2 classes</td>
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</tbody>
</table>

**HPCIAs**
- Third-, fourth- and fifth-generation cephalosporins, Eg: Cefotaxime
- Quinolones and fluoroquinolones, Eg: Levofloxacin

**CIAs**
- Aminoglycosides, Eg: amikacin
- Penicillins
- Ansamycins, Eg: Rifampicin
- Drugs used solely to treat tuberculosis or other mycobacterial disease

**HPCIAs**
- Macrolides and ketolides, Eg: Erythromycin
- Quinolones and fluoroquinolones, Eg: Ciprofloxacin

**CIAs**
- Aminoglycosides, Eg: streptomycin
- Penicillins

**HPCIAs**
- Quinolones and fluoroquinolones, Eg: Ciprofloxacin
And these multiple pathways (beekeeping, livestock and fisheries)… have been active for a long time!

Antibiotics in honey, 2010
Antibiotic use in poultry, 2014
Antibiotic use in aquaculture, 2016
Antibiotic use in fast food supply chain, 2017
Antibiotic use in feed, 2020
Antibiotic use in fast food supply chain, 2020
Antibiotic use in dairy, 2020
Use of ethnoveterinary medicines in dairy sector, 2021
These food/animal pathways are driven by growing intensification of food production systems which is in-turn fuelled by ease of antibiotic use/misuse

<table>
<thead>
<tr>
<th>Drivers</th>
<th>Characteristics leading to more disease/antibiotic use</th>
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<tbody>
<tr>
<td>• Growing food demand <em>(protein, animal protein)</em></td>
<td>• Large-scale units with <strong>high stocking density</strong> of animals/birds/ fish</td>
</tr>
<tr>
<td>• Growing population</td>
<td>• Genetically selected similar <strong>breeds</strong> for productivity (not disease resilience)</td>
</tr>
<tr>
<td>• Growing <strong>incomes</strong> / purchasing power</td>
<td>• Kept under <strong>confined conditions</strong> and in <strong>close proximity</strong>; limited focus on animal husbandry; high stress</td>
</tr>
<tr>
<td>• Urbanization</td>
<td>• <strong>Dependence on commercial feed</strong>, inputs (also known as animal feeding operations, factory farms)</td>
</tr>
<tr>
<td>• Changing <strong>food habits</strong>, evolving taste</td>
<td>• Often <strong>geographically concentrated</strong>; vertically integrated by large players; involves <strong>contract farming</strong></td>
</tr>
<tr>
<td>• Less <strong>people</strong> and less <strong>land</strong> to grow food</td>
<td>• <strong>Industrial systems</strong> but considered agriculture; can bypass required regulatory attention</td>
</tr>
<tr>
<td>• Political mandate - for <strong>exports, livelihood opportunities</strong></td>
<td></td>
</tr>
<tr>
<td>• Availability of <strong>inputs</strong> - machines, feed, drugs and chemicals</td>
<td></td>
</tr>
</tbody>
</table>
Intensive animal farming systems
Pathways – cropping systems

- Use/misuse/overuse of streptocycline (streptomycin + tetracycline) in crops highlighted (fruits, vegetables, etc.)

- Streptocycline registered as fungicide

- Ministry of Agriculture, notified the draft order on ‘Prohibition of Streptomycin + Tetracycline in agriculture’.

- Prohibiting import, manufacture or formulation of these antibiotics from Feb 22 and ban on use from Jan 24.
Consensus on what should be done at the global level is increasing pressure on India - GLG’s call to action on Antimicrobial Use in Food Systems

Infection prevention and control

Reducing antimicrobial use

- Reduce overall use of antimicrobials, particularly HPCIsAs for terrestrial and aquatic animals and plants
- End the use of medically important antimicrobials for growth promotion, starting immediately with the HPCIsAs
- Limit antimicrobial prophylaxis and metaphylaxis in animals and plants to well-defined situations, with a goal of markedly reducing use

Oversight and governance

- All countries should ensure effective governance and professional oversight of the sales and use of antimicrobials and stewardship of antimicrobials in all sectors.
What should be done in India?

- First and foremost - we need to stop growth promoter use
- On CIAs, India should consider developing a road map and necessary policy framework to conserve the use of CIAs in non-human sector

1. New/revised guidelines that recommend antimicrobials for all food-animal sectors. They should aim to **phase out use of CIAs for all non-therapeutic purposes**, with priority given to HPCIAs:

   - Use of CIAs for therapeutic purposes should not be resorted to, when **alternative effective** antibiotics are available.
   - Their use for treatment should always be under professional **supervision** and based on appropriate **diagnosis**.
   - **HPCIAs** used for treatment shall also be considered for phase-out, be allowed only as a **last resort** through necessary policy instruments.
   - **Fluoroquinolones** and third-, fourth- and fifth-generation cephalosporins are examples of **restricted-use HPCIAs** in other parts of the world. A careful consideration should be made on the basis of Indian data.
2. Antimicrobial use for **disease prevention** (including control) should be recognized as **non-therapeutic** and all measures should be adopted and/or promoted to discourage such use in farms. In particular, group preventive use should receive immediate attention.

- Necessary action should also be placed on promoting and incentivizing use of non-antimicrobial alternatives, biosecurity, hygiene and sanitation, and good animal-rearing practices. These are often lacking in Indian farms and are substituted by mass use of antimicrobials to prevent and control diseases, which does more harm than good.
What should be done in India?

3. The **definition of “drug”** in the Drugs and Cosmetics Act, 1940 includes the word “prevention”. It is important to revise and/or clarify the definition to ensure that it is not used to justify the use of antimicrobials in disease prevention in food-producing animals:

   - The definition also needs to **ensure that antimicrobials in feed are regulated**. As of now these are left unregulated, but should ideally fall under the purview of this Act which could be also used in poultry sector.

4. A long-term research agenda should be developed and implemented for non **antimicrobial alternatives** and their effectiveness understood in managing diseases in animal farms.
5. Setting up systems and mechanisms to **gather data** and enhance understanding on CIAs **use** and **resistance** in food-producing animals. This data on sector-wise use should be analysed with resistance in animals and humans and the reports should be made public annually.

- Investment in **creating awareness** among farmers and building capacity for good animal-rearing practices to prevent occurrence and spread of disease at farms.

- Programmatic interventions to ensure that veterinarians **prescribe** antimicrobials responsibly only and when necessary.

6. **Routine monitoring** by the central food regulator (FSSAI) and state food regulators on antimicrobial use and residues to ensure that withdrawal periods are followed and residue standards are met. FSSAI should also modify its standards as soon as use of a specific critically important antimicrobial is restricted or banned as in the case of colistin.
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### Interpretation of global guidance on use of critically important antimicrobials in food-producing animals

<table>
<thead>
<tr>
<th></th>
<th>WHO</th>
<th>OIE</th>
<th>FAO</th>
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<tbody>
<tr>
<td><strong>Highest priority critically important antimicrobials</strong></td>
<td><em>(Quinolones and fluoroquinolones, third- and fourth-generation cephalosporins and colistin)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth promotion</td>
<td>Should not be used</td>
<td>Should not be used</td>
<td>Should not be used</td>
</tr>
<tr>
<td>Prevention</td>
<td>Should not be used</td>
<td>Should not be used</td>
<td>Should not be used</td>
</tr>
<tr>
<td>Control</td>
<td>Should not be used</td>
<td>Could be used</td>
<td>Should not be used</td>
</tr>
<tr>
<td>Treatment</td>
<td>Should not be used</td>
<td>Could be used</td>
<td>Should not be used</td>
</tr>
</tbody>
</table>

| **Highest priority critically important antimicrobials** | *(Macrolides and ketolides, polymyxins other than colistin, glycopeptides and lipoglycopeptides, fifth-generation cephalosporins)* | | |
| Growth promotion          | Should not be used   | Should not be used   | Should not be used   |
| Prevention                | Should not be used   | Could be used        | Should not be used   |
| Control                   | Should not be used   | Could be used        | Should not be used   |
| Treatment                 | Should not be used   | Could be used        | Should not be used   |

| **Critically important antimicrobials**^
| Growth promotion          | Should not be used   | Should not be used*  | Should not be used   |
| Prevention                | Should not be used   | Could be used        | Should not be used   |
| Control                   | Should not be used   | Could be used        | Could be used**      |
| Treatment                 | Could be used        | Could be used        | Could be used        |

Note: For easy reference words used to reflect position are “should not be used” and “could be used”. **The red text highlights incoherence.**
* Could be used if there are no specific restrictions are mentioned in the OIE list, or if risk is low upon formal risk analysis
** Under exceptional circumstances; ^ Critically important antimicrobials other than highest priority critically important antimicrobials