Antibiotic Pollution from Food Production

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Workshop on Understanding the Environmental Dimensions of Antimicrobial Resistance
March 28-29, 2023
UNEP report recognizes ‘Agriculture and Food’ as one of the Key economic-sector value chains affecting AMR in the environment

• ‘Several points in the agriculture value chain serve as entry points for antimicrobials and antimicrobial resistant organisms into the environment such as the use of antimicrobials to treat infection and promote growth, use of reclaimed wastewater for irrigating crops, use of manure as fertilizer and inadequate waste management’

• ‘Unless broader steps are taken towards making food systems more sustainable and curbing the use of antimicrobials in animal husbandry practices, the use of antimicrobials in food production will continue to grow’

• ‘In intensive animal production systems, antimicrobials are frequently relied upon to maintain livestock health, welfare and productivity, including for control of diseases. In some jurisdictions, antimicrobials are still used as growth promoters’

• ‘Management options to address releases, effluent and waste from animal production:
  • Reduce antimicrobial use in food animals by improving animal health through implementing biosafety, biosecurity, vaccination and good animal husbandry programmes
  • Develop market incentives that would help motivate aquaculture producers to invest and adopt alternative management practices that curb the use of antimicrobials’
CSE’s work on food and environment aspects of AMR in India (few examples)

- Antibiotics in honey, 2010
- Antibiotic use in poultry, 2014
- Antibiotic use in aquaculture, 2016
- AMR in poultry environment, 2017
- Antibiotic use in fast food supply chain, 2017
- Antibiotic use in crops, 2019
- 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
- Use of ethnoveterinary medicines in dairy sector, 2022
Antibiotic use/misuse/overuse in food systems

- **Therapeutic**
  - Therapeutic doses
  - Clinically diagnosed infectious disease

- **Non-therapeutic**
  - Increase the rate of weight gain and efficiency of feed utilization
  - Mass, routine use largely through feed at sub-therapeutic doses

  - **Growth promotion**
    - Individual or group of animals
    - With no clinical sign
    - Often routine/intermittent use

  - **Prevention** (prophylaxis)
    - In a group of healthy animals where one or more animal is already infected
    - Other animals presumed to be infected or sub-clinically infected or at risk of infection

  - **Prevention – (control / metaphylaxis)**

Non-therapeutic use but continues to be promoted/justified and/or positioned as therapeutic
Key problems w.r.t antibiotic use in food systems (animal systems in particular)...

- **Problem 1:** antibiotic use/misuse is very high
  - Due to non-therapeutic purposes (e.g. growth promotion), large animal population, ease of antibiotic availability/use as a cheap substitute

- **Problem 2:** use/misuse of critically important antimicrobials (antibiotics)
  - Life-saving antibiotics in hospitals/ICUs are misused to grow meat in farms (for multiple reasons but some of which are avoidable)

- **Problem 3:** antibiotic use/misuse to prevent diseases
  - Whereas prevention with chemicals/antibiotics is no real prevention; but antibiotics pushed/promoted/justified as therapeutic use for prevention

- **Problem 4** (the biggest): antibiotic use/misuse is fueling intensive practices to rear animals for food
CSE’s latest report on conserving the use of critically important antimicrobials in food-producing animals

- **India**
  - Presents the **on-the-ground situation** in India wrt use of critically important antimicrobials in food-animal sector
  - Provides a series of policy measures including a roadmap to contain the misuse of critically important antimicrobials in food-animal production

- **Global**
  - Analyses the **global guidance of the Tripartite organizations** with regard to critically important antimicrobials
  - Calls for coherence and uniformity in **global guidance** on use of critically important antimicrobials in food-animals
Key findings: Critically important antibiotics are misused and overused in Indian food-animal production sector

- 27 critically important antimicrobials from seven classes were found to be used in dairy, poultry and aquaculture for both therapeutic and non-therapeutic purposes.
- Eighteen were from three highest priority critically important antimicrobial classes, i.e. macrolides and ketolides; third-, fourth- and fifth-generation cephalosporins; and quinolones and fluoroquinolones.
- Antimicrobials, apart from treatment used for prevention and control of diseases; in viral and fungal infections, along with feed (poultry sector).

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

**HPCIs**
- 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

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

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

**HPCIs**
- Quinolones and fluoroquinolones, Eg: Ciprofloxacin
### Critically important antimicrobials used in the Indian dairy sector to prevent, control or treat diseases

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Antimicrobial class</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Highest priority critically important antimicrobials considered veterinary critically important antimicrobials</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefoperazone</td>
<td>Third-, fourth- and fifth- generation cephalosporins</td>
<td>Mastitis</td>
</tr>
<tr>
<td>Ceftiofur</td>
<td></td>
<td>Mastitis, haemorrhagic septicaemia, anthrax</td>
</tr>
<tr>
<td>Ceftiraxone</td>
<td></td>
<td>Mastitis, haemorrhagic septicaemia; viral disease: foot and mouth disease</td>
</tr>
<tr>
<td>Cefquinome</td>
<td></td>
<td>Mastitis</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Quinolones and fluoroquinolones</td>
<td>Anthrax, diarrhoea; viral disease: foot and mouth disease</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>Quinolones and fluoroquinolones</td>
<td>Mastitis, haemorrhagic septicaemia, diarrhoea; viral disease: foot and mouth disease, infectious bovine rhinotracheitis</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td></td>
<td>Diarrhoea</td>
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<tr>
<td>Ofloxacin</td>
<td></td>
<td>Diarrhoea</td>
</tr>
<tr>
<td><strong>Critically important antimicrobials considered veterinary critically important antimicrobials</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Penicillins</td>
<td>Mastitis; viral disease: foot and mouth disease</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Penicillins</td>
<td>Mastitis, black quarter, brucellosis; viral disease: foot and mouth disease, infectious bovine rhinotracheitis</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Aminoglycosides</td>
<td>Mastitis, brucellosis</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Aminoglycosides</td>
<td>Mastitis, diarrhoea; viral disease: foot and mouth disease</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Aminoglycosides</td>
<td>Mastitis, black quarter, brucellosis, tuberculosis; viral disease: foot and mouth disease</td>
</tr>
<tr>
<td><strong>Critically important antimicrobials considered veterinary highly important antimicrobials</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Ansamycins</td>
<td>Brucellosis, tuberculosis</td>
</tr>
<tr>
<td><strong>Highest priority critically important antimicrobials not mentioned in OIE list</strong></td>
<td></td>
<td></td>
</tr>
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<td>Cefotaxime</td>
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</tr>
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<td>Ceftazidime</td>
<td></td>
<td>Mastitis</td>
</tr>
<tr>
<td>Ceftizoxime</td>
<td></td>
<td>Mastitis</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>Quinolones and fluoroquinolones</td>
<td>Mastitis</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>Quinolones and fluoroquinolones</td>
<td>Mastitis</td>
</tr>
<tr>
<td><strong>Critically important antimicrobials not mentioned in OIE list</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Drugs used solely to treat tuberculosis or other mycobacterial disease</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
<td>Tuberculosis</td>
</tr>
</tbody>
</table>

Note: In addition to the above, antimicrobials which are not critically important and used in Indian dairy sector include tetracycline, oxytetracycline, doxycycline, trimethoprim, sulfamethoxazole, sulfadimidine, cloxacillin, benzylpenicillin, nitrofurantoin, cefalexin, ornidazole and metronidazole.
## Critically important antimicrobials used in the Indian poultry sector to prevent, control or treat diseases

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<tr>
<td>Ciprofloxacin</td>
<td>Quinolones and fluoroquinolones</td>
<td>Pullorum disease, fowl typhoid, colibacillosis, salmonellosis</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td></td>
<td>Fowl cholera, infectious coryza, pullorum disease, fowl typhoid, colibacillosis, necrotic enteritis, salmonellosis, chronic respiratory disease; viral diseases: Ranikhet disease, infectious bronchitis, avian influenza, Marek’s disease, infectious bursal disease</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td></td>
<td>Colibacillosis</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Macrolides and ketolides</td>
<td>Infectious coryza</td>
</tr>
<tr>
<td>Tylosin</td>
<td></td>
<td>Chronic respiratory disease; fungal disease: mycotoxicosis</td>
</tr>
<tr>
<td>Tylvalosin</td>
<td></td>
<td>Chronic respiratory disease</td>
</tr>
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## Critically important antimicrobials considered veterinary critically important antimicrobials

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</tr>
<tr>
<td>Ampicillin</td>
<td></td>
<td>Necrotic enteritis</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Aminoglycosides</td>
<td>Infectious coryza, pullorum disease, fowl typhoid, colibacillosis, salmonellosis</td>
</tr>
<tr>
<td>Gentamicin</td>
<td></td>
<td>Pullorum disease, fowl typhoid, salmonellosis</td>
</tr>
<tr>
<td>Neomycin</td>
<td></td>
<td>Pullorum disease, colibacillosis, necrotic enteritis; fungal disease: aspergillosis, mycotoxicosis</td>
</tr>
<tr>
<td>Streptomycin</td>
<td></td>
<td>Fowl cholera</td>
</tr>
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## Highest priority critically important antimicrobials not mentioned in OIE list

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<td>Azithromycin</td>
<td>Macrolides and ketolides</td>
<td>Fowl cholera</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>Quinolones and fluoroquinolones</td>
<td>Fowl cholera, infectious coryza, pullorum disease, fowl typhoid, colibacillosis, necrotic enteritis, salmonellosis; viral disease: Ranikhet disease</td>
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Note: In addition to the above, antimicrobials that are not critically important and are used in the Indian poultry sector include tetracycline, oxytetracycline, doxycycline, trimethoprim, sulfamethoxazole, tiamulin, cefalexin, furazolidone and chloramphenicol.
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<tr>
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<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ciprofloxacin</strong></td>
<td>Quinolones and fluoroquinolones</td>
<td>For one or more of the following:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infections caused by <em>Aeromonas</em> spp.: e.g. motile aeromonadsepticaemia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hemorrhagic septicemia, red sore, tail rot and fin rot, furunculosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infections caused by <em>Vibrio</em> spp.: e.g. vibriosis, intestinalnecrosis, anaemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infections caused by <em>Pseudomonas</em> sp.: e.g. pseudomonassepticaemia, fin rot</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infections caused by <em>Flavobacterium</em> sp.: e.g. columnarisdisease, bacterial gill disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infections caused by <em>Edwardsiella</em> sp.: e.g. edwardsiellosis</td>
</tr>
</tbody>
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Note: In addition to the above, antimicrobials that are not critically important and are used in the Indian aquaculture sector include tetracycline, oxytetracycline, doxycycline, trimethoprim, sulfamethoxazole, cefalexin, furazolidone, chloramphenicol and nitrofurans.
Indian practices reflect the collective impact of the global guidance and national policy-related actions

Analyses the **global guidance of the Tripartite organizations** with regard to critically important antimicrobials reflect three key issues

**Key Issue 1:** Significant overlap in antimicrobials considered critical for humans and food-producing animals

**Key Issue 2:** Need for coherence in position on use of critically important antimicrobials in food-producing animals

**Key Issue 3:** Need for clarity and strong action on use of antimicrobials for disease prevention in food-producing animals
• The overall positioning of antimicrobials that need attention (to be conserved etc.) has reduced due to changes made in categorization/prioritization
  • Problem appears to be related to only a limited set of antibiotics
  • Frequent shifts in antimicrobials falling under HPCIA and CIA categories make it look like a less-serious exercise
  • What the stakeholders/nations are expected to interpret w.r.t. antimicrobials authorised only for humans to be made amply clear

• The basis of using for authorization of antimicrobials is not clear and can potentially mislead. It needs to be addressed and made clear
  • Antimicrobial authorisations can vary across countries; on-the-ground antimicrobial use practices can vary
  • Need to know/clarity on rationale to use authorisations, which national-level/global database were referred, what a country is expected to do in case a contradiction

• Macrolides (as well as certain penicillins) getting off the radar of HPCIAs /CIAs may not be a good idea
  • Extensively used in Indian food-animal sector as well as in human health; Becoming ineffective due to growing resistance

• Contradiction/confusion regarding the future animal use of antimicrobials authorised only for humans currently

• While crops are not being considered as part of non-human use, all caution must be exercised to avoid under-playing the problem of antibiotic misuse in crops and its connections with AMR
India should consider developing a road map and necessary policy framework to conserve the use of CIAs for both human and non-human sector initiatives

- Use of highest priority critically important antimicrobials for treatment should also be considered for phase-out. They should only be allowed in exceptional situations as a last resort.

- Prohibition of antibiotic growth promoters in food-producing animals (e.g., poultry sector).

- 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.

- Necessary focus should also be placed on promoting and incentivizing use of non-antimicrobial alternatives, biosecurity, hygiene and sanitation, and good animal-rearing practices.

- A long-term research agenda should be developed and implemented for non-antimicrobial alternatives and their effectiveness understood in managing diseases in animal farms. Programmatic interventions should be made for their greater promotion and adoption.

- Setting up systems and mechanisms to gather data and enhance understanding on critically important antimicrobial 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.

- 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.
Ethnoveterinary Medicine in the Indian Dairy Sector

Results: effectiveness of EVM

CSE assessment of the National Dairy Development Board’s EVM project implemented with technical support from Trans-Disciplinary University, Karnataka
## Mastitis Control Popularization Project: Overall results

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of unions/producer companies treating with EVM</th>
<th>Total number of cases treated across unions (in thousands)</th>
<th>Cure rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastitis</td>
<td>25</td>
<td>255</td>
<td>78.4</td>
</tr>
<tr>
<td>Fever</td>
<td>18</td>
<td>163</td>
<td>82.2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20</td>
<td>151</td>
<td>84.4</td>
</tr>
<tr>
<td>Indigestion</td>
<td>19</td>
<td>32</td>
<td>83.4</td>
</tr>
<tr>
<td>Wound</td>
<td>16</td>
<td>9</td>
<td>80.5</td>
</tr>
<tr>
<td>Bloat</td>
<td>18</td>
<td>7</td>
<td>76.0</td>
</tr>
<tr>
<td>Retention of placenta</td>
<td>17</td>
<td>6</td>
<td>71.2</td>
</tr>
<tr>
<td>Lumpy skin disease</td>
<td>8</td>
<td>3</td>
<td>66.2</td>
</tr>
<tr>
<td>Prolapse</td>
<td>17</td>
<td>2</td>
<td>69.6</td>
</tr>
<tr>
<td><strong>Sub-total</strong></td>
<td><strong>628</strong></td>
<td></td>
<td><strong>80.9</strong></td>
</tr>
<tr>
<td><strong>Other ailments</strong></td>
<td><strong>152</strong></td>
<td></td>
<td><strong>78.3</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>25</strong></td>
<td><strong>780</strong></td>
<td><strong>80.4</strong></td>
</tr>
</tbody>
</table>

- **Key four diseases** covering 77% (6.01 lakhs) of total cases; 81.2% cure rate
- 2016-October 2022
- 7.8 lakh disease cases across all 25 unions
- Overall 80.4% cure rate
- Nine diseases which are treated with antibiotics, 80.9% cure rate
- 4 diseases covering 77% of total cases; 81.2% cure rate
- In general, in most disease cases, 4 out of every 5 animal were cured using EVM.
What do these results mean?

- **Safe milk and milk products for consumer**
  - antibiotic free milk
  - cattle reared without antibiotics leading to reduction in AMR drivers/pathways through food and environment (AMR safe manure useful for growing organic movement in India)

- **Reduction in overall treatment expenses**
  - reduced consumption of antibiotics, veterinary medicines
  - reduced veterinary visits; farmer dependence on vets reduced

- **Improved livelihood of farmers**
  - reduction in loss of milk productivity
  - lesser rejection of milk at the district co-operative society level
Key problems w.r.t antibiotic use in food systems (animal systems in particular)...

• Problem 1: antibiotic use/misuse is very high
  – Due to non-therapeutic purposes (e.g. growth promotion), large animal population, ease of antibiotic availability/use as a cheap substitute

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• Problem 3: antibiotic use/misuse to prevent diseases
  – Whereas prevention with chemicals/antibiotics is no real prevention; but antibiotics pushed/promoted/justified as therapeutic use for prevention

• Problem 4 (the biggest): antibiotic use/misuse is fueling intensive practices to rear animals for food
High stocking density in intensive animal farms
Chemical-dependent Intensive food systems – drivers, characteristics and impacts; impacts are much beyond AMR

**Drivers of Intensification**

- Growing food demand (protein, animal protein)
- Growing population
- Growing incomes / purchasing power
- Urbanization
- Changing food habits, evolving taste
- Less people, less land to grow food
- Political mandate for exports, livelihood opportunities
- Availability of inputs - machines, feed, drugs and chemicals

**Characteristics of Intensification**

- Large-scale units with high stocking density of animals/birds/ fish
- Genetically selected similar breeds for productivity (not disease resilience); amplification of pathogens due to monoculture effect
- Kept under confined conditions and in close proximity; limited focus on animal husbandry; high stress
- Dependence on commercial feed, inputs (also known as animal feeding operations, factory farms)
- Often geographically concentrated; vertically integrated by large players; involves contract farming
- Industrial systems but considered agriculture; can bypass required regulatory attention

**Impacts of Intensification**

- AMR – through two key routes – food and farm waste; untreated manure/litter/waste water application to crops, fish ponds.
- Zoonoses, pandemics (e.g. swine flu)
- Food-borne illnesses, nutritional deficiencies
- Loss of biodiversity/agro-diversity/dietary diversity
- Natural resource degradation (water quality and reserves, soil fertility, nutrient availability etc.)
- Growing pest attacks; loss of disease resilience; increasing dependence on chemicals (pesticides, fertilisers) and high yielding varieties
- Land use changes, loss of forests; often diffuses boundaries b/w human-animal-wild-life
- Rising GHG intensive processes, vulnerability to climate crisis
- Small holder farmer livelihood crisis and distress
Post COVID-19 pandemic, One Health approach is gaining momentum to contain AMR

- Growing realization that the way we produce our food and the way we manage our environment is connected to our health and the health of planet

- Importance of One Health is becoming clear:
  - connected to development, trade, commerce etc.
  - only a true One Health AMR response on-the-ground is effective
  - A ONE HEALTH RESPONSE TO AMR has co-benefits related to:
    - Limiting zoonoses and pandemics
    - Ecological conservation
    - Livelihood security
    - Climate resilience

Quadripartite call to action for One Health for a safer world, March 27, 2023
There are real challenges in implementing the One Health approach... More so for emerging economies...

- **Limited resources and competing priorities** like – food, nutrition and livelihood security, access to life-saving medicines, primary healthcare and education

- There are **issues related to stakeholder ownership, denial, conflict of interest and apportioning of blame; and lack of coherent communication/ guidance**;

- **Limited understanding of connections so far**; no real estimates of cost of action as well as cost of inaction; issues around data sharing/interpretation

- **Complexity and scale of the problem and solution** also makes it hard to create public awareness and build pressure

- There are **hardly any established multi-sectoral mechanisms and implementation systems**
But we have also learned that we cannot afford AMR

- LMICs/emerging economies cannot first pollute, chemicalize and toxify the environment and then invest in clean up, because we cannot afford the high cost of cleanup
- We also cannot afford the high cost of treatment when basic drugs fail
- So, we have to do things differently...
We need to **Re-invent** ...the agenda/pathways

- Conserve what we have. Ensure that antibiotics critically important for human health are conserved. We call this the **Conservation agenda**.

- Ensure that we can continue to increase food production without the use of antimicrobials. The **Development agenda**. This needs food systems to be transformed. Unlearn the dependence on chemicals. Counter commercially-driven narratives.

- Ensure that the waste from pharma/other sources is tracked and contained. The **Environmental agenda**. This needs cost effective waste management.

- But all this will require serious re-invention of the way we do business with our food and environment. We have to prevent pollution and overuse of chemicals – **Prevention agenda**.
Thank you!

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