

CSE Workshop on
Roadmap to Reduce the
Use of CIAs in the
Indian Dairy Sector
Feb 25, 2022



CSE report: Use of critically important antimicrobials in the Indian Dairy sector

Conserving the Use of Critically Important Antimicrobials in Food-producing Animals

Gaps and Possibilities in Global Guidance and Indian Policy Framework
Deepak Bhati & Gursimrat K Sandhu, Sustainable Food Systems Programme, CSE

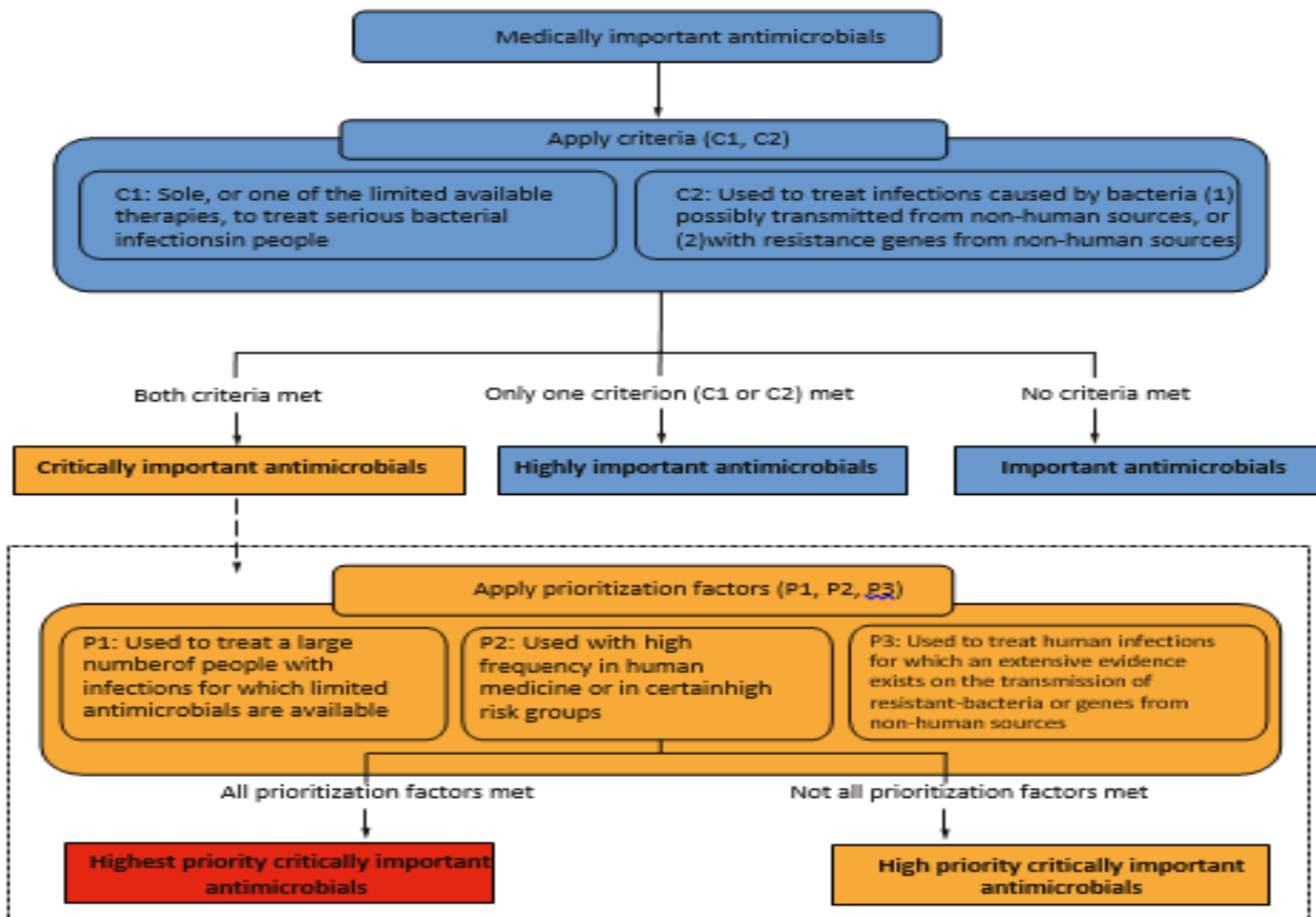
WHO's Critically Important Antimicrobials for Human Medicine (6th Revision, 2018)

- Total 178 antimicrobials
- 17 classes of CIAs
- Five out of which are HPClAs



Highest priority critically important antimicrobials
Cephalosporins (third-, fourth- and fifth-generation)
Glycopeptides (Also includes lipoglycopeptides)
Macrolides and ketolides
Polymyxins
Quinolones (also includes fluoroquinolones)
Critically important antimicrobials (other than HPClAs)
Aminoglycosides
Ansamycins
Carbapenems and other penems
Glycylcyclines
Lipopeptides
Monobactams
Oxazolidinones
Penicillins (antipseudomonal)
Penicillins (aminopenicillins)
Penicillins (aminopenicillins with beta-lactamase inhibitors)
Phosphonic acid derivatives
Drugs used solely to treat tuberculosis/mycobacterial diseases

Categorisation of medically important antimicrobials



AMR a big problem; against CIAs even bigger

Lancet study- Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

- Estimated **4.95 million deaths** associated with bacterial AMR; including **1.27 million deaths** attributable to bacterial AMR
- Resistance in *E.coli* against third-generation Cephalosporins; in *E. coli* against flouroquinones; in *K. pneumoniae* against third-generation Cephalosporins each caused 50,000-100,000 deaths

Most CIAs under EML, 2019 are categorized as “Watch” or “Reserve”

- 19 CIAs in AWaRe category; **Seven in Reserve category**: last-resort, highly selected patients; **11 in Watch category**: first-or-second choice antibiotics; only for specific and limited infective syndromes

WHO global priority pathogens list, 2017 includes pathogens resistant to CIAs; same is the case for India's PPL

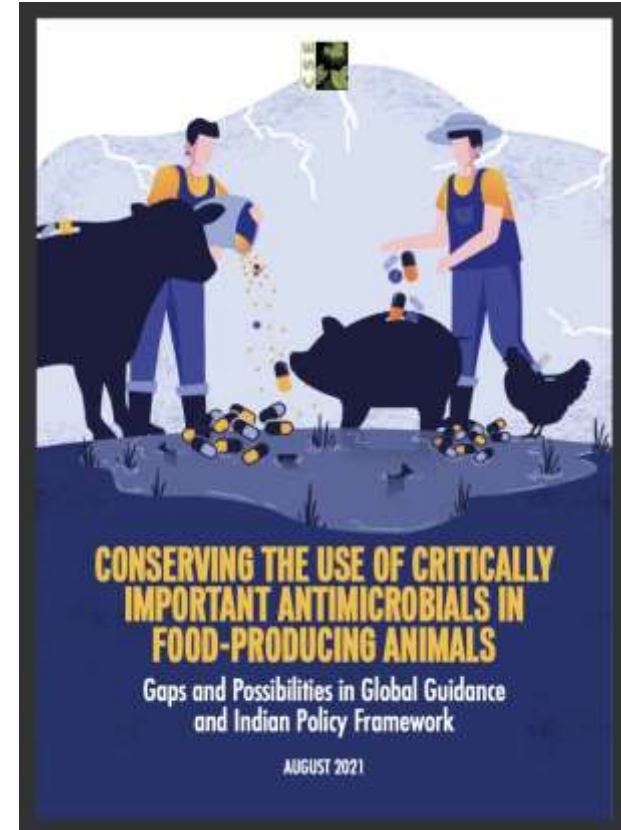


CSE Report of 2021: Conserving the use of critically important antimicrobials in food-producing animals

Highlights key issues with global guidance on CIA use in food-animals

- 1) **Significant overlap** in antimicrobials considered critical for humans and food- producing animals;
- 2) Need for **coherence in position** on use of critically important antimicrobials in food- producing animals; and
- 3) Need for **clarity and strong action** on use of antimicrobials for disease prevention in food-producing animals.

Highlights CIA use in the Indian dairy, poultry and aquaculture sector along with **policy gaps**; provides recommendations for a roadmap to reduce CIA use



Interpretation of global guidance on use of CIAs in food-producing animals

For easy reference words used to reflect position are “should not be used” and “could be used”. The exact wording is mentioned in text. 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

	WHO	OIE	FAO
Highest priority critically important antimicrobials (Quinolones and fluoroquinolones, third- and fourth-generation cephalosporins and colistin)			
Growth promotion	Should not be used	Should not be used	Should not be used
Prevention	Should not be used	Should not 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
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



Summary of CIA use: explains why dairy sector is potentially a big concern; more CIAs; large population; big size animals

Sector	CIA	HPCIA
Dairy	21 (6 Classes)	13 (2 Classes)
Poultry	14 (4 Classes)	8 (2 Classes)
Aquaculture	-	3 (1 Class)



HPClAs used in the Indian dairy sector

Antimicrobial	Antimicrobial class	Disease
Cefoperazone	Third-, fourth- and fifth-generation cephalosporins	Mastitis
Ceftiofur*		Mastitis, haemorrhagic septicaemia, anthrax
Ceftriaxone		Mastitis, haemorrhagic septicaemia; viral disease: foot and mouth disease
Cefquinome		Mastitis
Cefotaxime		Mastitis, haemorrhagic septicaemia
Ceftazidime		Mastitis
Ceftizoxime		Mastitis
Ciprofloxacin	Quinolones and fluoroquinolones	Anthrax, diarrhoea; viral disease: foot and mouth disease
Enrofloxacin*		Mastitis, haemorrhagic septicaemia, diarrhoea; viral disease: foot and mouth disease, infectious bovine rhinotracheitis
Norfloxacin		Diarrhoea
Ofloxacin		Diarrhoea
Levofloxacin		Mastitis
Moxifloxacin		Mastitis



CIAs used in the Indian dairy sector

Antimicrobial	Antimicrobial class	Disease
Amoxicillin	Penicillins	Mastitis; viral disease: foot and mouth disease
Ampicillin		Mastitis, black quarter, brucellosis; viral disease: foot and mouth disease, infectious bovine rhinotracheitis
Amikacin	Aminoglycosides	Mastitis, brucellosis
Gentamicin		Mastitis, diarrhoea; viral disease: foot and mouth disease
Streptomycin		Mastitis, black quarter, brucellosis, tuberculosis; viral disease: foot and mouth disease
Rifampicin	Ansamycins	Brucellosis, tuberculosis
Ethambutol	Drugs used solely to treat tuberculosis or other mycobacterial disease	Tuberculosis
Isoniazid		Tuberculosis



HPCIAs and CIAs used in the Indian poultry sector

Antimicrobial	Antimicrobial class	Disease
Highest priority critically important antimicrobials		
Ciprofloxacin	Quinolones and fluoroquinolones	Pullorum disease, fowl typhoid, colibacillosis, salmonellosis
Enrofloxacin*		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
Norfloxacin		Colibacillosis
Levofloxacin		Fowl cholera, Infectious coryza, pullorum disease, fowl typhoid, colibacillosis, necrotic enteritis, salmonellosis ; viral disease: Ranikhet disease
Erythromycin	Macrolides and ketolides	Infectious coryza
Tylosin*		Chronic respiratory disease; fungal disease: mycotoxicosis
Tylvalosin*		Chronic respiratory disease
Azithromycin		Fowl cholera
Critically important antimicrobials		
Amoxicillin	Penicillin	Necrotic enteritis; viral disease: Ranikhet disease
Ampicillin		Necrotic enteritis
Amikacin	Aminoglycosides	Infectious coryza, pullorum disease, fowl typhoid, colibacillosis, salmonellosis
Gentamicin		Pullorum disease, fowl typhoid, salmonellosis
Neomycin		Pullorum disease, colibacillosis, necrotic enteritis; fungal disease: aspergillosis, mycotoxicosis
Streptomycin		Fowl cholera



HPClAs used in the Indian aquaculture sector



Antimicrobial	Antimicrobial class	Disease
Highest priority critically important antimicrobials		
Ciprofloxacin	Quinolones and fluoroquinolones	For one or more of the following: Infections caused by <i>Aeromonas</i> spp.: e.g. motile aeromonad septicaemia, hemorrhagic septicemia, red sore, tail rot and fin rot, furunculosis
Enrofloxacin*		Infections caused by <i>Vibrio</i> spp.: e.g. vibriosis, intestinal necrosis, anaemia
Oxolinic acid		Infections caused by <i>Pseudomonas</i> sp.: e.g. pseudomonas septicaemia, fin rot Infections caused by <i>Flavobacterium</i> sp.: e.g. columnaris disease, bacterial gill disease Infections caused by <i>Edwardsiella</i> sp.: e.g. edwardsiellosis

Specific examples wherein CIAs used in the Indian dairy are recommended for human health in India

- **Cefoperazone** for treatment of obstetric sepsis during pregnancy, microbiologically infected burn wounds, infection of vascular catheters, ventilator-associated or hospital-acquired pneumonia, catheter-associated urinary tract infection in adults.
- **Ceftriaxone** for use in adults but is also in children for septicaemia, neonatal meningitis, severe pneumonia, complicated or severe UTI, antimicrobial coverage for paediatric surgical procedures.
- **Ciprofloxacin** for treatment of cornea infections, multi-drug resistant bacterial infections, acute inflammatory infective diarrhoeas, serious infected diabetic ulcers, infected burn wounds, severe acute pelvic inflammatory disease, acute prostatitis.
- **Amikacin** for pyelonephritis, pneumonia and in children for urinary tract infection, septicaemia or pneumonia in infants with severe sepsis.
- **Gentamicin** for endocarditis, obstetric sepsis during pregnancy, corneal infections, osteomyelitis, septic arthritis and in children for the treatment of neonatal meningitis, septicaemia, pneumonia.
- **Ampicillin** for infective endocarditis, group B streptococcal disease, septic abortion, peritonitis, vancomycin resistant enterococcus and neonatal meningitis, severe pneumonia, neonatal septicaemia.
- **Amoxicillin** is advised for the treatment of cellulitis, acute pharyngitis, rhinosinusitis, acute bacterial exacerbation of chronic obstructive pulmonary disease, asymptomatic bacteriuria (an obstetrics and gynaecology infection), obstetric sepsis during pregnancy, acute otitis media, acute rheumatic fever and other acute ear infection.



Gaps in policies, and guidelines on critically important antimicrobial use in India



Policy/guideline (stakeholder)	Key features and gaps
Gazette Notification dated July 19, 2019 (Ministry of Health and Family Welfare)	<p>Prohibited the sale, manufacture and distribution of colistin and its formulations in food-producing animals, poultry, aqua-farming and animal feed supplements.</p> <p>Gaps: No action/roadmap on other critically important antimicrobials.</p>
Farmer Manual (dairy sector) (Department of Animal Husbandry and Dairying)	<p>Recommends the use of four antibiotics (penicillin, gentamicin, streptomycin, and enrofloxacin) for treatment of various diseases.</p> <p>Gaps: All recommended antibiotics for use are critically important antimicrobials.</p>
Drugs and Cosmetics Act, 1940 (Central Drugs Standards Control Organization)	<p>The definition of drug mentioned is “all medicines for internal or external use of human beings or animals and all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals, including preparations applied on human body for the purpose of repelling insects like mosquitoes”.</p> <p>Gaps: The word “prevention” is found to be used to justify antimicrobial use for disease prevention. Another gap is that it does not refer to antimicrobials in feed, therefore antimicrobial for growth promoter use in feed gets out of its purview and has remained unregulated so far.</p>

Examples of global measures to restrict CIA use in food-producing animals

EU- Antimicrobial Advice Ad Hoc Expert Group (AMEG) of the European Medicines has classified antibiotics for veterinary use into **four categories**- A—Avoid, B—Restrict, C—Caution and D—Prudence;

Most classes of critically important antimicrobials are positioned under categories A, B and C

Effective Jan '22, EU ban **preventive use** of antibiotics in groups of animals and via medicated feed; as a **control treatment**; for **promoting growth**.

Some EU countries already had taken stronger action/measures to conserve CIAs such as cephalosporins, fluoroquinolones and macrolides; e.g. **France, Denmark, Netherlands, Sweden**;

USA- fluoroquinolones and cephalosporins- prohibited for extra label use



Recommendations for Indian policy framework to conserve use of critically important antimicrobials



India should consider developing a road map and necessary policy framework to conserve the use of CIAs in non-human sector (example – dairy sector)

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

- Use of critically important antimicrobials 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.
- HPClAs 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 HPClAs in other parts of the world. A careful consideration should be made on the basis of Indian data.



India should consider developing a road map and necessary policy framework to conserve the use of CIAs in non-human sector (example – dairy sector)

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.



India should consider developing a road map and necessary policy framework to conserve the use of CIAs in non-human sector (example – dairy sector)

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.



India should consider developing a road map and necessary policy framework to conserve the use of CIAs in non-human sector (example – dairy sector)

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.



For information, contact:

Amit Khurana
Director
Sustainable food systems programme
k_amit@cseindia.org

Rajeshwari Sinha
Programme Manager
Sustainable food systems programme
s_rajeshwari@cseindia.org

Gursimrat Sandhu
Deputy Programme Manager
Sustainable food systems programme
Gursimrat@cseindia.org

Deepak Bhati
Programme Officer
Sustainable food systems programme
deepak.bhati@cseindia.org

Website: www.cseindia.org
Email: cse@cseindia.org

