Action on Antibiotic Resistance

Antibiotic Use in Food Animals: India Overview

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ReAct

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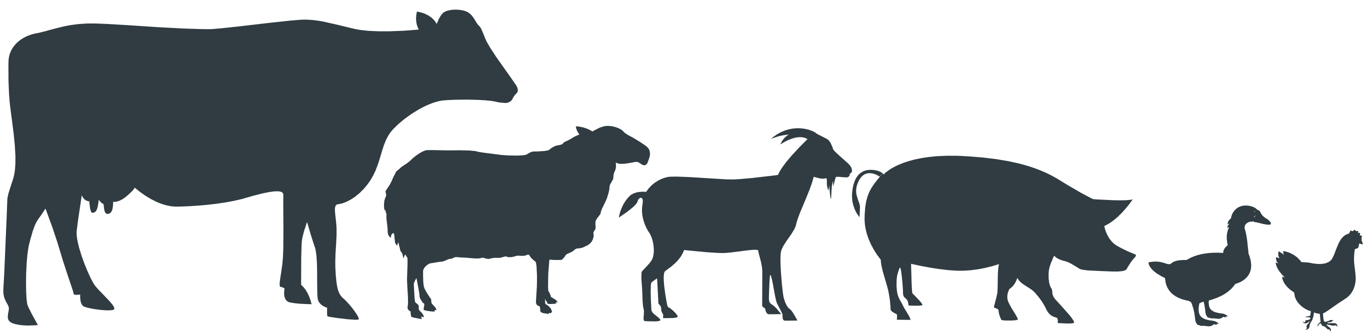

Antibiotic Use in Food Animals: India Overview

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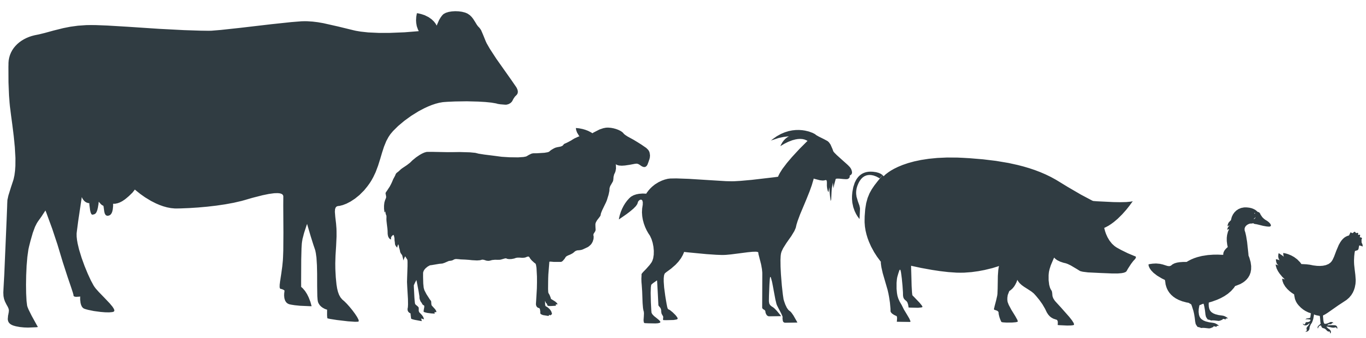


Preface

In recent years, India has emerged as a global hotspot for antibiotic resistance (ABR), with increasing resistance rates to most antibiotics in common pathogens and rising number of treatment failures.

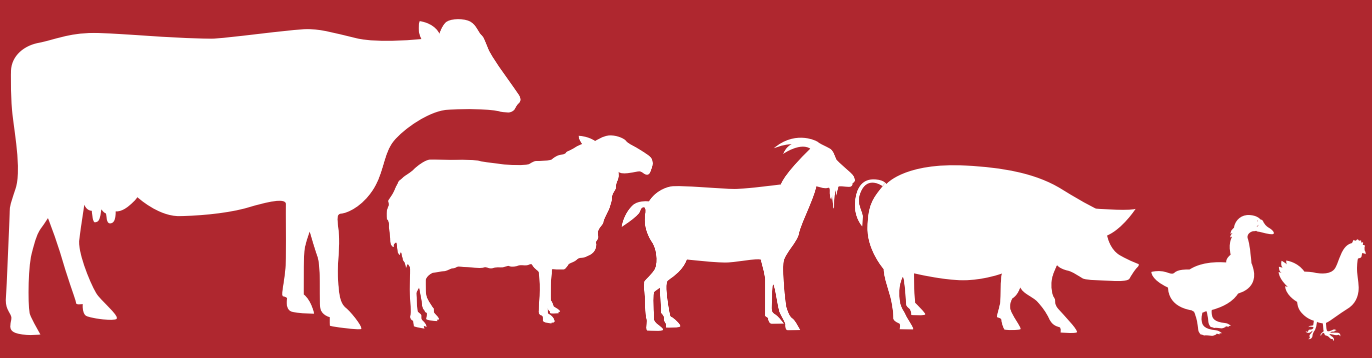
Apart from the human health sector an additional area of concern in India is the rampant use of antibiotics in the food-animal production sector. There are few regulations governing the use of antimicrobials for cattle, chicken, and pigs raised for domestic consumption in India, with no stringent implementation protocols even when there are regulations. Several studies show the use of antimicrobials as growth promoters is quite widespread. Non-therapeutic usage of antibiotics has been especially common in poultry production.

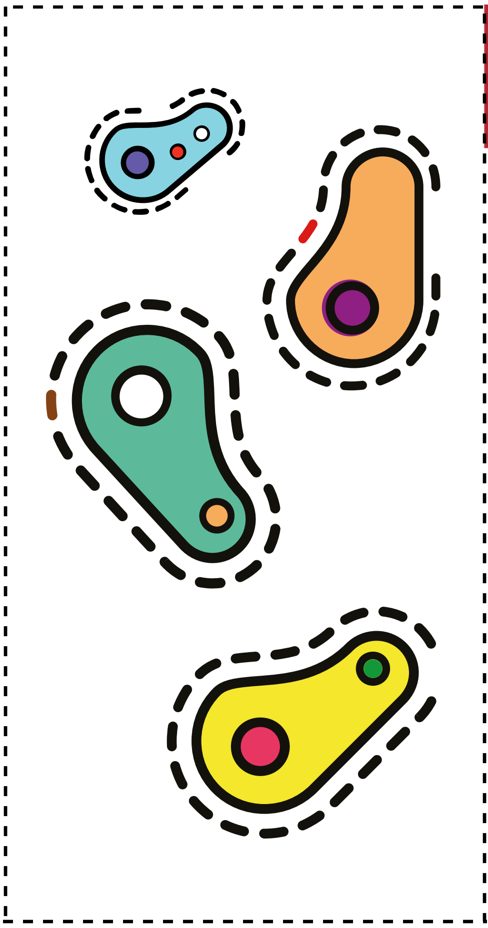
On the positive side, in recent years, the issue of ABR has gained high profile among Indian policymakers, with the announcement of a National Action Plan, setting up of a basic surveillance system, inter-sectoral cooperation initiatives and public awareness campaigns supported by official health agencies and civil society groups.

This booklet provides a brief round-up of the problems and suggested steps needed to reduce antibiotic use in food-animal production in India. It is meant as a very basic introduction to this vast subject and aimed at policymakers, media, health professionals and concerned citizen groups.

Section A

Understanding antibiotics and its use in food animals





What are bacteria?

Bacteria are tiny single-celled organisms that can be found all over the planet, including soil, water, plants, animals, humans - except places which have been sterilised.

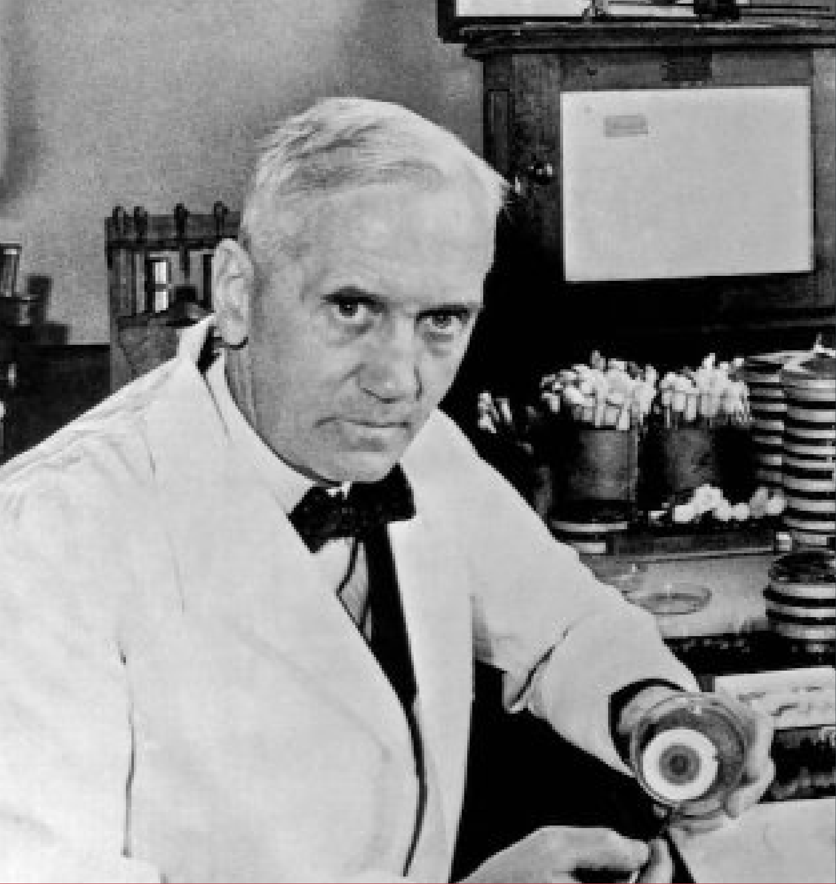
Bacteria are among the most abundant organisms on Earth. The majority of the bacteria play a positive role in nature. They help sustain the existence and continuity of all life forms on our planet.

Bacteria decompose and recycle dead animals and plants; digest sewage into simple chemicals; extract nitrogen from the air for plants; and play an essential role in production of food. Scientists and industries also utilise bacteria to produce a lot of useful products.

What if bacteria enter our bodies...

Nevertheless, not all bacteria are friendly. Pathogenic bacteria cause harm to our bodies. When bacteria manage to get through our first line of defence which is our body's skin and mucous membranes and enter our bodies, they make us sick. For healthy people, the immune system will detect the presence of foreign organisms and activate different types of white blood cells in the bloodstream. Neutrophils engulf and kill the bacteria; Eosinophils and monocytes swallow up the foreign organisms and particles; Basophils help to intensify inflammation to facilitate specialised white blood cells to reach the site of the injury, protecting against a bacterial infection from worsening.

Bacteria are believed to be the first life forms on Earth, which appeared about 4 billion years ago.



"When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic, or bacteria killer. But I guess that was exactly what I did."

Accidental Discovery of First Antibiotic - Penicillin

In 1928, Sir Alexander Fleming was investigating staphylococcus, a type of bacteria that causes boils (infection of hair follicle causing an inflamed pus-filled swelling on the skin). Before he left for vacation, he forgot to place the petri dishes containing staphylococcus culture into incubator. When he was back to his lab, Fleming noted that a mold called Penicillium notatum had contaminated his Petri dishes. After inspecting, he was amazed to find that the mold inhibited the normal growth of the staphylococci. He named this active antimicrobial substance "penicillin."

Discovery of Antibiotics?

Antibiotics are agents with biological activities to kill or inhibit the growth of bacteria. Ever since antibiotics were discovered eight decades ago, they have been used widely in modern medicine and are extremely effective against bacterial infections, which once used to be major cause to morbidity and mortality.

Antibiotics are not only used to treat bacterial infections in humans, but also used to protect the health and welfare of animals.

Type of Antibiotics

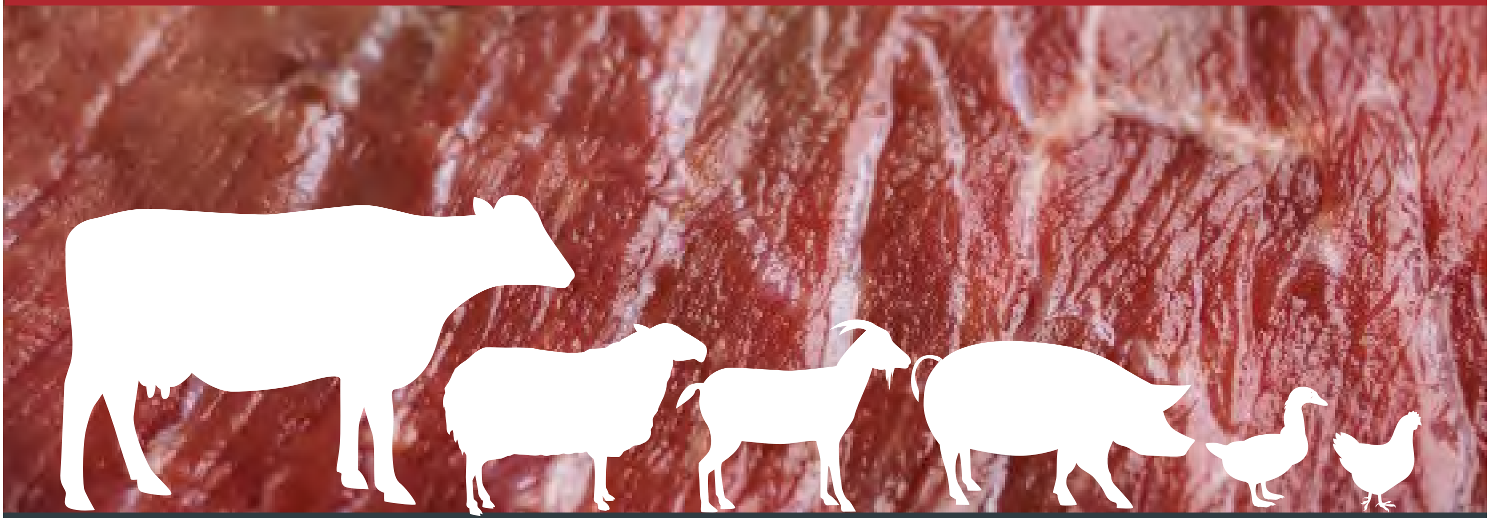
Bacteriocidal Antibiotics

Antibiotics that kill bacteria include aminoglycosides, beta lactams, fluoroquinolones, glycopeptides, lipopeptides, nitroimidazoles and nitrofurans.

Bacteriostatic Antibiotics

Antibiotics that inhibit bacterial growth include glycylcyclines, lincosamides, macrolides, oxazolidinones, streptogramins and sulphonamides.

Antibiotics use in food-animal production



What are food animals?

Animals that are raised and bred to produce food for human consumption such as eggs, meat and milk.

Example: Beef cattle, dairy cattle, goat, sheep, deer, pigs, broiler chicken, layer chicken and ducks

Why antibiotics are used in animals?

There are three main reasons why antibiotics are used by farmers:

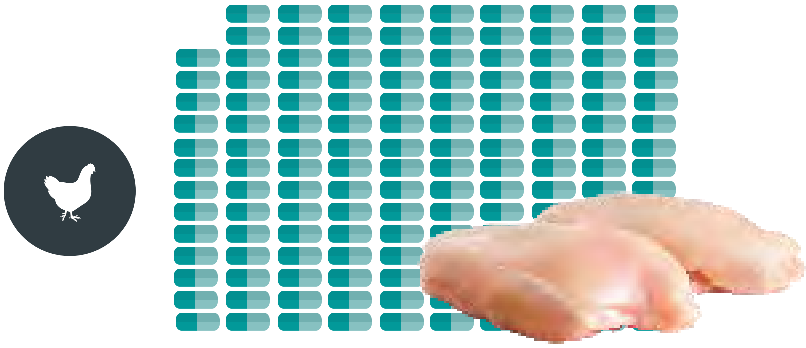
- As treatment for animals that show clinical signs of an infectious disease
- As metaphylaxis to treat a group of clinically healthy animals and minimise an expected outbreak of a disease or as prophylaxis to prevent those at risk from being infected
- As growth promoter to boost the weight of the animals.

Reference:
1. National Pharmaceutical Regulatory Agency (NPRA). Registration and Regulatory Control of Veterinary Products in Malaysia. ppt. Available at http://vam.org. my/home/wp-content/uploads/2017/11/Pn Asnida_V MP-Registration-and-Control.pdf. (accessed on 28 December 2017)

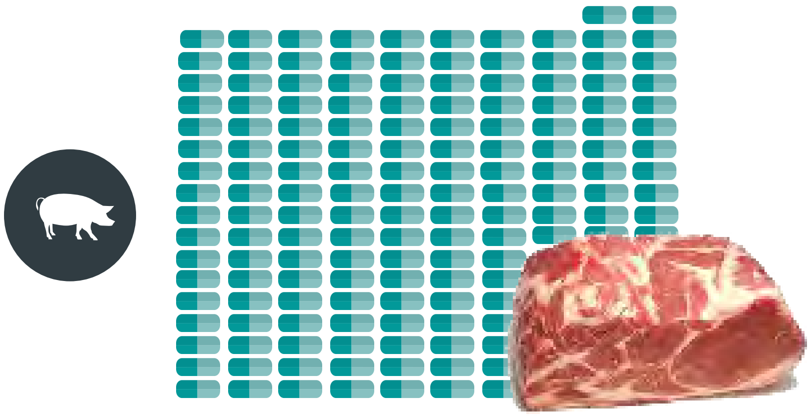
Global trends in antimicrobial use in food animals

Organisation for Economic Cooperation and Deveopment (OECD) estimates that the amount of antimicrobials used in food animals will escalate globally from 63,151 tons in 2010 to 105,596 tons by 2030 - an increase of 67%. The followings are the estimated global average annual consumption of antimicrobials to produce one kilogram of meat:

45mg of antimicrobials are used to produce 1kg of beef



148mg of antimicrobials are used to produce 1kg of chicken



172mg of antimicrobials are used to produce 1kg of pork

?

The term "antimicrobial" refers to any agent that kills microorganisms and inhibits their growth. An antimicrobial agent can be further categorised into groups according to the microorganisms it acts against. For example, antibiotics are used against bacteria whereas antifungals are against fungi.

Reference:
1. Laximinarayan, R., Van Boeckel, T., Teillant, A. 2015. Global Antimicrobial Use in the Livestock Sector. Organisation for Economic Co-operation and Development. TAD/CA/APM/WP(2014)34/FINAL.
2. Van Boeckel T.P. et. al. Global trends in antimicrobial use in food animals. PNAS. 2015: 112 (18); 5649 - 5654.

Top 5 countries with the largest shares of global antimicrobial consumption in food-animal production

In the United States, 80% of annual antimicrobial consumption is used in food animals.

1. China (23%)
2. The United States (13%)
3. Brazil (9%)
4. India (3%)
5. Germany (3%)

Reference:
1. Van Boeckel T.P. et. al. Global trends in antimicrobial use in food animals. PNAS. 2015: 112 (18); 5649 - 5654.

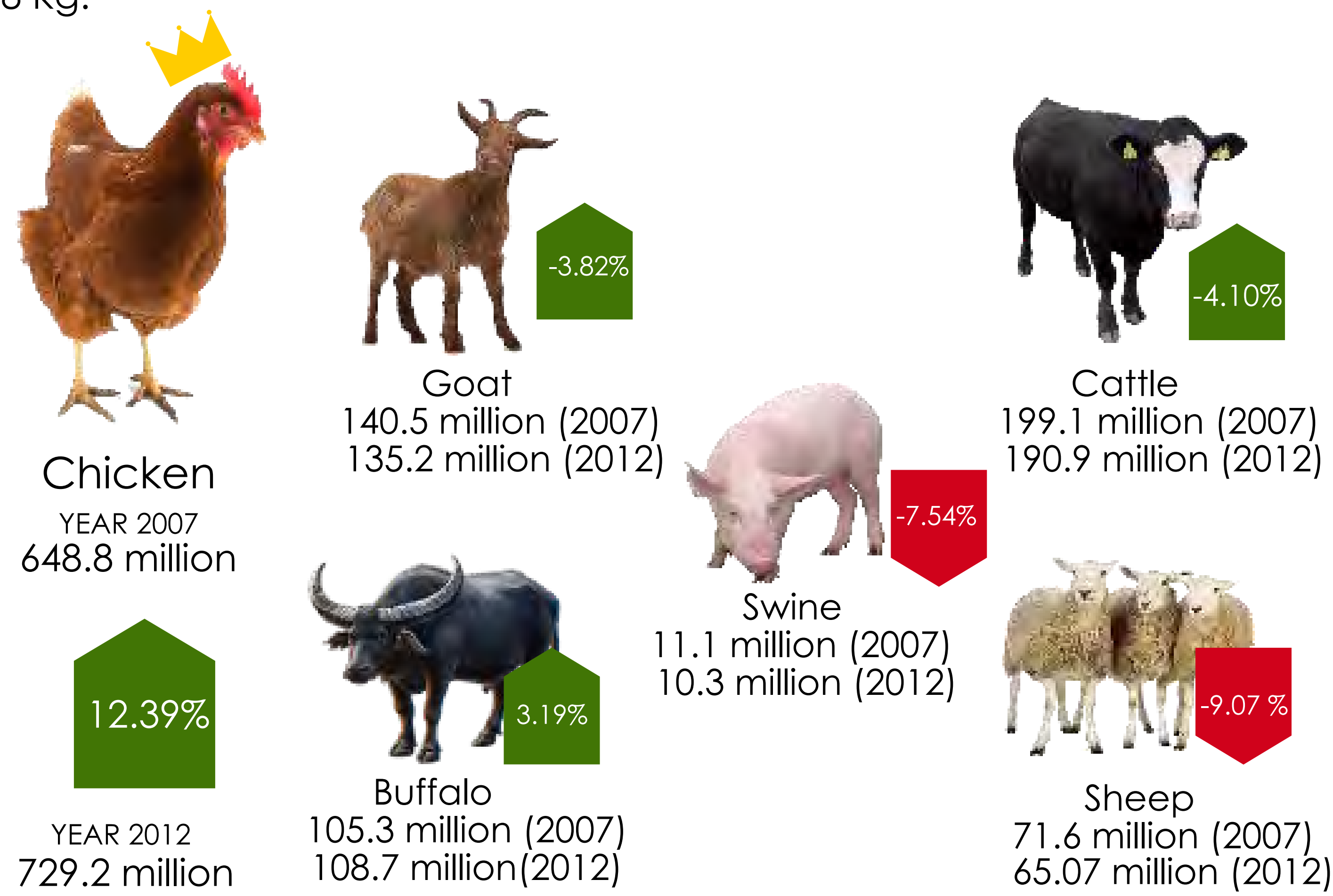
Livestock in India

India's livestock sector is one of the largest in the world, accounting for 11.6% of the world's livestock population.

India is the world's 5th largest meat producer, with an estimated production of around 7 million tonnes in 2015–16, of which 54% was red meat, the rest being poultry meat. India is also the world's largest producer of milk, the third-largest egg producer after China and USA and the fourth-largest chicken[1] producer after China, Brazil and USA.

Chicken is the most consumed meat in India as it is cheaper than other meats and is subject to fewer religious prohibitions or cultural taboos. Buffalo meat or carabeef is India's second most consumed animal protein after chicken meat due to its affordability. The annual per capita consumption of carabeef is around 2 kg, whereas for chicken it is 3.6 kg.

India's annual per capita fish and shrimp consumption is estimated at around 6 Kg, which is low in comparison to the global average of around 18 Kg.



Reference:
1. SCENARIO OF LIVESTOCK AND POULTRY IN INDIA AND THEIR CONTRIBUTION TO NATIONAL ECONOMY. M.M. Islam et al. International Journal of Science, Environment ISSN 2278-3687 (O) and Technology, Vol. 5, No 3, 2016;956–965.
2. Annual Report 2016–17, Department of Animal Husbandry, Dairying & Fisheries, Ministry of Agriculture & Farmers Welfare, Government of India (http://dahd.nic.in/sites/default/files/Annualpercent20Reportpercent202016-17.pdf, accessed on 3 December 2017).
3. ibid
4. Poultry Production in India - The Current Scenario. APEDA Agri Exchange. http://agriexchange.apeda.gov.in/news/NewsSearch.aspx?newsid=22055 (accessed on 11 December 2017).
5. GAIN Report Number: IN7034. February 2017. Prepared by Vijay Intodia, Mark Wallace. http://agriexchange.apeda.gov.in/marketreport/Reports/Livestock_and_Products_Semi_annual_New%20Delhi_India_3-2-2017.pdf (accessed on 19 March 2018).

Fisheries in India

In India, the annual fisheries production increased from 0.75 million tonnes in 1950–51 to 10.79 million tonnes in 2015–2016. Globally, the country now takes the second position, after China, contributing to 5.7% of global fish production.

Aquaculture constituted over a third of the country's total fish production. Specifically, freshwater aquaculture experienced over a tenfold growth from 0.37 million tonnes in 1980 to 4.03 million tonnes in 2010. This quantity is almost fully consumed on the domestic market, except for shrimps and freshwater prawns, which are mainly exported.

India's cultured shrimp production in 2014 was estimated at 426 500 MT while wild production was estimated at 450 000 MT. From 2004–2014, cultured shrimp production increased at a compound annual growth rate of 13%.

From 2010 to 2015, shrimp export volume increased at a compound annual growth rate of 15.8%. India's shrimp export volume reached 382 959 Tons in 2015, equivalent to US$33.19 billion.

With the rapid growth and demand for aquaculture, the industry faces challenges in the form of diseases such as white spot virus, enterocytozoon hepatopenaei (EHP), running mortality syndrome, and white feces. Any disease to the species might result in the loss of the complete culture. So as a preventive measure farmers started using antibiotics, and found good results. Finally this has resulted in over usage of antibiotics out of which several are unapproved antibiotics.

As a result of antibiotic residues being found in shrimp exports from India are banned in 4 countries. The Food and Drug Administration of United States also announced that they would increase the testing for aquaculture products.

The EU has also expressed concern over the use of antibiotics in Indian shrimps and shown its dissatisfaction with the response it got from the Indian authorities. In 2016, the EU changed the necessary number of fish exports inspected from 10% to 50%, among other actions taken, to control the export of antibiotic-contaminated shrimp to the EU.

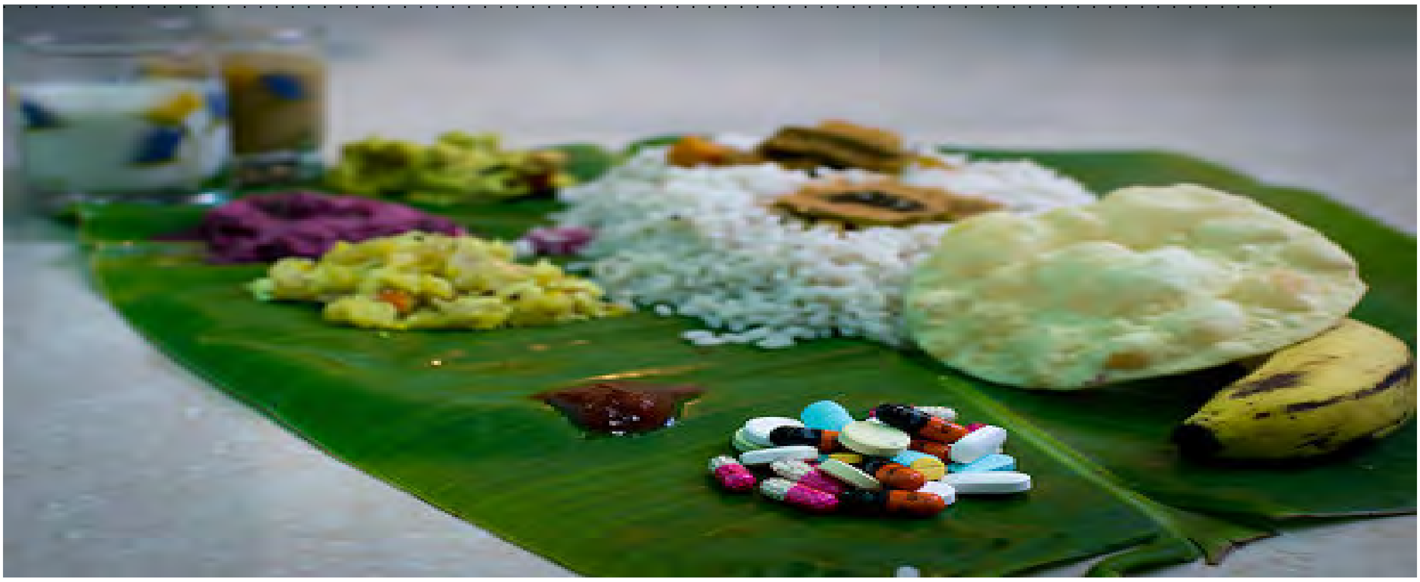
Reference:
1. Statistical Analysis of Fish Production in India, Chandasudha Goswami , Dr. V. S. Zade. International Journal of Innovative Research in Science, Engineering and Technology, IJIRSET, Vol. 4, Issue 2, February 2015. http://www.rroij.com/open-access/statistical-analysis-of-fish-production-in-india.pdf (accessed on 10 March 2018).
2. Aquaculture in India, Jelte de Jong. https://www.rvo.nl/sites/default/files/2017/04/aquaculture-in-india-report-2017.pdf (accessed on 20 March 2018).
3. FAO. 2014. National Aquaculture Sector Overview India, p. 13.
4. India's Shrimp Sector Grows Steadily. February 2017. GAIN Report Number: IN 7030. https://gain.fas.usda.gov/Recent%20GAIN%20Publications/India%E2%80%99s%20Shrimp%20Sector%20Growing%20Steadily_New%20Delhi_India_2-22-2017.pdf (accessed on 18 March 2018).
5. Ban Antibiotics – Save Indian Aqua culture Industry and Exports. 15 September 2017. Aquadeals. httidp://blog.aqua.deals/ban-antibiotics-save-indian-aqua-culture-industry-and-exports/(accessed on 20 March 2018).

Antibiotic use in livestock in India

Currently, there is little accurate data available in India on antimicrobial use in food animals or resistant infections linked to animals and its impact on public health. It is accepted though, that there is widespread use of antibiotics in food animals for prevention, treatment of infection as well as growth promoters. In particular, non-therapeutic usage of antibiotics has been especially common in poultry production and aquaculture.

A recent study estimating global antibiotic use in poultry, swine and cattle in 2010 indicates that India accounts for 3% of global consumption and is among the top consumers worldwide, along with China, the United States, Brazil and Germany. Projections for 2030 estimate an overall increase of about two-thirds in animal antibiotic consumption worldwide.

The use of antibiotics in animal feed, the study said, will increase by 82% in India by 2030. Their use in chickens, in particular, is expected to triple in India by 2030. The study found that globally penicillins, tetracyclines and quinolones are some of the most widely used antibiotics, with the use of these antibiotics higher in countries with meat-heavy diets.



The WHO's list of Critically Important Antimicrobials is made up of antibiotics which are critically important for human health and their use should be restricted in the veterinary sector. These include ampicillin, amoxycillin, cefadroxil, chlortetracycline, doxycycline, erythromycin, flumequinegentamycin, veneomycin, oxytetracycline, spiramycin, sulfadiazine, sulfadimethoxine.

Reference:
1. National Pharmaceutical Regulatory Agency, Ministry of Health Malaysia. List of Registered Veterinary Products (Updated November 2017). Available at http://npra.moh.gov.my/images/reg-info/Veterinary/2017/LIST_OF_REGISTERED_VETERINARY_PRODUCTS_2017.pdf (accessed on 22 December 2017)
2. Health Action International Asia Pacific (HAIAP), Third World Network Penang, Consumers' Association of Penang. Antibiotic Use and Antibiotics Resistance in Food Animals in Malaysia: A Threat to Human And Animal Health. 10 October 2013.
3. Van Boeckel TP, Brower C, Gilbert M, et al. Global trends in antimicrobial use in food animals. Proc. Natl. Acad. Sci. U.S.A.. 2015;112(18):5649-5654.

ABR in Poultry

In 2017 the Center for Science and the Environment, a non-profit based in Nnew Delhi released a study titled – ‘Antibiotic Resistance in Poultry Environment’. As part of the study it collected samples of litter and soil from in and around 12 randomly selected poultry farms in four key poultry-producing states in north India – Uttar Pradesh, Haryana, Rajasthan and Punjab.

A total of 217 isolates of three types of bacteria – E. coli, Klebsiella pneumoniae and Staphylococcus lentus – were extracted and tested for resistance against 16 antibiotics. Ten of these antibiotics have been declared Critically Important (CI) for humans by the World Health Organization (WHO).

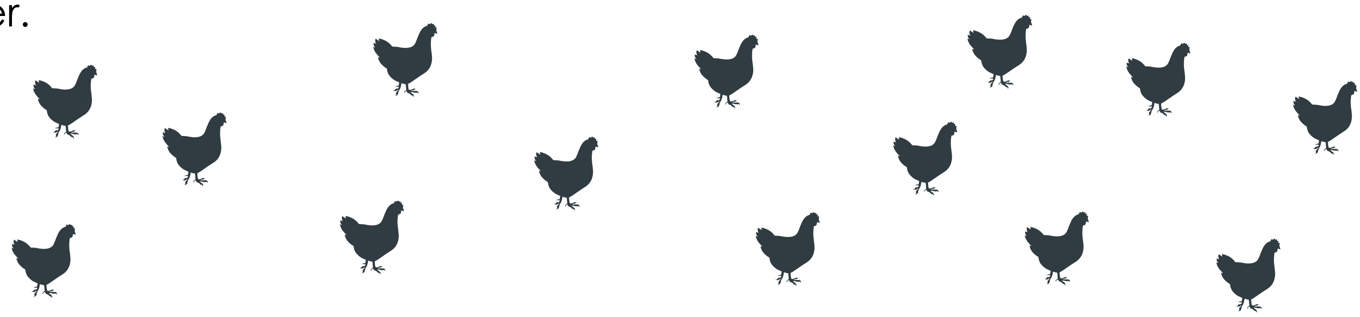
The study found that antibiotics were being used in these poultry farms, and that the litter was used as manure in neighbouring agricultural lands. As a control the study also collected 12 soil samples at a distance of 10 to 20 kilometers from the respective farms, where the litter was not being used as manure.

The study found that 100% of the E. coli, 92% of K. pneumoniae and 78% of S. lentus isolated from the poultry environment were multi-drug resistant. About 40% of E. coli and 30% of K. pneumoniae isolates were resistant to at least 10 out of 13 antibiotics against which these bacteria were tested for resistance.

Both E. coli and K. pneumoniae had very high resistance to antibiotics such as penicillins, fluoroquinolones, third and fourth generation cephalosporins and carbapenems, which is a last resort antibiotic used in hospitals.

Overall, the study found high degree of resistance to all critically important classes of antibiotics. Of the critically important antibiotics used in the study, five belonged to the ‘highest priority’ category and the rest were ‘high priority’.

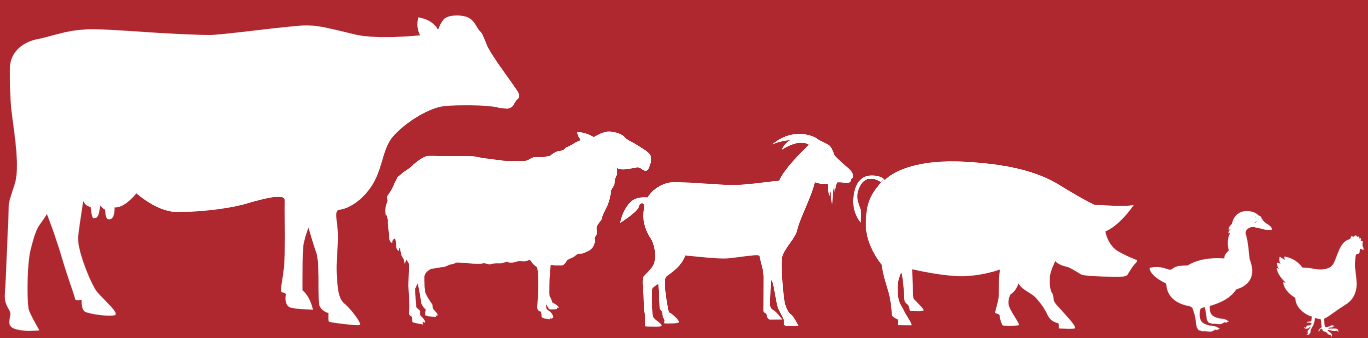
The CSE study also found strong similarity in the resistance pattern of E. coli from the litter and from agricultural soil in the surrounding areas where the litter was used as manure. This indicated that the multi-drug resistant E. coli being created in the poultry farms was entering the environment through litter.



Reference:
1. Chandra Bhushan, Amit Khurana, Rajeshwari Sinha and Mouna Nagaraju, 2017, Antibiotic Resistance in Poultry Environment: Spread of Resistance from Poultry Farm to Agricultural Field, Centre for Science and Environment, New Delhi
http://www.cseindia.org/userfiles/Antibioticspercent20npercent20Chickenpercent2030percent20july.pdf (accessed on 19 October 2017).

Section B

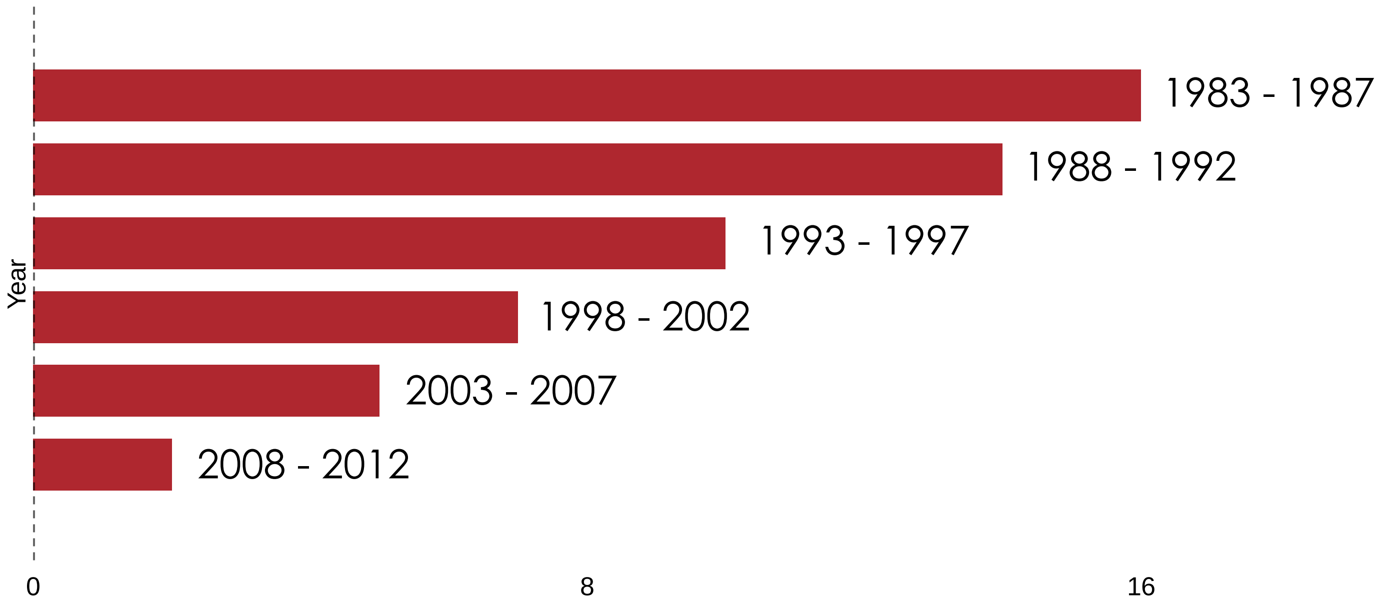
The emergence of antibiotic resistance



Antibiotics Begin to Fail

The post-World War II period witnessed a 'golden era' of antibiotic discovery. New antimicrobial agents were discovered, developed and marketed from the late 1940s to the early of 1970s. Nevertheless the discovery rate started dwindling 1980s onwards, leaving a discovery void. This is because of an increasingly arduous discovery process and declining interest by companies and government in the research and development of antibiotics due to less promising returns on investment (ROI). Around the same time, antibiotic resistance began to emerge due to primarily rampant misuse of antibiotics. Today antibiotic resistance could be detected nearly as quickly as newer antibiotics were developed.

Total Number of New Antibacterial Agents



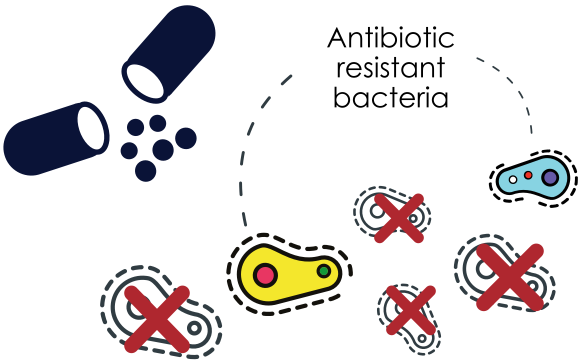
Similarly, overuse and inappropriate use of antibiotics in the food-producing animals have also given rise to antibiotic resistance in animal pathogens. Antibiotic regimes no longer work on sick animals. Worse still, the resistant bacteria can spread from animals to humans through the food chain.

The emergence of antibiotic resistance progressively undermines the viability of many antibiotics. Resistant bacteria cause thousands of deaths every year. If there[2] is no immediate and radical actions taken collectively against this trend, soon humans will be running out of options to save lives and the world will go backward to a pre-antibiotic era.

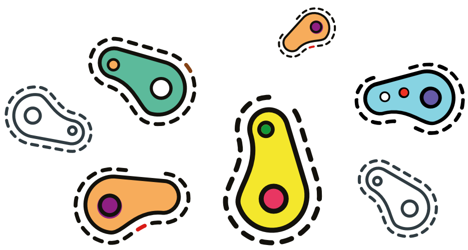
Reference:
1. The Epidemic of Antibiotic-Resistance Infections, CID 2008: 46 (15 January) Clin Infect Dis. (2011) May 52 (suppl 5): S397-S428.
2. WHO. Tackling antibiotic resistance from a food safety perspective in Europe, World Health Organisation, Geneva, 2011. 2011.

What is antibiotic resistance?

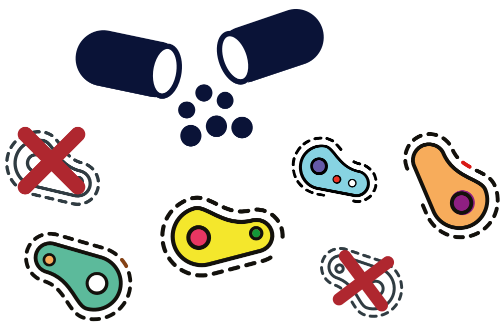
Antibiotic resistance (ABR) is the ability of some bacteria to protect themselves against the effects of an antibiotics. Clinical resistance means that a bacterium can grow in the antibiotic concentrations reached in the body during therapy resulting in treatment failure.



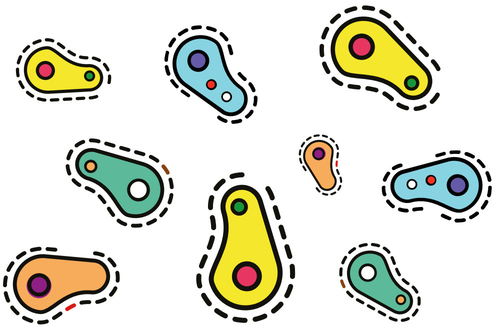
When an antibiotic is used it disables or kills only the susceptible bacteria but not the ones that have become resistant due to genetic mutations or variation.



Resistant bacteria now grow and multiply. Some bacteria even transfer their "drug-resistance" to other bacteria.



When antibiotics are used again they confront larger numbers of resistant bacteria.



Eventually antibiotic resistance results in treatment failure.

Reference:
1. ReAct. Antibiotic resistance. Available at https://www.reactgroup.org/toolbox/understand/antibiotic-resistance/ (accessed on 31 January 2018)

Spread of antibiotic resistance through food animals

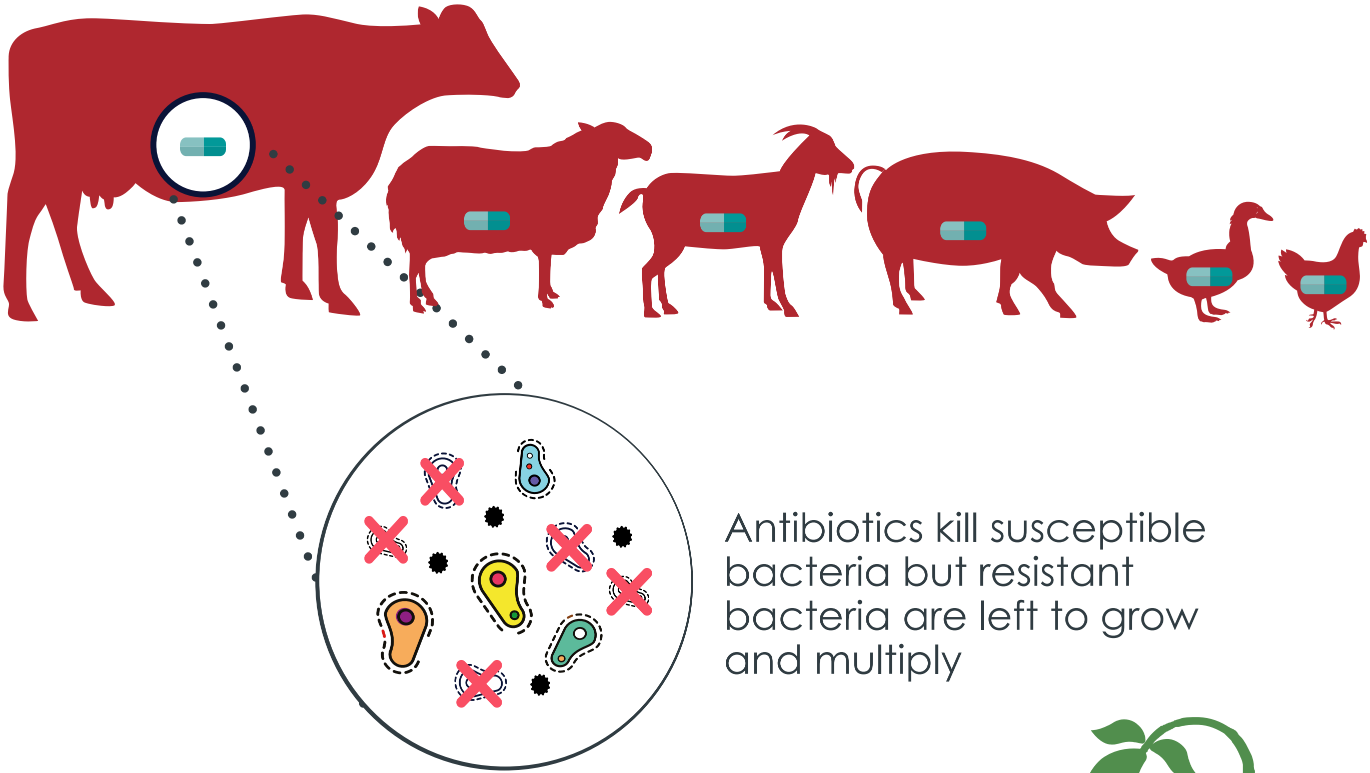
Many classes of antimicrobials that are used for humans are also being used in food animals. Apart from the use of these medicines for treatment of sick animas many food-animal producers also use them to promote growth or for routine disease prevention in crowded and unsanitary industrial conditions.

Such indiscriminate use of antibiotics accelerates the development of antibiotic resistant bacteria, which then escape and spread into communities. Farm and slaughterhouse workers, and veterinarians, who come in close contact with colonised or infected animals, are also at risk of carrying such resistant bacteria and passing them on to others.

Bacteria as well as antibiotic residues from food-animal production are also spread widely in the environment, mainly through manure, where it affects bacteria in the environment as well as in wild fauna.

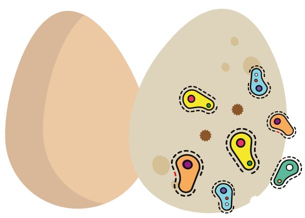
When people are exposed to these resistant bacteria from animals, this leads to resistant infections in humans. Multiple studies show an association between the use of antibiotics in animals and the spread of antibiotic resistance-related bacteria in humans.

Antibiotic resistance: from animals to humans

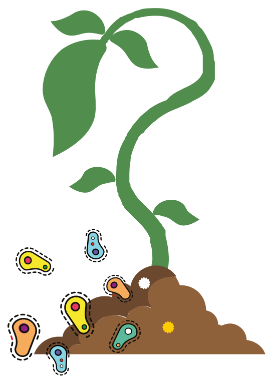


Antibiotics kill susceptible bacteria but resistant bacteria are left to grow and multiply

Resistant bacteria spread to animal meat



Resistant bacteria contaminate the eggs via animal faeces



Resistant bacteria contaminate environment e.g. soil and plants

Resistant bacteria can spread to humans from raw or inadequately cooked food when the raw materials are contaminated or cross-contaminated with other food and environment during preparation

Veterinary capacity in India

For the delivery of veterinary and allied services to the livestock keepers and other stakeholders, India has a sizable infrastructure available. There are an estimated 287 000 different kinds of service institutions, ranging from veterinary hospitals and polyclinics to slaughter houses and semen production centers in the country.

However, India's lack of veterinary human resources remains a major concern. In 2015, only around 34 500 veterinarians were employed for field services against the required 75 000, based on animal population and geographic coverage.

Apart from the veterinarians serving in health coverage programmes, there were about 2 500 serving in other organizations for managing livestock and poultry farms, defense services, banking, insurance, pharmaceuticals, immuno-biological units, feed industries etc. An additional 3 050 professionals were engaged in teaching institutions, research organizations and extension centers. It is estimated there is a shortfall of around 50% in field services as well as at teaching institutions and India will require over 100 000 professionals in veterinary, animal science and dairying by 2035.

Reference:
1. Human Resource needs in Veterinary and Animal Sciences. 2015. POLICY PAPER 2. National Academy of Veterinary Sciences (India) http://www.navsindia.org/downloads/files/n593137c054c72.pdf (accessed on 2 March 2018).

Surveillance of ABR in India

For a long time, antimicrobial/antibiotic resistance surveillance was limited to small-scale efforts by the state-funded Indian Council of Medical Research (ICMR) and some private agencies on a pilot basis. There was no systematic, national-level surveillance for ABR among human pathogens such as Salmonella, Shigella, Staphylococcus, Klebsiella, Acinetobacter etc. There was surveillance, however, of disease-specific pathogens as part of different national disease control programmes for tuberculosis, HIV, leprosy and kala-azar.

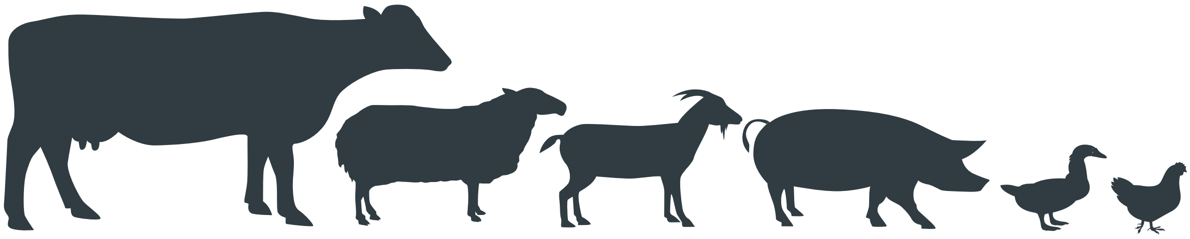
As part of the 'National Programme for Containment of AMR' (2012–2017), it was decided to establish a laboratory based surveillance system by strengthening laboratories for ABR in the country and to generate quality data on antimicrobial resistance for pathogens of public health importance.

The ICMR's Antimicrobial Resistance Surveillance and Research Network (AMRSN) is currently carrying out surveillance with a network of ten laboratories across the country. A total of 30 labs in state medical colleges are planned to be strengthened in a phased manner to carry out surveillance.

However, in the case of ABR in animals and food or antibiotics there is very limited surveillance. There are isolated studies, which have indicated high levels of ABR across animal commodities and systems, but they are yet to be unified under a nationally scaled programme.

While the Indian National Action Plan on AMR emphasizes a One Health approach, on the ground there is no such coordination in collection of data between the human and animal health sectors. Another weakness of the existing surveillance systems for ABR in India is that they do not account for antibiotic use.

The absence of a surveillance system that can establish the relationship between the antibiotic consumption patterns and emergence of AMR prevents the designing and evaluation of effective interventions. If such a link is established, then tracking antibiotic use or consumption data could also be used as a surrogate marker for the risk of potential AMR emergence.



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1. Standard Operating Procedures Bacteriology, 2015. https://icmr.nic.in/guidelines/Standard_Operating_Procedures.pdf (Accessed on 13 July 2016).
2. Mehndiratta PL, Bhalla P. Use of antibiotics in animal agriculture & emergence of methicillin-resistant Staphylococcus aureus (MRSA) clones: Need to assess the impact on public health. Indian J Med Res. 2014;140(3):339-344.
3. NATIONAL POLICY FOR CONTAINMENT OF ANTIMICROBIAL RESISTANCE, Directorate General of Health Services Ministry of Health & Family Welfare. 2011.

Antibiotic residues in food products

Honey

A study by the Centre for Science and the Environment found most honey brands sold in India contained varying amounts of antibiotics.

For the study, 12 samples were picked in Delhi, all well-known brands, including one each from Australia and Switzerland. Antibiotics found included Chloramphenicol and broad-spectrum drugs such as Ciprofloxacin and Erythromycin.

Milk

Presence of antimicrobial residues in milk has been reported from different parts of India, indicating wide antimicrobial use in food animal production in India.

One of the most common clinical issues encountered in the dairy farms is mastitis and milk from cows and buffaloes, affected by the disease, have been shown to contain bacteria, with a wide spectrum of resistance against commonly used antibiotics.

In some cases, multiple drug resistant bacteria have been seen to co-infect animals suffering from mastitis.

Fisheries

A survey in freshwater fish hatcheries of West Bengal was conducted in 2010–11 and the susceptibility of hatchery bacterial flora to selected antibiotics were studied. Aquadrugs such as oxytetracycline, althrocin, ampicillin, sparfloxacin, enrofloxacin, acriflavine, formalin, potassium permanganate, malachite green, tannic acid and herbal extracts were found to be used at varying levels for prophylactic as well as curative purposes.

Reference:
1.Busting the myth about 'pure and natural' honey. http://www.cseindia.org/cse-lab-study-busting-the-myth-about-pure-and-natural-honey-2022 (accessed on 18 October 2017).
FSSAI & BIS move to regulate antibiotics in honey. http://www.cseindia.org/fssai-bis-move-to-regulate-antibiotics-in-honey--4183(accessed on 18 October 2017).
3. Ramesh Kumar Nirala, Kumari Anjana, K.G. Mandal and Jayachandran, C. 2017. Persistence of Antibiotic Residue in Milk under Region of BiharInt. J.Curr.Microbiol.App.Sci. 6(3): 2296–2299.
4. Bharathkumar G and Jawahar Abraham T. Antibiotic susceptibility of Gram-negative bacteria isolated from freshwater fish hatcheries of West Bengal, India. July 2011. Indian Journal of Fisheries 58(3),

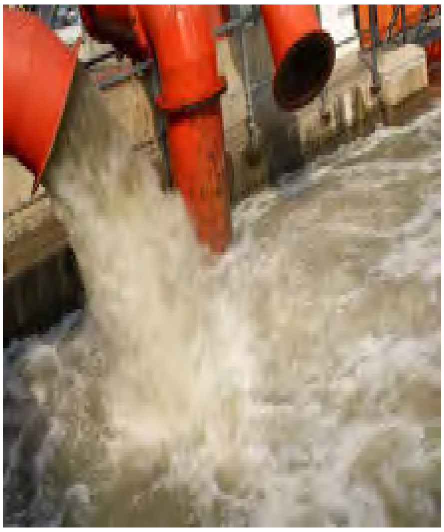
With its large domestic drug industry, India is also facing the problem of pollution from antibiotics production facilities in different parts of the country.

Antibiotics, when released into water bodies and the environment, are capable of stimulating bacterial resistance that is then transferred to human commensal and pathogenic bacteria.

In 2007, Swedish researchers reported very high emissions of pharmaceuticals from drug manufacturers at an industrial estate in Patancheru, near Hyderabad, India that had around 90 manufacturing units. The treatment plant from the estate released drugs in its effluent water at levels sometimes equivalent to the high doses that are given therapeutically. In particular, high levels of several broad-spectrum fluoroquinolone antibiotics were documented in both effluent and surface water, with ciprofloxacin being the most abundant.

In another study of the effluents released from the Patancheru effluent treatment facility at three sites downstream of the plant, researchers – using a DNA sequencing technique called 'shotgun metagenomics' to test effluent - found that resistance genes made up almost 2% of the DNA samples taken there.

The analysis identified very high levels of several classes of resistance genes as well as elements for horizontal gene transfer, including integrons, transposons and plasmids—which are bits of genetic material that let resistance genes jump from one bacteria to another.



An investigative report commissioned by Nordea Investment Management, one of the world's largest investment funds, accused some of the world's biggest pharmaceutical companies of ignoring "disturbing" environmental damage caused by the manufacturing they outsource to India.

The Nordea report said that water pollution caused by drug manufacturers in India, which supply many of the world's largest pharmaceutical companies, is having a harmful impact on local communities, leading to skin diseases and killing fish.

Reference:
1. Rutgersson C, Fick J, Marathe N, Kristiansson E, Janzon A, Angelin M, et al. Fluoroquinolones and qnr genes in sediment, water, soil, and human fecal flora in an environment polluted by manufacturing discharges. Environmental science & technology. 2014;48(14):7825–32. doi: 10.1021/es501452a pmid:24988042.
2. Carlsson, G. et al. Environ. Toxicol. Chem. 28, 2656–2662 (2009).
3. Kristiansson E. et al. PLoS ONE 6, e17038 (2011), http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0017038 (accessed on 19 October 2017).

Consequences of antibiotic resistance

Antibiotic resistance poses great threat to food safety and public health when the resistant bacteria spread from food animals to humans through the food chain. Antibiotics used in the first line treatment are no longer effective to eradicate common food-borne disease-causing bacteria such as Salmonella and Campylobacter.

Infections which used to be common become more difficult to treat

The length of hospital stay increases to, on average, more than 25 days

Treatment cost is higher

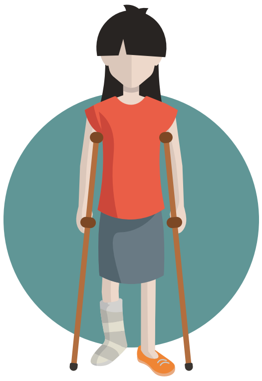
Risk of bloodstream infections and death is higher

Who are at risk?

In general, certain groups of people whose immune systems are week and who have an increased risk for getting infections are at a higher risk of being infected by antibiotic resistant bacteria.

Infants, especially premature babies

Seniors, particularly those living in long term care facilities



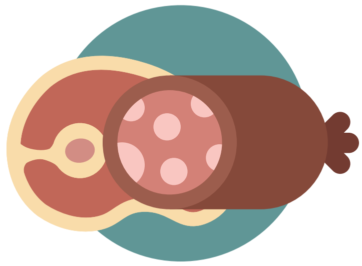
People with weakened immune systems due to illnesses or injury

Farmers who may have direct contact with sick animals

People who are living in a crowded and unhygienic place

People who do not practice good hygiene habits like hand hygiene

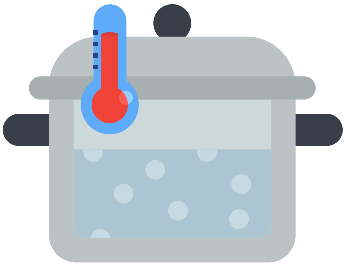
Personnel who work in healthcare facilities and day care centres such as doctors, nurses etc.



Slaughter house and meat processing plant workers or butchers

Reduce the chances of infection

Follow simple food safety tips: COOK, CLEAN, CHILL, SEPARATE [1]



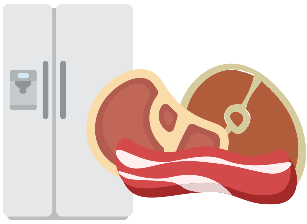
COOK

Food should be cooked to a safe internal temperature.

- 68°C for whole beef, pork, lamb, and veal (allowing the meat to rest for 3 minutes before carving or consuming) or 72°C for ground meats
- 74°C for for all poultry, including ground chicken and ground

CLEAN

- Wash hands before handling raw foods to avoid contamination especially after contact with animals or animal environment.
- Wash hands after touching raw meat, poultry or seafood.
- Wash the work surfaces, cutting boards, utensils and grill before and after cooking.



CHILL

Keep the temperature of the refrigerator below 4°C and refrigerate foods within 2 hours of cooking.

SEPARATE

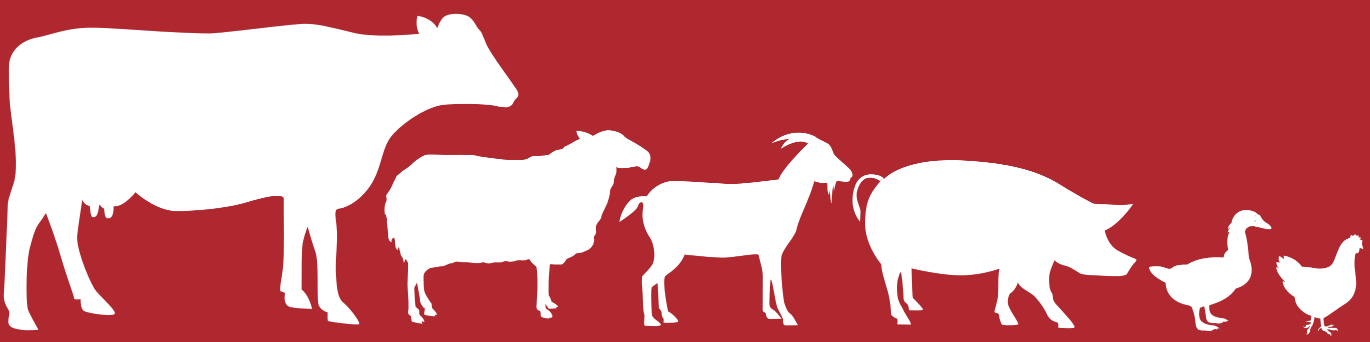
Bacteria from raw meat, poultry, seafood, and eggs may spread to ready-to-eat foods.

- Do not store raw and cooked food in the same space.
- Handle raw meats and ready-to-eat foods separately Use different cutting boards to prepare raw meats and any food that will be eaten without cooking.

Reference:
1. Centers for Disease Control and Prevention. Antibiotic Resistance, Food and Food-producing Animals. Available at https://www.cdc.gov /features/ antibiotic-resistance-food/index.html (accessed on 10 January 2018)

Section C

Responding to antibiotic resistance



National Action Plan on AMR

As one of the countries most affected by antimicrobial resistance (AMR), India is now taking strides to address the growing problem.

In 2017, Indian health authorities released their National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017–2021, that outlines the various challenges that need to be tackled to manage the phenomenon.

There are six key areas that the NAP-AMR has identified as being strategic priorities for Indian health authorities to take action on. These include:

- Improved awareness of AMR through effective communication;
- Strengthening knowledge and evidence through surveillance;
- Reducing the incidence of infection through effective infection prevention and control;
- Optimizing the use of antimicrobial agents in health, animals and food;
- Promoting investments for AMR activities, research and innovations; and
- Strengthening India's commitment and collaborations on AMR at international, national and sub-national levels.

Significantly, all the strategic priority areas identified by India's NAP-AMR clearly mention the animal, food and environment sectors as priority areas for strengthened surveillance, prevention of disease, regulation and optimizing use of antimicrobials. The NAP-AMR further promotes the One Health perspective of integrating human and animal health sectors.

Despite the new, comprehensive National Action Plan, in practice there have been few steps taken to implement the plan. For example, there is no money allocated yet specifically for implementation of India's multi-year National Action Plan on Antimicrobial Resistance (AMR).

The fact remains that India also does not have a stringently framed and implemented regulatory framework to limit the use of antimicrobials in livestock and food animals. The lack of regulations is particularly glaring when it comes to use of antimicrobials for non-therapeutic purposes, like growth promotion, or for routine prevention, both of which have been the drivers of antibiotic overuse at the farm level

Reference:
1. National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017 – 2021 , Government of India, April 2017.
2. https://www.cseindia.org/cse-slams-indian-poultry-industry-for-using-its-name-to-misrepresentfacts-8497 (accessed on 22 March 2018).

Guidelines on antibiotic use

Different state agencies however, from time to time, have issued guidelines on use of antimicrobials in food-animal production or recommended standards for permissible levels of antibiotic residues in food products. Some of these include:

The Second Amendment of the Drugs and Cosmetics Rules (2006) contains a list of 536 drugs that fall under Schedule H, which means they can be sold only based on the prescription of a Registered Medical Practitioner.

- In 2007, poultry feed specification from the Bureau of Indian Standards recommended that antibiotics with systemic action not be used as growth promoters, and phasing out of antibiotics that act in the gut in five years.
- In January 2012, the Central Drugs Standard Control Organization introduced a new norm that specifies the withdrawal period, or the timeframe for poultry, livestock and marine products to be kept off antibiotics before they enter the food chain. According to the new insertion eggs and milk products will have to be off antibiotics for seven days before they enter the food chain. The corresponding figure for poultry and livestock items will be 28 days.
- In 2013, a new category of H1 drugs was added through an amendment to the Drugs and Cosmetics Rules. Use of these drugs now, including many important antibiotics, requires a prescription. Pharmacists must provide separate prescription documentation subject to review, and non-compliance with the regulations can incur penalties.
- In 2014, the Department of Animal Husbandry, Dairying and Fisheries issued a circular to its officials across India, advising them to use antibiotics judiciously for treatment of all food producing animals and animal feeding. It also advised that the use of all antibiotics and hormones in animal feed should be stopped immediately.
- Another directive issued in January 2015 by the Food Safety and Standards Authority of India outlines certain principles that include limiting the use of antibiotics in livestock rearing.

Reference:
1. http://cdsco.nic.in/writereaddata/Advisorypercent20onpercent20antimicrobialpercent20resistancepercent202.pdf (accessed on 14 December 2017).

New standards

The Food Safety and Standards Authority of India FSSAI, which defined standards for fisheries products through the Food Safety and Standards Regulations (FSSR 2011) has amended this regulation in 2017 to include standards for all food-animal products.

Under the proposed Food Safety and Standards (Contaminants, Toxins and Residues) Amendment Regulation 2017 the tolerance limit of antibiotics and pharmacology active substances in food of animal origin will be clearly specified to ensure antibiotic residue in food from animals does not threaten human health. The amended regulation states that for a list of 21 antibiotics the tolerance limit, used in human beings and animals will be 0.01mg/kg for the following types of foods namely:

(i) All edible animal tissue;
(ii) Fats derived from animal tissues; and
(iii) Milk.

The amendments prescribe the maximum permissible limits of 21 antibiotics and 77 other veterinary drugs for use in food-animal production. The ministry has invited stakeholder objections and suggestions, which will be placed before the FSSAI scientific panel on residues of pesticides and antibiotics. The panel's recommendations will be considered by the scientific committee and then the food authority for approval, following which it will be notified in the Gazette of India.

Unfortunately, none of these recommendations have been formalized as laws so far. According to a critique of the situation even where there are rules prescribed there are no specifics, no timelines and no punitive

Reference:
1. http://foodsafetyhelpline.com/2017/11/fssai-drafts-regulations-related-tolerance-limit-antibiotic-residues-food/ (accessed on 15 December 2017).

Compared to other food-animal production sectors, there are many more rules and standards governing antimicrobial use in aquaculture production, especially because they are meant for exports.

The Government of India's Marine Products Export Development Authority (MPEDA) regulates aquaculture production, which includes shrimp. Through a variety of policies and activities, MPEDA supports aquaculture production, development of processing infrastructure and value addition, and establishing standards for quality control and market promotion.

MPEDA has set up 19 ELISA screening laboratories at various centers in the maritime states of India to conduct the pre-harvest testing/screening of the aquaculture products (shrimp/fish) for the presence of antibiotics residues like chloramphenicol & nitrofuran metabolites before the produce is harvested.

The MPEDA's list of 20 antibiotics and pharmacologically active substances banned for use in aquaculture include:

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

Reference:
1. http://foodsafetyhelpline.com/2017/11/fssai-drafts-regulations-related-tolerance-limit-antibiotic-residues-food/ (accessed on 15 December 2017).

Export related rules

The veterinary health certificate required for exports is issued by Government of India's Export Inspection Council (EIC) under Ministry of Commerce and Industry. The EIC regulates establishments that process fish and fishery products meant for export and also regulates traceability and antibiotic residue for shrimp products. The Council also monitors antibiotic residues in eggs, honey, milk and poultry meat, meant for export.

In 2002, new restrictions were placed for antibiotic residue levels in fresh, frozen, and processed fish and fishery products intended for export. The amendment includes maximum residue limits for tetracycline, oxytetracycline, trimethoprim, and oxolinic acid, and it prohibits the use of certain antibiotics in units processing all types of seafood.

In 2003, through an amendment to an existing law regulations were introduced on antibiotic residues in eggs and egg products. Maximum Residue Limits (MRL) for antibiotics in food products consider an acceptable daily intake, based on an assumed average daily intake, with a margin of safety.

In 2003, order S.O. 1227(E) prohibited the use of 'antibacterial substances, including quinolones' from the culture of, or in any hatchery for producing the juveniles or larvae or nauplii of, or any unit manufacturing feed for, or in any stage of the production and growth of, shrimps, prawns or any other variety of fish and fishery products without authorization from qualified veterinary surgeons or fishery scientists.

In addition, this order bans the following antibiotics from feed, treatment, or use in any stage of production of egg powder for export: chloramphenicol, dimetridazole, metronidazole, nitrofurans, including metabolites of furazolidone and nitrofurazone.

Monitoring

The Ministry of Health and the Drug Controller General of India have responsibility for enforcing regulations related to food safety and the quality and use of antibiotics for both humans and animals in India.

State Drug Controllers also have some responsibilities. However, the absence of uniform regulations for dairy and poultry farming in India poses a serious challenge to the enforcement of rational use of antibiotics.

Anecdotal evidence also suggests a general lack of awareness in India about regulations for antibiotic use and an absence of routine testing, making it likely that consumers are receiving products with more than the maximum permissible level of antibiotic residues.

Within the Ministry of Agriculture, the Directorate of Marketing & Inspection runs the Agricultural Marketing Information Network (AGMARK). This organization certifies manufacturers of selected products, including eggs and chilled or frozen raw meat.

In the early 2000s, AGMARK began upgrading some of its laboratories to measure antibiotic residues in animal products. However, limits on antibiotic residues in animal products are not yet widely established as a part of AGMARK certification.

Reference:
1. http://agmarknet.gov.in/

Recommendations

Groups of health professionals such as the signatories of the Chennai Declaration and civil society organizations, like Center for Science and the Environment working on AMR have made recommendations on controlling the use of antimicrobials in the food-animal production sector, fisheries, aquaculture and to limit pollution of the environment. While they accept the appropriate use of antimicrobials for treatment of bacterial infections in animals as being legitimate they point out that their use purely as growth promoters and for some prophylactic purposes is both unnecessary and avoidable.

Their recommendations are aimed at reducing use of antibiotics without causing harm to either human or animal health.

Some of the recommendations include:

- Allocation of appropriate funds to implement India's National Action Plan on AMR 2017–2021.
- Studies to understand the economic, medical and social factors that are propelling the use of antimicrobials in food-animal production.
- Track rates of veterinary antibiotic use, resistance, and residues through a nationwide surveillance and monitoring system.
- Change incentives to discourage unnecessary antibiotic use in animals.
- Educate farmers, veterinarians, and consumers on the dangers of antimicrobial resistance.
- Phase out the non-therapeutic use of antibiotics in animals.
- Ban the use of critically important antibiotics in food-animal production.
- Set antibiotic residue limits for food products of animal origin.
- Implement washout periods between the use of antibiotics and animal slaughter.
- Frame biosecurity guidelines for food-animal producers.
- Promote alternative growth promoters where possible.
  Reduce overall demand for antibiotics, by improving sanitation and limiting use to instances where antibiotics can be effective.

Antibiotic Use in Food Animals:
India Overview