ICAR initiatives on AMR Surveillance: preparedness, laboratory networks and future plans

By

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ICAR

INDIAN COUNCIL OF AGRICULTURAL RESEARCH

Indian Council of Agricultural Research is an apex body for coordinating, guiding and managing research and education in agriculture including horticultural Science, fisheries Science and animal sciences in the entire country. With over **101** ICAR institutes and **73** agricultural universities.

The challenge now with ICAR is to ensure nutritional security to ever-growing population of our country with little potential for increase in cultivable land area, ensuing shortage of water and global warming.

Animal Science Institutes under ICAR

- There are 20 institutes under Animal Science Division of ICAR including two Deemed Universities:

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Animal Health Institutes of ICAR

) \ ., zatnagar
) , ukteswar/ , hubaneswar
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) ., engaluru
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hese institutes are undertaking animal health programmes working in the areas of development of diagnostics, prophylactics, vaccines, epidemiology based forecasting models, animal health management protocols, zoonotic diseases from one health perspective.

One Health Approach

- One Health is a concept which acknowledges that human health is interconnected with animals, fisheries agriculture and environment.

- Diseases can pass between animals and humans and indiscriminate and inappropriate use of antimicrobials can further drive antimicrobial resistance(AMR), even though judicious use of antimicrobials is required.

- AMR containment therefore requires close collaboration between human and veterinary, fisheries health and environment including wildlife.

Antimicrobial Resistance

Single biggest global threat to mankind's efforts in combating communicable diseases in human and animals

Antibiotics in animal production

- Modern animal production practices/intensified farming is associated with regular/inappropriate use of antimicrobials, potentially increasing selection pressure on bacteria to become resistant.
- The estimated global average annual consumption of antimicrobials per kilogram of animal produced Cattle: 45 mg/kg
- Chicken: 148 mg/kg
- Pig: 172 mg/kg
- At this rate it is estimated that between 2010 and 2030, the global consumption of antimicrobials will increase by 67%, from 63,151 tons to 1,05,596 tons.

Antibiotics and human health

- The presence of antimicrobial residues in aquaculture and animal products is harmful to the consumer.
- The development and spread of antimicrobial-resistant bacteria and resistance genes ultimately reach human food chain and causes severe economic losses.

- Even though Antimicrobial agents are essential to ensure human health, animal health, welfare, and food security------judiciously
- AMR challenges control of infectious diseases
- AMR compromises health security and damages economies
- Historical lack of coherent global approaches to prevention / containment Antimicrobial Resistance (AMR)
- The human, animal and plant sectors have a shared responsibility to prevent or minimise the development of antimicrobial resistance by both human and non-human pathogens: this requires effective stewardship.

National programme on AMR – activities

- AMR surveillance network (14 labs)
  - ICMR network
  - MoHFW/NCDC network – 10 labs(Four pathogens)
- Promote rational use of antibiotics as per
  (National Treatment Guidelines for antimicrobial use in infectious diseases)
- Hospital infection control
  (Hospital infection prevention and control guidelines)
- Schedule H1/ Schedule X to regulate sale of antibiotics
- Antimicrobial stewardship activities

AMR surveillance: India

- Surv system in Public health programmes for specific diseases/pathogens e.g. RNTCP, NVBDCP, NLEP, NACO
- GASP for Gonococcus (network of 15 labs)
- IndiaCLEN surveillance
  for Pneumococcus, *Haemophilus influenzae;* through invasive bacterial infection surveillance (IBIS) & community antimicrobial resistance study (CAMR)
- (INSAR) (2009-2012) network of 20 labs with WHO support
- MoHFW/NCDC : AMR surveillance network (10 labs)
- ICMR : AMR Surveillance Network (4 institutions/6 labs)
- Veterinary/fisheries/ agriculture sector proposed

The Bad Bugs we generally encounter in animals

- **Extended spectrum β-lactamase producers**
- **AmpC type β-lactamase producers**
- **FQS resistant *enterobacteriaceae***
- **XDR and hyper-virulent- *Klebsiella pneumoniae* and *K. oxytoca***
- **ESBL & ACBL producing ExPEC**
- Multiple β-lactamase producing KP and KO
- **Methicillin resistant *S. aureus* and *S. epidermidis* (MRSA/MRSE**
- **Mettalo-β-lactamase producering *enterobacteriaceae* (EC & KP)**
- **Vancomycin resistant and intermediate *S. aureus***

AMR agents in the eastern and north-eastern India (IVRI, Kolkata Studies)

Bugs	Occurrence (Sample positivity %)
ESBL producing Klebsiella pneumonia In organized poultry farm In bovine milk	16.2% (OD, JH, WB) (32/185) 10.14% (JH, WB, TR, MEG) (20/268)
ESBL producing Escherichia coli In organized poultry farm In bovine milk In bovine mastitis Almost, 20-30% of the ESBL-EC/KP are resistant to carbapenem Pigs	10.5% (OD, JH, WB) (18/178) 1.5% (WB, OD) (2/132) 10.2% (WB, TR, OD, JH) 6% (WB) (12/200)
NDM producing KP/EC	0.5% (Detected in bovine and canine only)
MRSA (Bovine milk)	3.35% (11/358)
MRCoNS (Bovine milk)	8.9% (42/358)
FQS resistant enterobacteriaceae	12.8% (JH, WB, OD, SK, TR, MEG) (46/658)

Multi-drug resistant ESBL producing enterobacteriaceae are commonly detected from animals (eastern India)

- The isolates were frequently detected in organized poultry and dairy farms as well as in backyard farmed pigs.
- Most of the isolates carried multiple ESBL genes.
- The genes *bla*CTX-M-15, *bla*CTX-M-9, *bla*SHV-12 and non ESBL gene *bla*TEM-1 were more common.
- Presence of multiple resistance gene cassettes (dfrA12 and aadA12) leads to MDR phenomenon. No ESBL in backyard poultry

Studies on antimicrobial resistance in Fishes (CIFT)

- Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected in 9.5% of 63 samples from different retail markets and aquaculture farms of Kerala.
- MRSA isolates belonged to SPA ridom types t002, t657, t334, t311
- Multi-locus sequence typing (MLST) of MRSA isolates revealed that the isolate which was t657 ridom spa type belonged to ST772 which is commonly called as Bengal Bay clone reported in many parts of India as community-associated MRSA in clinical infections.
- A new spa type of MRSA was identified and was assigned SPATYPE, t15669 in the RIDOM server.
- Antibiotic sensitivity profile of twelve MRSA cultures revealed that all the strains were multidrug resistant (MDR).
- MDR of the strains ranged from 3 to 8 classes of antibiotics.

Carbapenems resistance in *E. coli and Salmonella* *(CIFT Studies)*

- **Fifty two isolates of *Escherichia coli* and twelve isolates of *Salmonella* isolated from marine fish and freshwater fish were tested for their susceptibility to carbapenems namely meropenem, imipenem and ertapenem.**
- **A low percentage (3.9%) of *E.coli* showed resistance to meropenem.**
- **11.5 & 17% of *E.coli* and 8.3 & 25% of Salmonella showed intermediate sensitivity to meropenem and ertapenem, respectively.**
- **100% of *E. coli* and Salmonella were sensitive to imipenem.**
- **Meropenem resistant *E.coli* was also found to be resistant to other antibiotics such as ciprofloxacin, gentamicin, nalidixic acid, norfloxacin and tetracycline.**
- **The results indicate that carbapenem resistance in *E. coli* and *Salmonella* isolated from fish was marginal but nevertheless needs continuous monitoring.**

AMR Issues Aquatic foods

- Aquaculture accounts for 6.5% of all protein for human use
- Global aquaculture production increased in last 3 decades from 5 million to 63 trillion tons
- Global fish supply projected to 187 million tons by 2030
- Increased use of antibiotics in aquaculture including in India → Potential source of AMR to humans
- Insufficient regulations on use of Antibiotics in Aquaculture (matter of concern)

Advisory on use of antibiotics in foc

- Antibiotics/antimicrobial growth promoter – a major concern.
- AGP not to be allowed in feed or feed supplement.
- Prophylactic, metaphylactic or therapeutic use of antibiotics need to be done under the strict supervision of RVP.
- Identification of manufacturers to end users (for quantification of antimicrobial production and consumption).
- Use of alternatives like prebiotics, probiotics and phytotherapeutics.
- Appropriate bio-security measures for infection, prevention and control.

DADF, No: 102-74/204-Trade
02/12/2014

Other initiatives	Focal points
Bureau of Indian Standards – Poultry Feed- Specification – 5th revision 1374:2007	▪ Antibiotics with systemic action should not to be used as **AGPs in feed** (chloramphenicol, doxycycline, tetracycline, nitrofuran, furazolidone)
Food Safety and Standards (contaminants, toxins, and residues) Regulations, 2011	▪ **Maximum residue limits (MRLs) for four antibiotics** - tetracycline, oxytetracycline, trimethoprim, and oxolinic acid was set for sea foods including shrimps, prawns.
Circular regarding sub rule 3A of rule 97, Drugs and Cosmetics Rules, 1945, 2013	▪ The container of the medicine for treatment of food-producing animals shall be labeled with the **withdrawal period of the drug** for the species on which it is intended to be used. If the specific withdrawal period is not mentioned, it should not be less than 28 days for meat from poultry.
National Policy on containment of antimicrobial resistance - 2011 and National	▪ Address the need for **regulation for usage of antimicrobials in poultry** as well as the requisite labeling requirements in food ▪ Establishment of a **laboratory-based surveillance** system in the country

Expectations from Vety/Agri / Aquaculture Sector

- Create structure/system for national AMR surveillance
- Establish surveillance of antimicrobial use/Presence in Veterinary sector/Fisheries
- activities for raising awareness about AMR in animals
- Promote rational use of abs in Veterinary/fisheries sector/Agriculture sector
- Stop/Restrict use of Abs as Animal Growth Promoters(AGP)
- Strengthen regulations and possibly have separate regulations for use of Abs in Vety/Agri sector
- Strengthen Biosecurity/Biosafety in farm animals

Critical gaps

1. **No systematic epidemiological database** to identify the disease determinants or risk factors for drug resistant pathogens in livestock.

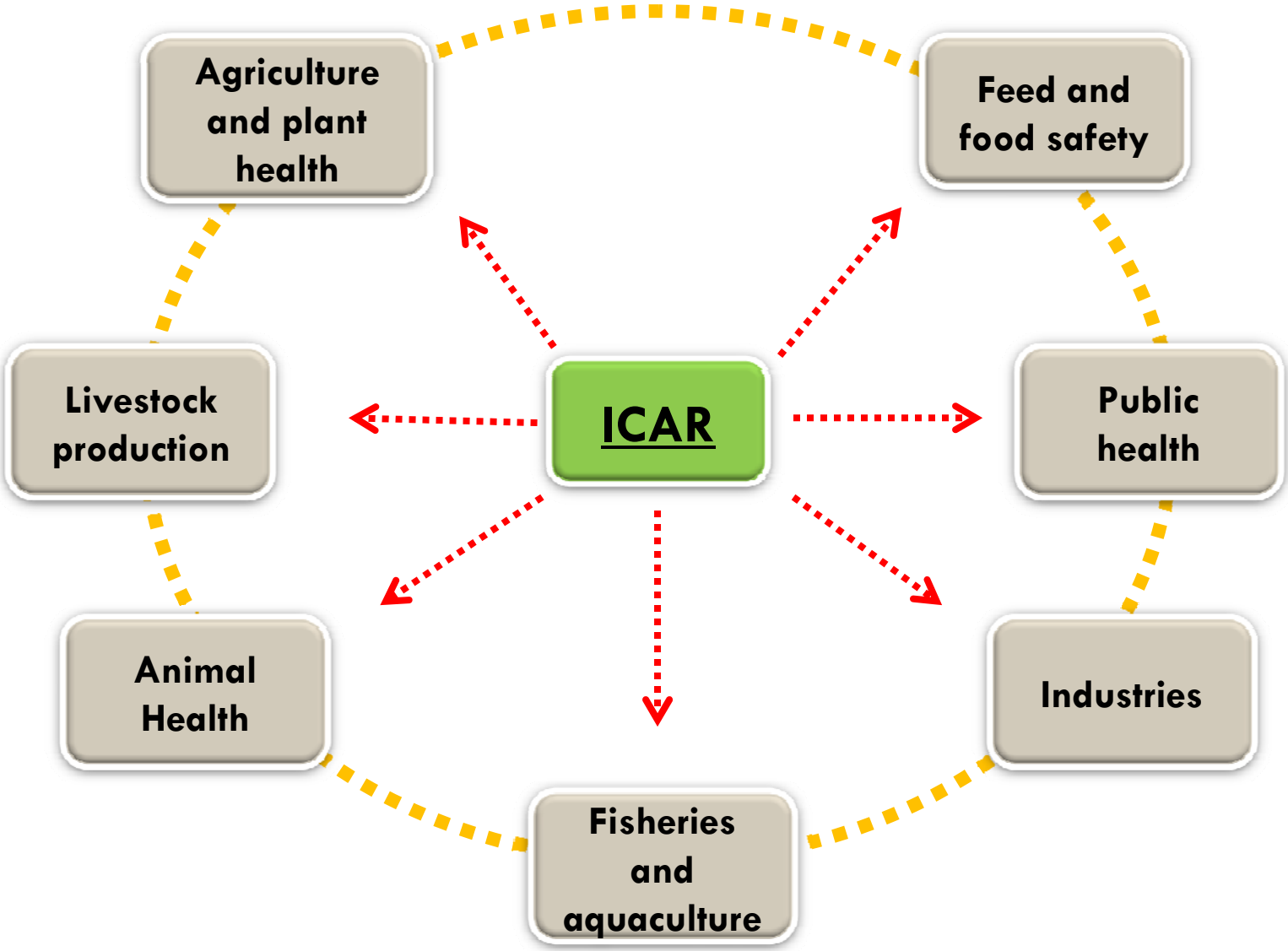
2. **Lack of information on genetic environment** of major ESBL/beta-lactamase genes which is urgently required to understand the transmission of such genes within or across the species.

3. **Limitation of current diagnostic tests** - frequent cause of false negative results.

What is required

- Need to develop the national laboratory systems by enhancing the cross sectoral partnership
- Time to share the experiences on laboratory preparedness and enhancing the networking on animal health/fisheries and human health labs
- Stewardship activities for Rational Ab use
- Strengthen implementation of regulations for Ab sale/use
- Increase awareness of AMR among all the stakeholders

ICAR to advise and advocate….



ICAR Strategies on combating antibiotic-resistant bacteria

- Check the emergence and the spread of resistant bacteria in agriculture, veterinary and fishery sector.
- To streamline the nation wide efforts to identify and report cases of AMR.
- To strengthen the surveillance mechanism for AMR.
- Development and use of rapid diagnostic tests for the identification and characterization of superbugs.
- To promote the basic and applied research and development for new antibiotics as well as other therapeutics and vaccines.
- To facilitate national and international collaboration, capacities for antibiotic-resistance prevention, surveillance, control, and antibiotic research and development.

INFAAR – an ICAR-FAO initiative

A nation wide network programme for AMR – will be operational shortly.

It aims to develop/generate -

1. **Scientifically validated data regarding AMR/AMU in agriculture through constant surveillance and monitoring**
2. **Diagnostics to detect MDR in food animals and fisheries.**
3. **Alternative therapeutics**
4. **Economic analysis**

Indian Network for Fishery and Animals Antimicrobial Resistance (INFAAR)

- **Origin**: meeting to establish a National Network of Veterinary Laboratories for Antimicrobial Resistance (AMR) in India organized by FAO-ICAR at Kolkata on 7-8 March, 2017
- **Objective**: to generate nation wide, structured, quality data through surveillance and research on AMR, specific to livestock and fisheries sectors for strengthening knowledge and better understanding of AMR
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INFAAR

- Nine Veterinary Institutes and Eight fisheries institutes form the initial member laboratories of the INFAAR. Every institute identifies two scientists for doing AMR work under the INFAAR network.

- ICAR-National Institute of Veterinary Epidemiology and Disease Informatics, Bengaluru (ICAR-NIVEDI) coordinates the overall technical and data management operations of the network.

- ICAR-National Bureau of Fish Genetic Research, Lucknow (ICAR-NBFGR) collaborates with ICAR-NIVEDI in coordinating technical activities of labs from fishery sector.

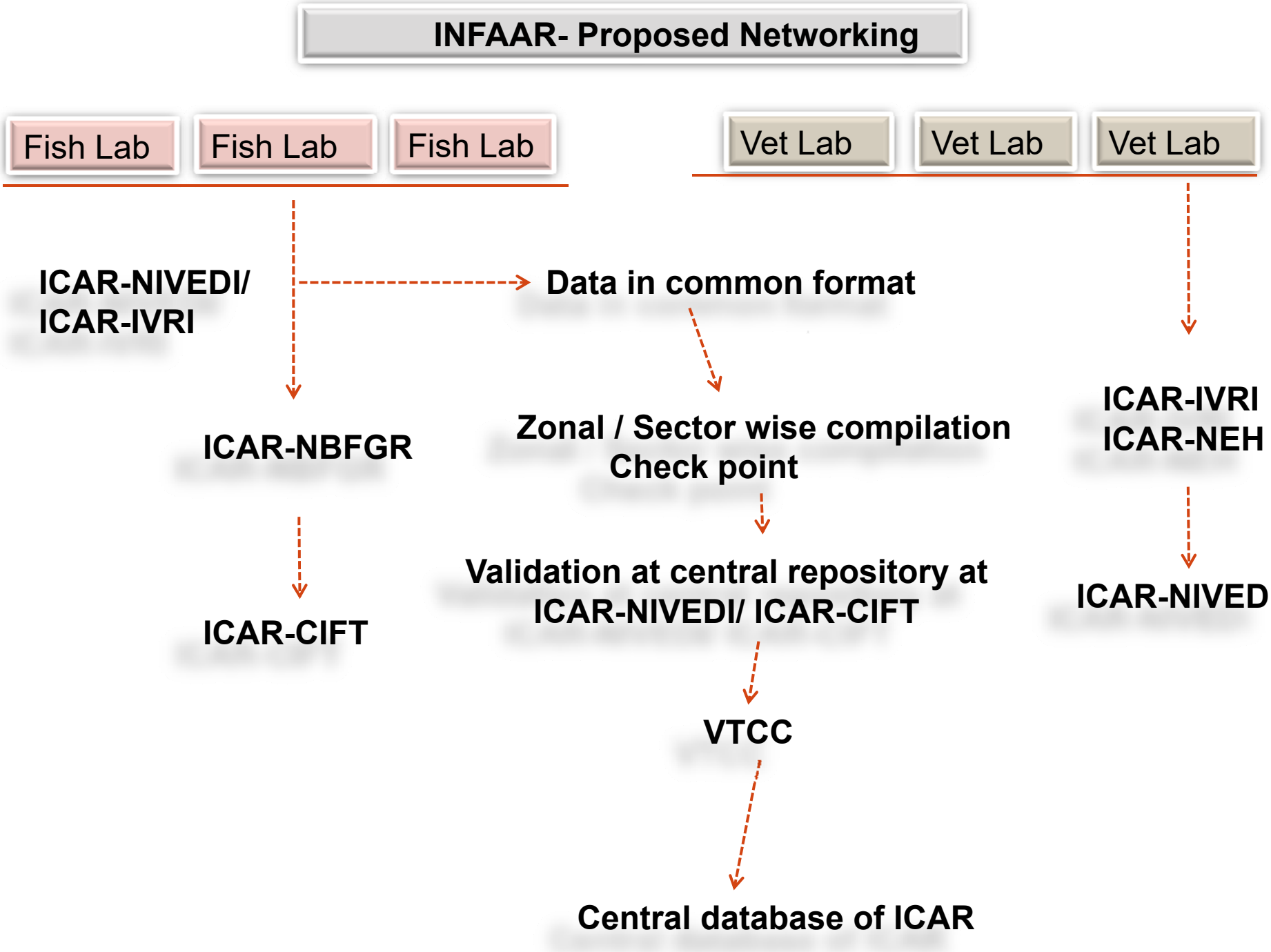
- The participation of the Veterinary and fisheries institutes in the network is through resources available with the respective institutions.

- INFAAR would be expanded to include laboratories (Universities) subject to their meeting the criteria on competence and willingness to agree to the mandate of the network.

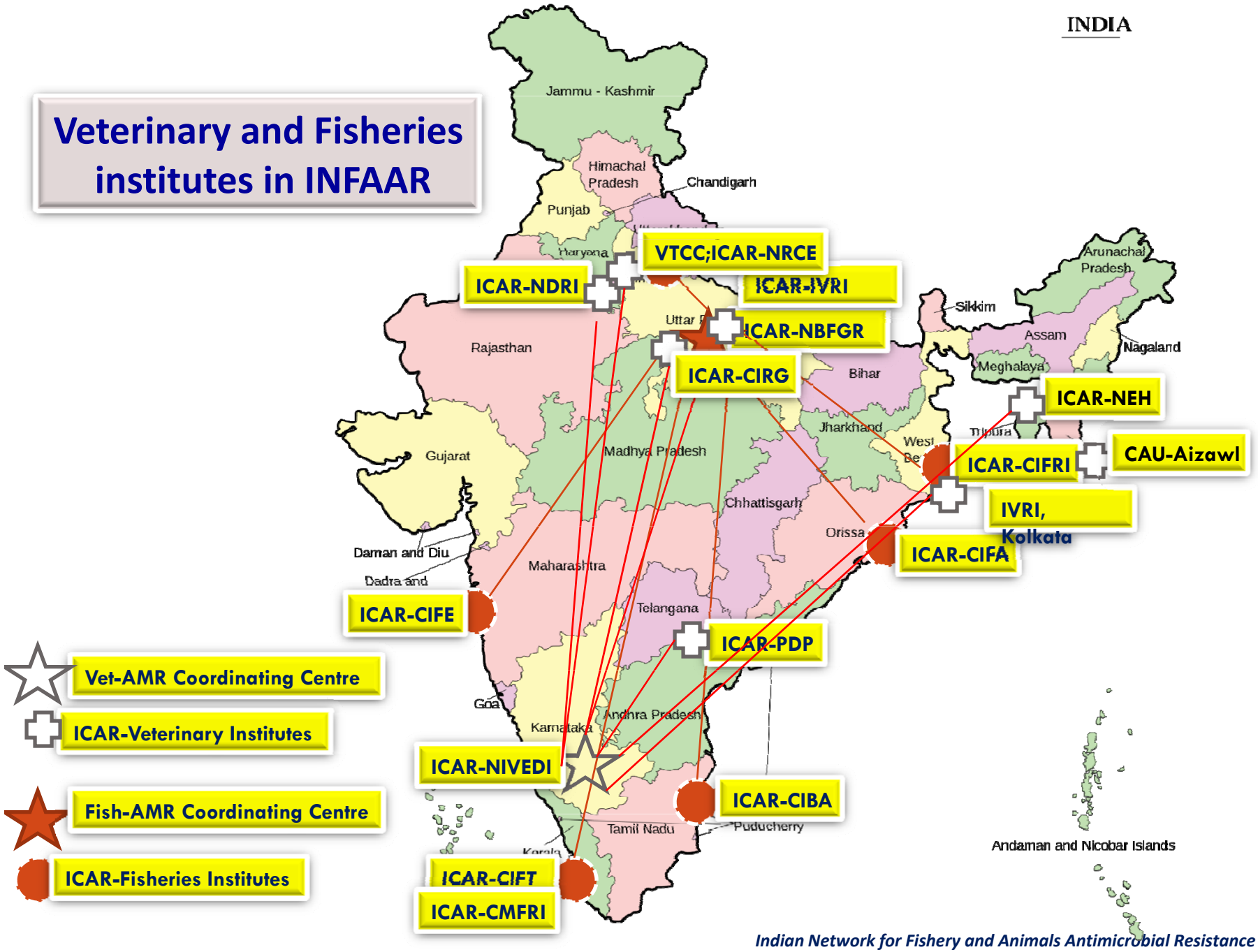
Work Plan

- Consolidated approach considering entire micro-biome of the agriculture ecosystem
- Develop and strengthen the antimicrobial resistance monitoring system in veterinary and aquaculture sector
- Strengthen the animal health monitoring system with better infection, prevention and control measures
- Implementation and conduction of long-term research network.
- Outreach and education/ awareness

- **Document and disseminate evidence based data regarding emergence of AMR in agriculture coupled with information on quantitative antibiotic drug with special reference to livestock and fisheries management practices.**
- **Identify the researchable issues to address recognized knowledge gaps and develop effective pragmatic mitigation strategies to maximize the effectiveness of antibiotics.**
- **Explore the possible novel strategic approaches to support better infection**


INFAAR- Proposed Networking
Fish Lab
Fish Lab
Fish Lab
Vet Lab
Vet Lab
Vet Lab
ICAR-NIVEDI/
ICAR-IVRI
Data in common format
ICAR-NBFGR
Zonal / Sector wise compilation
Check point
ICAR-IVRI
ICAR-NEH
ICAR-CIFT
Validation at central repository at
ICAR-NIVEDI/ ICAR-CIFT
ICAR-NIVEDI
VTCC
Central database of ICAR

Veterinary and Fisheries institutes in INFAAR



Indian Network for Fishery and Animals Antimicrobial Resistance (INFAAR)

Future Research Areas

- Transmission dynamics of antimicrobial resistant bacteria and resistance genes
- Source tracking of Antimicrobial resistant bacteria.
- Natural antimicrobials for aquaculture and seafood safety.
- Bacteriophages as bio-control agents
- Probiotic bacteria –are they carriers of resistance genes? or essentially required
- Break-points to be standarized.

Prediction of antibiotic resistance: time for a new preclinical paradigm

- Predicting the future is difficult, especially for evolutionary processes that are influenced by numerous unknown factors. This is what is required of drug developers when they assess the risk of resistance arising against a new antibiotic candidate during preclinical development.
- Traditional procedures that are used for the prediction of antibiotic resistance needs to be markedly improved by including a broader analysis of bacterial fitness, infection dynamics, horizontal gene transfer and other related factors.
- This will lead to more informed preclinical decisions for continuing or discontinuing the development of drug candidates.

Root of the proble

- Treatment by others than the registered veterinary personnel - practised extensively – increases this problem manifold.
- Use of substandard antimicrobials or under dosing associated with economic limitations of the farmers.
- Lack of veterinary laboratories with full scale diagnostics facility
- Lack of awareness among the farmers, owners, pharmacists, industry persons and to some scale among the veterinarians.
- Unavailability of a standard therapeutic guidelines to the registered veterinarians.
- Lack of bio-safety measures and vaccination strategy covering the nation wide animal population.

Research and surveillance imp

- Lack of committed research funding
- No established research network for AMR surveillance in animals in India
- Dearth in diagnostic methods for detection of AMR in animals which again needs to be standardized and synchronized for their uniform use in all the laboratories across the country.
- Unavailability of ready to use or simple diagnostic tools.
- Lack of knowledge and research for use of alterative medicines / methods in animal diseases to optimize the use of antimicrobials in animals.
- Lack of simple tools or mechanism for estimation of antimicrobial use and their residues in animals or animal products.

What we need to do?

- Judicious use of antimicrobials by registered clinicians only with ban on over-the-counter sales.
- Development of new antimicrobials or use of other alternative strategies – phage therapy.
- One Health approach
- We need a more specific and sensitive test for ESBLS/ACBL, MRSA/ VRSA in animals – laboratory friendly or handy phenotypic tools are preferable.

- Antibiotic residue need to be screened in foods of animal origin- Whether is it a concern in Indian context?
- Withdrawal period needs to be considered and antibiotic usage certificate may be introduced before marketing the animals or their products.
- Hospital or health care refusal must be prevented to contaminate animal food chain by not allowing their entry in pasture or aquatic bodies.
- Regular health check up of animal handlers and farm personnel.
- Demographic surveillance – does over populated or overcrowded place have any role?
- Analysis to determine the risk factor of animals for such colonization.
- Evolution or adjustment of the system to exist with such pathogens as in SCM

Enough food …. but without hidden contaminating antibiotics or resistant microbes in food or environment for sound public health.

भाकृअनुप
ICAR

THANK YOU…