International partnership for AMR: Challenges and Opportunities

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Outlines

- Introduction
- Challenges
- Global Action Plan on AMR and integrated surveillance
- International commitment and partnership for containment of AMR
- Quadripartite initiative for containment of AMR
- Take home messages

Use of antibiotics in animals (and plants) intended for food can result in resistant bacteria being transmitted to human through the food chain

The use of antimicrobial agents for food animal production is expected to nearly double in some countries by 2030 (Van Boeckel *et al.*, 2015).

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Resistance: Biological phenomenon

- Antibiotics are extensively used for **treatment, prophylaxis and growth promotion**
- The antibiotics also **kill innocent by standers bacteria** which are non-pathogens
- The use of antibiotics also promotes antibiotic **resistance in non-pathogens** too
- These non-pathogens may later pass their **resistance genes on to pathogens**

scientific reports

OPEN

High prevalence of *mcr-1*-encoded colistin resistance in commensal *Escherichia coli* from broiler chicken in Bangladesh

Shahana Ahmed[1], Tridip Das[2], Md Zohorul Islam[1,2,3,4], Ana Herrero-Fresno[1], Paritosh Kumar Biswas[2] & John Elmerdahl Olsen[1]

Front Microbiol. 2017; 8: 562.
Published online 2017 Apr 4. doi: 10.3389/fmicb.2017.00562

PMCID: PMC5378783
PMID: 28421056

High Prevalence of Colistin Resistance and *mcr-1* Gene in *Escherichia coli* Isolated from Food Animals in China

Xianhui Huang,† Linfeng Yu,† Xiaojie Chen, Chanping Zhi, Xu Yao, Yiyun Liu, Shengjun Wu, Zewen Guo, Linxian Yi, Zhenling Zeng, and Jian-Hua Liu*

Globally, 73% of all antimicrobials sold on Earth are used in animals raised for food. Van Boeckel et al., Science 365, 1266 (2019)

Since 2000, meat production has grown by 68%, **64%**, and 40% in **Africa, Asia**, and South America respectively - http://www.fao.org/faostat/en/#home

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Antibiotic use: Human health vs animal health

1. Self-medication	1. Use of antibiotic growth promoters
2. Patient compliance, i.e. under dose vs overuse	2. Withdrawal period or milk discard time – Food safety concern
3. Antibiotic sensitivity test	3. Only for companion animals
4. Over the Counter Sale	4. Same problem
5. Use of new and expensive drug	5. Economic factor plays a role
6. Life, duration of illness	6. Trade, prod. and food security
7. Counterfeit drugs - Major issue	7. Minor issue- Cost factor

Geographic distribution of antimicrobial resistance in LMICs

(A) P50, the proportion of antimicrobial compounds with resistance higher than 50%.

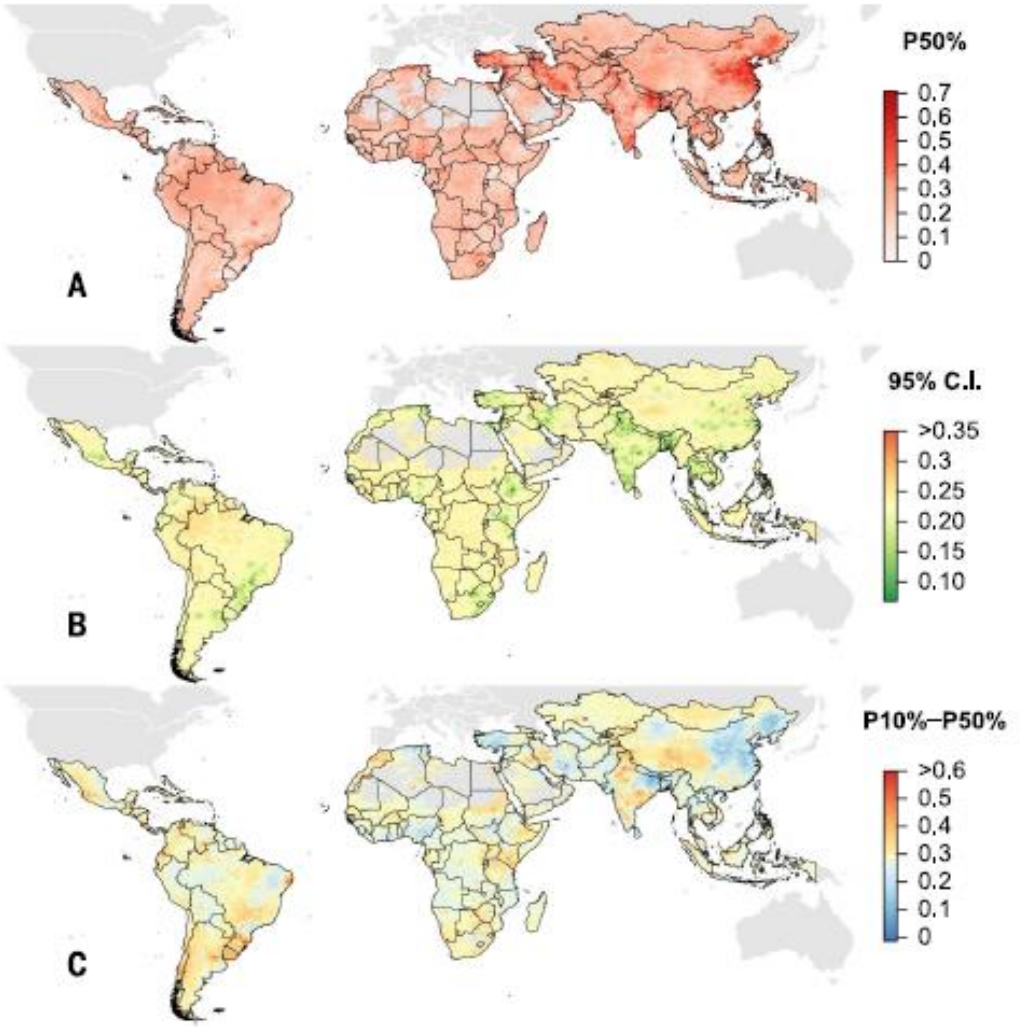
(B) 95% confidence intervals on P50 (supplementary materials).

(C) Difference in the proportion of antimicrobials with 10% resistance and 50% resistance.

Red areas indicate new hotspots of resistance to multiple drugs; blue areas are established hotspots.

Maps are available at resistancebank.org.

Source: Van Boeckel et al., Science 365, eaaw1944 (2019)



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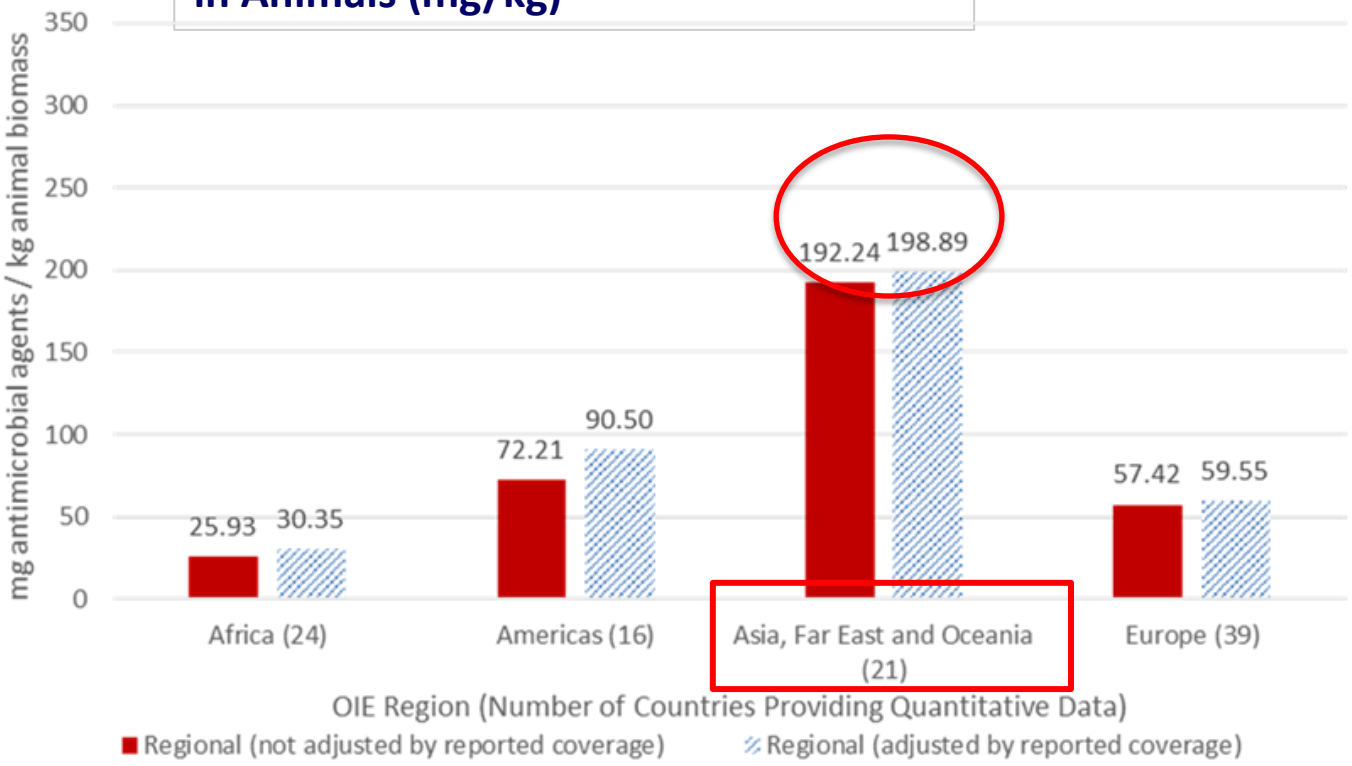
Asia-Pacific Region: Hotspot for emerging AMR gene!

Global consumption of antimicrobials =

117.48 mg/kg of animal biomass

Quantity of Antimicrobial Agents used in Animals (mg/kg)



Source: Fifth OIE Annual Report Antimicrobial Agents Intended for Use in Animals

AMU data submitted by - 156 OIE members

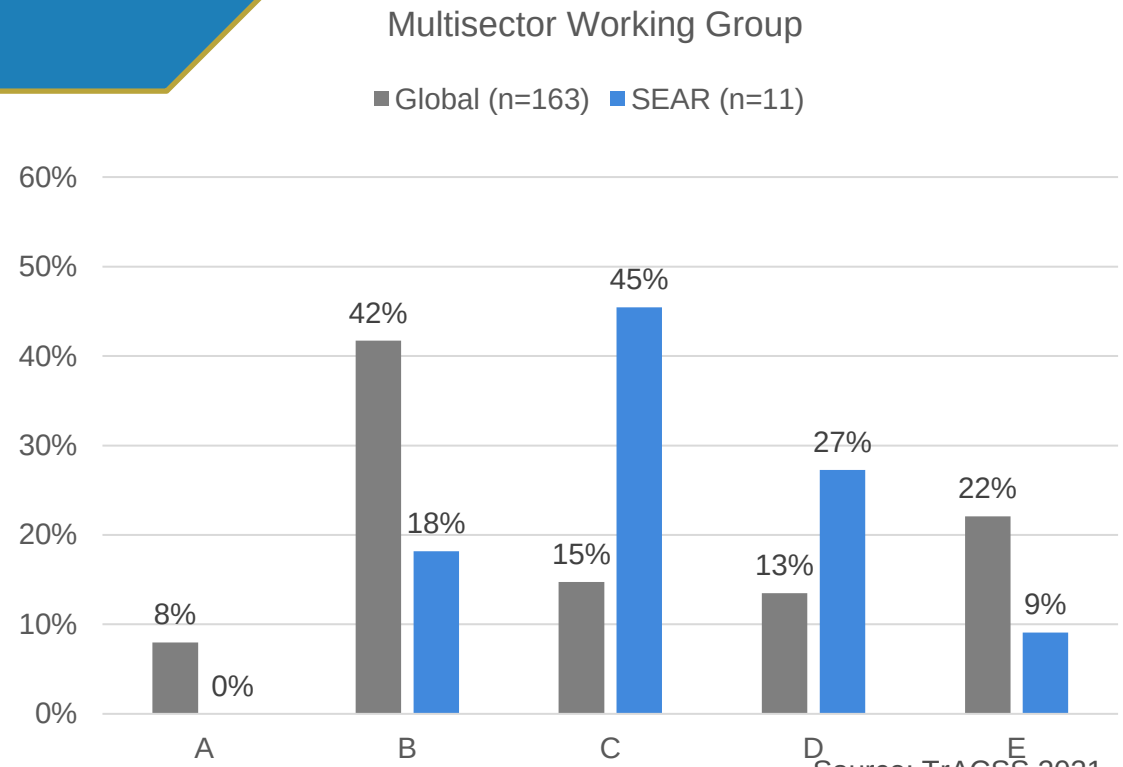
Asia-Pacific Region

Highest antimicrobial usage in animals

AMU vs AMR

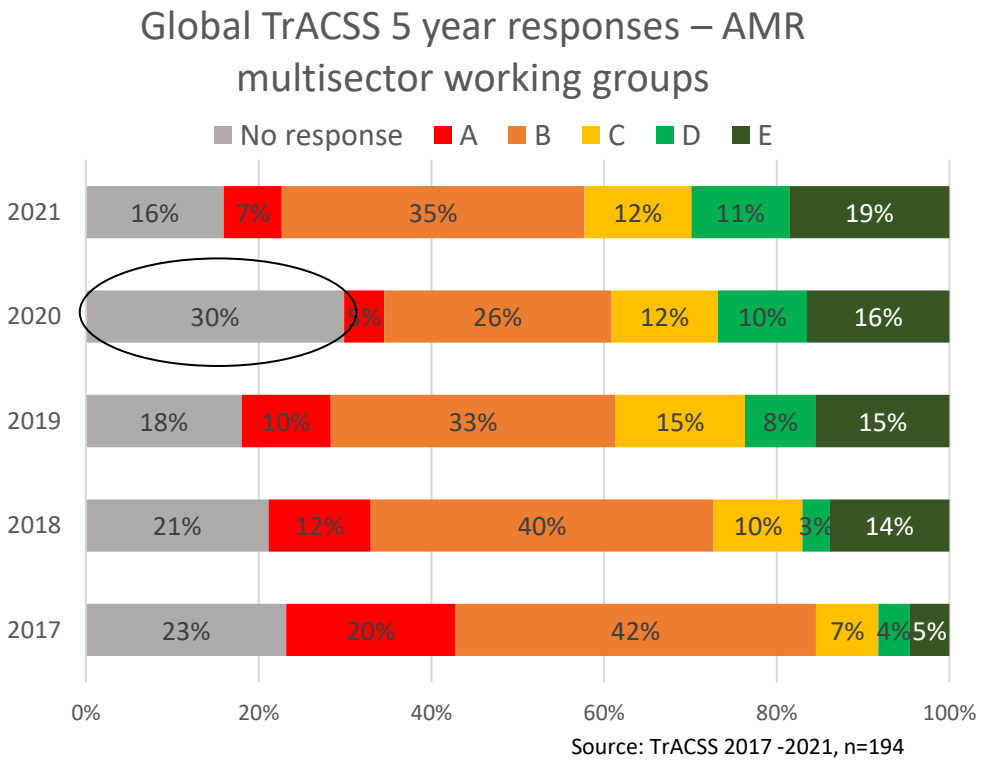
More we use ⇨ more threat of AMR

AMR MULTISECTOR WORKING GROUPS



Source: TrACSS 2021

A	No formal multi-sectoral governance or coordination mechanism on AMR exists.
B	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership.
C	Multi-sectoral working group(s) is (are) functional, with clear terms of reference, regular meetings, and funding for working group(s) with activities and reporting/accountability arrangements defined.
D	Joint working on issues including agreement on common objectives.
E	Integrated approaches used to implement the national AMR action plan with relevant data and lessons learned from all sectors used to adapt implementation of the action plan.



Source: TrACSS 2017 -2021, n=194

Increase in functional AMR WG over the past few years, but most common response has been that committees have been established with government leadership, but not yet functional (B).

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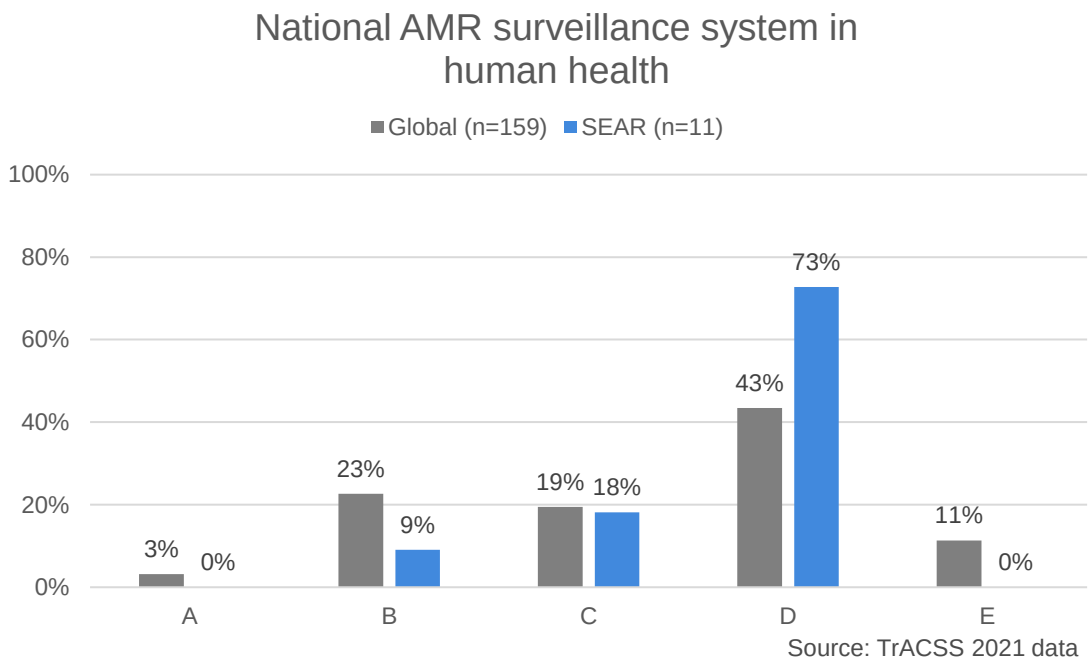
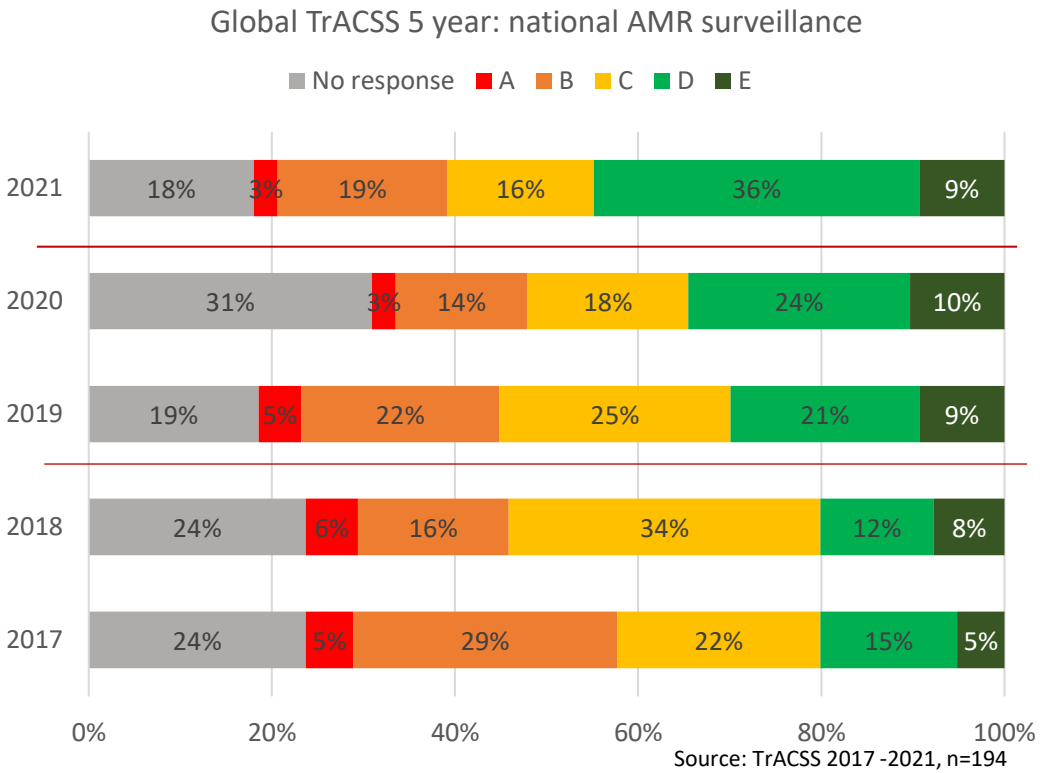
GAP IN AMR SURVEILLANCE



Source: TrACSS 2021 data



Source: TrACSS 2017 -2021, n=194

Red line represents changes to wording over the years

A No capacity for generating data (antibiotic susceptibility testing and accompanying clinical and epidemiological data) and reporting on antibiotic resistance.

B AMR data is collated locally for common bacterial infections in hospitalized and community patients, but data collection may not use a standardized approach and lacks national coordination and/or quality management.

C AMR data are collated nationally for common bacterial infections in hospitalized and community patients, but national coordination and standardization are lacking.

D There is a standardized national AMR surveillance system collecting data on common bacterial infections in hospitalized and community patients, with established network of surveillance sites, designated national reference laboratory for AMR,, and a national coordinating centre producing reports on AMR.

E The national AMR surveillance system links AMR surveillance with antimicrobial consumption and/or use data for human health.

Overall, there is an increase in countries with AMR data collated nationally (C-E) over the years, and shifts can be seen even between years without any changes

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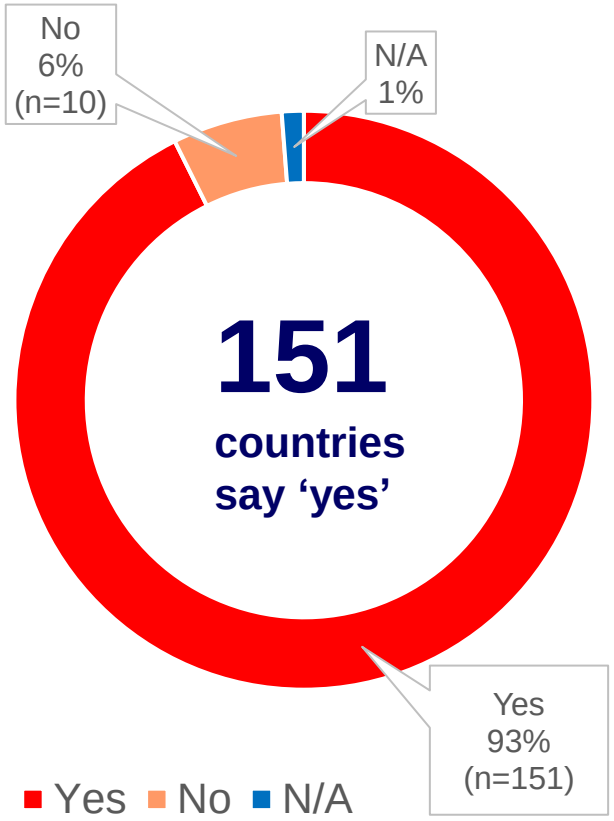
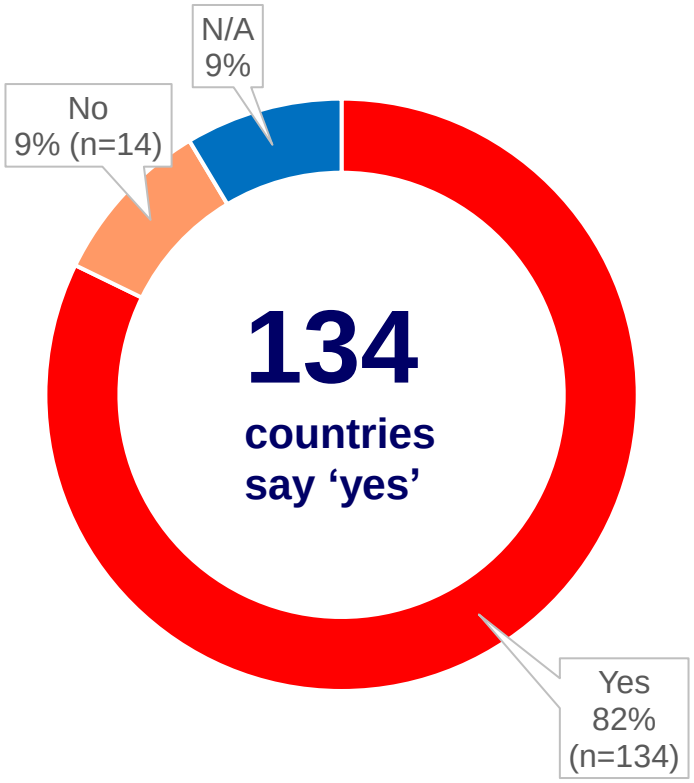
COVID-19 IMPACT on AMR NAPs

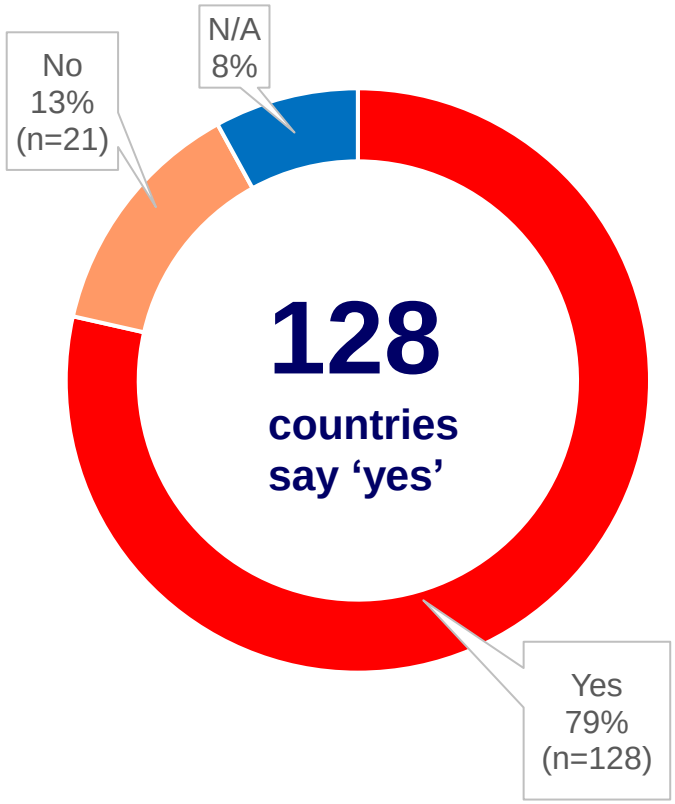
Has COVID-19 impacted your AMR NAP development and implementation?



Were there governance and administrative impacts: AMR NAP Committee meetings deferred; reduced government funding for addressing AMR available



Were there operational impacts: awareness campaigns deferred; monitoring and data collection activities impacted; technical capacity building activities deferred



AMR and International trade

- Importing countries or trade bloc put food safety and quality requirement to exporting countries which may include livestock and poultry products, fish, seafood and honey

- What are critical to make decision for import?
  - Evaluation of national veterinary services (PVS - OIE)
  - Risk assessment
    - Regulatory framework
    - Animal disease surveillance system
    - Laboratory capacity for investigation, detection and validation
    - Residue monitoring system (Veterinary drugs, pesticides, mycotoxin)
    - Veterinary drug supply, sale and use in feed
    - Farming practice (Biosecurity, vaccination and management)

AMR concern: Trade implication

- EU Régulations 2019/6, in particular Article 118 aimed at implementing the global consensus on addressing the global health risk of AMR by preventing the use of medically important antimicrobials for growth promotion purposes.

- Revision of **code of practice** to minimize and contain Antimicrobial Resistance (CAC/RCP 61-2005)

- Guidelines on **Integrated Monitoring and Surveillance of Foodborne Antimicrobial Resistance**

AMR: High-level political interest and commitment

2015

Global Action Plan on AMR adopted at the World Health Assembly

2016

UN General Assembly Political Declaration September in 2016

OIE and FAO governing bodies endorsed Global Action Plan

2017

Interagency Coordination Group (IACG) on AMR was established

2018

WHO, FAO and OIE sign an MoU to strengthen their long-standing partnership, with a strong focus on AMR in a One Health context

2019

The **IACG launched its final report** with recommendations in April 2019

Establishment of a **standing Tripartite Joint Secretariat (TJS), hosted by WHO**

Political declaration on UHC (endorsed in Sept 2019) calls for a dedicated high-level meeting on AMR

2021

On April 29, the **high-level dialogue on AMR** was held calling for urgent action to tackle AMR

The Global Leaders Group on Antimicrobial Resistance

WHO ARE WE?

The Global Leaders Group (GLG) on Antimicrobial Resistance was established following the recommendation of the ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance (AMR) to strengthen global political momentum and leadership on AMR.

The GLG is composed of heads of state, serving or former ministers and/or senior government officials acting in their individual capacities, together with senior representatives of foundations, civil society organizations and the private sector. It also includes principals of the Tripartite organizations - the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and the World Health Organization (WHO), as well as the UN Environment Programme (UNEP) - in an ex-officio capacity.

The GLG is co-chaired by Their Excellencies Sheikh Hasina, Prime Minister of Bangladesh and Mia Amor Mottley, Prime Minister of Barbados.

WHAT DO WE DO?

The GLG performs an independent global advisory and advocacy role with the primary objective of maintaining urgency, public support, political momentum and visibility of the AMR challenge on the global agenda.

The **mission** of the GLG is to collaborate globally with governments, agencies, civil society and the private sector through a One Health approach* to advise on and advocate for prioritized political actions for the mitigation of drug resistant infections through responsible and sustainable access to and use of antimicrobials.

H.E. Sheikh Hasina
Prime Minister of Bangladesh

H.E. Mia Amor Mottley
Prime Minister of Barbados

Co-Chairs, Global Leaders Group on Antimicrobial Resistance

"The Global Leaders Group is about catalysing political action to address the enormous challenges of AMR and seize the opportunities it presents to create a healthier, safer, more prosperous and equitable world. As GLG members we will use our voices in as many ways as we can to help ensure that action on AMR is among the highest priorities across national and global efforts to reach the Sustainable Development Goals".

* *A One Health approach to antimicrobial resistance refers to designing and implementing programmes, policies, legislation and research in a way that enables multiple sectors and stakeholders engaged in human, terrestrial and aquatic animal and plant health, food and feed production and the environment to communicate and work together to achieve better public health outcomes. (Ref: IACG Report, 2019)*

Tripartite Joint Secretariat on Antimicrobial Resistance | Food and Agriculture Organization of the United Nations | OIE World Organisation for Animal Health | World Health Organization

The Global Leaders Group (GLG) on Antimicrobial Resistance

Strengthening global political momentum and political leadership on AMR

The GLG's six priority action areas for 2021-22

Advocate for sustained political action on AMR by seizing critical opportunities including embedding it in the SDGs and through a One Health approach

Advocate for transforming the food, animal and human health, plant and environment eco-systems focusing on infection prevention and control and the responsible and sustainable use of antimicrobials

Advocate for improved surveillance and monitoring of antimicrobial use and resistance across all sectors to inform ambitious, science- and risk-based, global and national targets and interventions

Advocate for increased mobilization of internal and external financial resources, with a focus on LMICs, to support the development and implementation of multisectoral national action plans

Advocate for increased, effective and affordable innovations across all sectors and stakeholders to secure a sustainable pipeline for new antimicrobials (particularly antibiotics), vaccines, diagnostics, waste management tools, and safe alternatives to antimicrobials, and to ensure their equitable access

Advocate for better understanding of environmental pathways on the development and transmission of AMR including the linkages between antimicrobial production, use and waste disposal in all sectors

GAP Strategic Objectives

1. Improve awareness and understanding of AMR through education and training
2. **Strengthen knowledge and evidence base through surveillance and research**
3. Reduce the incidence of infection through effective hygiene and IPC measures
4. Optimize the use of antimicrobial medicines in human and animal health
5. Ensure sustainable investment through research and development

www.who.int/publications/i/item/9789241509763

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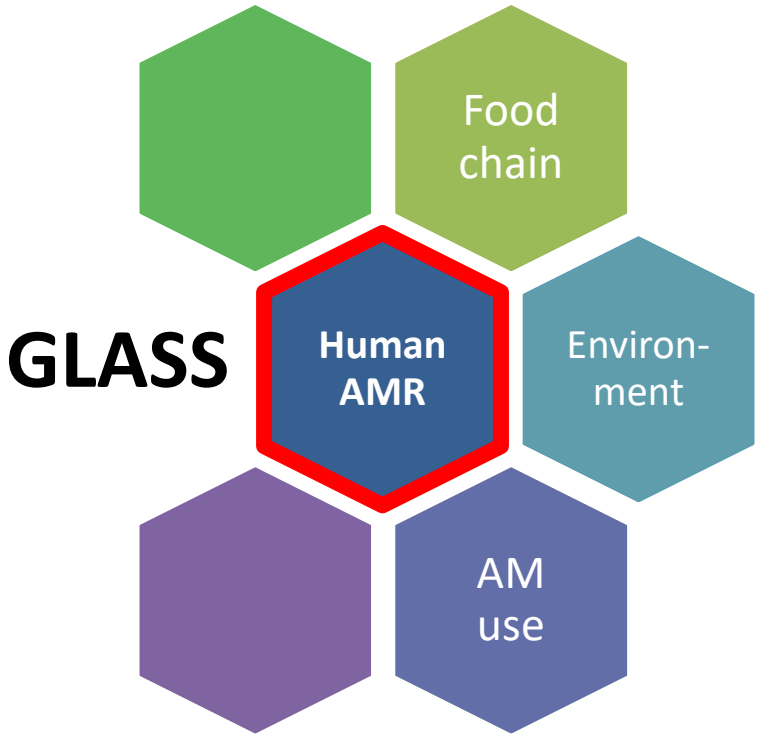
Global AMR Surveillance System!

- Initial steps of a global AMR surveillance system
- Further development to include other related AMR data



8 bacteria

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Acinetobacter* spp.
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Salmonella* spp.
- *Shigella* spp.
- *Neisseria gonorrhoeae*

4 specimen types

- blood
- urine
- stool
- genital swabs

More information can be obtained

http://www.who.int/drugresistance/surveillance

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WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance

- Containment of AMR from the food chain
- Capacity building for integrated surveillance of AMR
- Monitoring of antimicrobial use
- WHO List of critically important antimicrobials (CIA list) for human medicine
- FAO/OIE/WHO tripartite activities and *Codex Alimentarius* activities on AMR

AGISAR

Support

GAP

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GAP Strategic Objectives

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WHO Guideline for Use of Medically Important Antimicrobials in Food-Producing Animals

- Goals:
  - Help **preserve the effectiveness of medically important antimicrobials**, particularly those antimicrobials judged to be critically important to human medicine.
  - Provide **formal recommendations for limitations of specific uses of medically important antimicrobials in food-producing animals**, particularly antimicrobials judged to be critically important for humans
- Supports the Global Action Plan on Antimicrobial Resistance

WHO list of Critically Important Antimicrobials for Human Medicine (WHO CIA list)

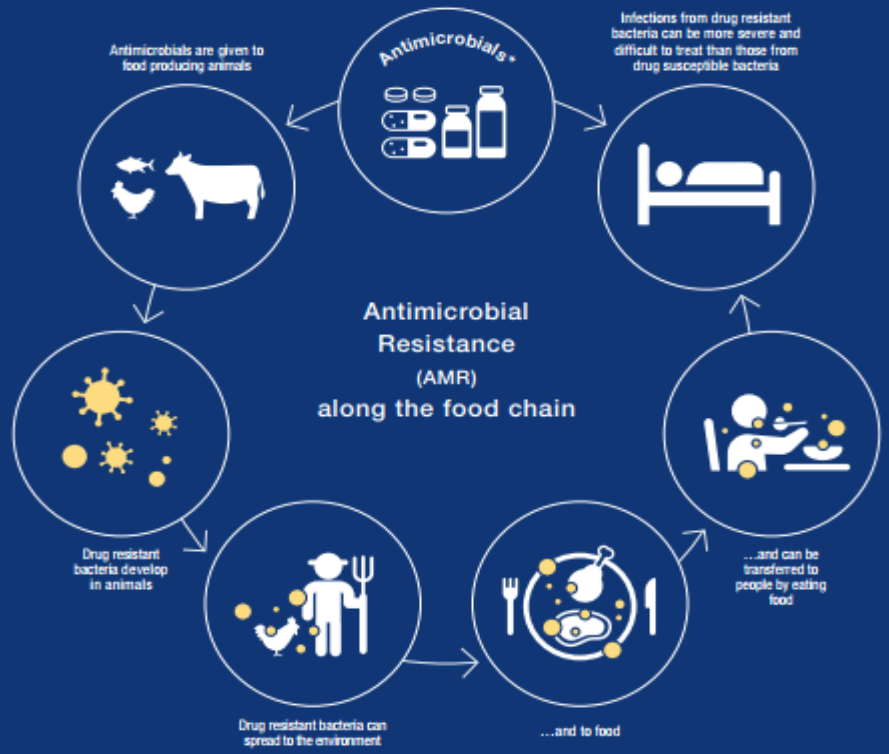
Since 2005, WHO has produced a regularly updated list of all antimicrobials currently used for human medicine (mostly also used in veterinary medicine), grouped into 3 categories based on their importance to human medicine. The list is intended to assist in managing antimicrobial resistance, ensuring that all antimicrobials, especially critically important antimicrobials, are used prudently both in human and veterinary medicine.

Critically Important
Highly Important
Important

Prioritize
by Prioritization Criterion 1, 2, 3

Highest Priority
High Priority

Classify
by Criterion 1, 2



WHO supports optimization of the use of antimicrobial medicines in human and animal to preserve their effectiveness by taking a One Health approach

*The scope of this list is limited to the antibacterial drugs (antibiotics).

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WHO Critically Important Antimicrobials for Human Medicine 5th revision

Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)
October 2016

Summary of classification and prioritization of antimicrobials categorized as Critically Important, Highly Important and Important

Medically Important Antimicrobials

Antimicrobial class	Criterion (Yes = ●)				
Critically Important					
CRITICALLY IMPORTANT ANTIMICROBIALS	**C1**	**C2**	**P1**	**P2**	**P3**
HIGHEST PRIORITY					
Highest Priority: *Cephalosporins (3rd, 4th and 5th generation)*	●	●	●	●	●
Highest Priority: *Glycopeptides*	●	●	●	●	●
Highest Priority: *Macrolides and ketolides*	●	●	●	●	●
Highest Priority: *Polymyxins*	●	●	●	●	●
Highest Priority: *Quinolones*	●	●	●	●	●
HIGH PRIORITY					
Aminoglycosides	●	●		●	●
Ansamycins	●	●	●	●	
Carbapenems and other penems	●	●	●	●	
Glycylcyclines	●	●	●		
Lipopeptides	●	●	●		
Monobactams	●	●	●		
Oxazolidinones	●	●	●		
Penicillins (natural, aminopenicillins, and antipseudomonal)	●	●		●	●
Phosphonic acid derivatives	●	●	●	●	
Drugs used solely to treat tuberculosis or other mycobacterial diseases	●	●	●	●	
Highly Important					
HIGHLY IMPORTANT ANTIMICROBIALS	**C1**	**C2**	**P1**	**P2**	**P3**
Amidinopenicillins		●	NA		
Amphenicols		●			
Cephalosporins (1st and 2nd generation) and cephamycins		●			
Lincosamides		●			
Penicillins (anti-staphylococcal)		●			
Pseudomonic acids		●			
Riminofenazines	●				
Steroid antibacterials		●			
Streptogramins		●			
Sulfonamides, dihydrofolate reductase inhibitors and combinations		●			
Sulfones	●				
Tetracyclines	●				
Important					
IMPORTANT ANTIMICROBIALS	**C1**	**C2**	**P1**	**P2**	**P3**
Aminocyclitols			NA		
Cyclic polypeptides					
Nitrofurantoins					
Nitroimidazoles					
Pleuromutilins					

C1 Criterion 1
The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people.

C2 Criterion 2
The antimicrobial class is used to treat infections in people caused by either: (1) bacteria that may be transmitted to humans from nonhuman sources, or (2) bacteria that may acquire resistance genes from nonhuman sources.

P1 Prioritization criterion 1
High absolute number of people, or high proportion of use in patients with serious infections in health care settings affected by bacterial diseases for which the antimicrobial class is the sole or one of few alternatives to treat serious infections in humans.

P2 Prioritization criterion 2
High frequency of use of the antimicrobial class for any indication in human medicine, or else high proportion of use in patients with serious infections in health care settings, since use may favour selection of resistance in both settings.

P3 Prioritization criterion 3
The antimicrobial class is used to treat infections in people for which there is evidence of transmission of resistant bacteria or resistance genes from non-human sources.

WHO CIA list 5th rev. : http://who.int/foodsafety/publications/antimicrobials-fifth/en/
AGISAR: http://who.int/foodsafety/areas_work/antimicrobial-resistance/agisar/en

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GLOBAL ACTION PLAN
ON ANTIMICROBIAL RESISTANCE

Strategic Objective 2

- Information on: the incidence, prevalence, range across pathogens and geographical patterns related to antimicrobial resistance is needed to be made accessible in a timely manner in order to guide the treatment of patients; to inform local, national and regional actions; and to monitor the effectiveness of interventions;

- Understanding how resistance develops and spreads, including how resistance circulates within and between humans and animals and through food, water and the environment, is important for the development of new tools, policies and regulations to counter antimicrobial resistance;

Need of integrated surveillance of AMR

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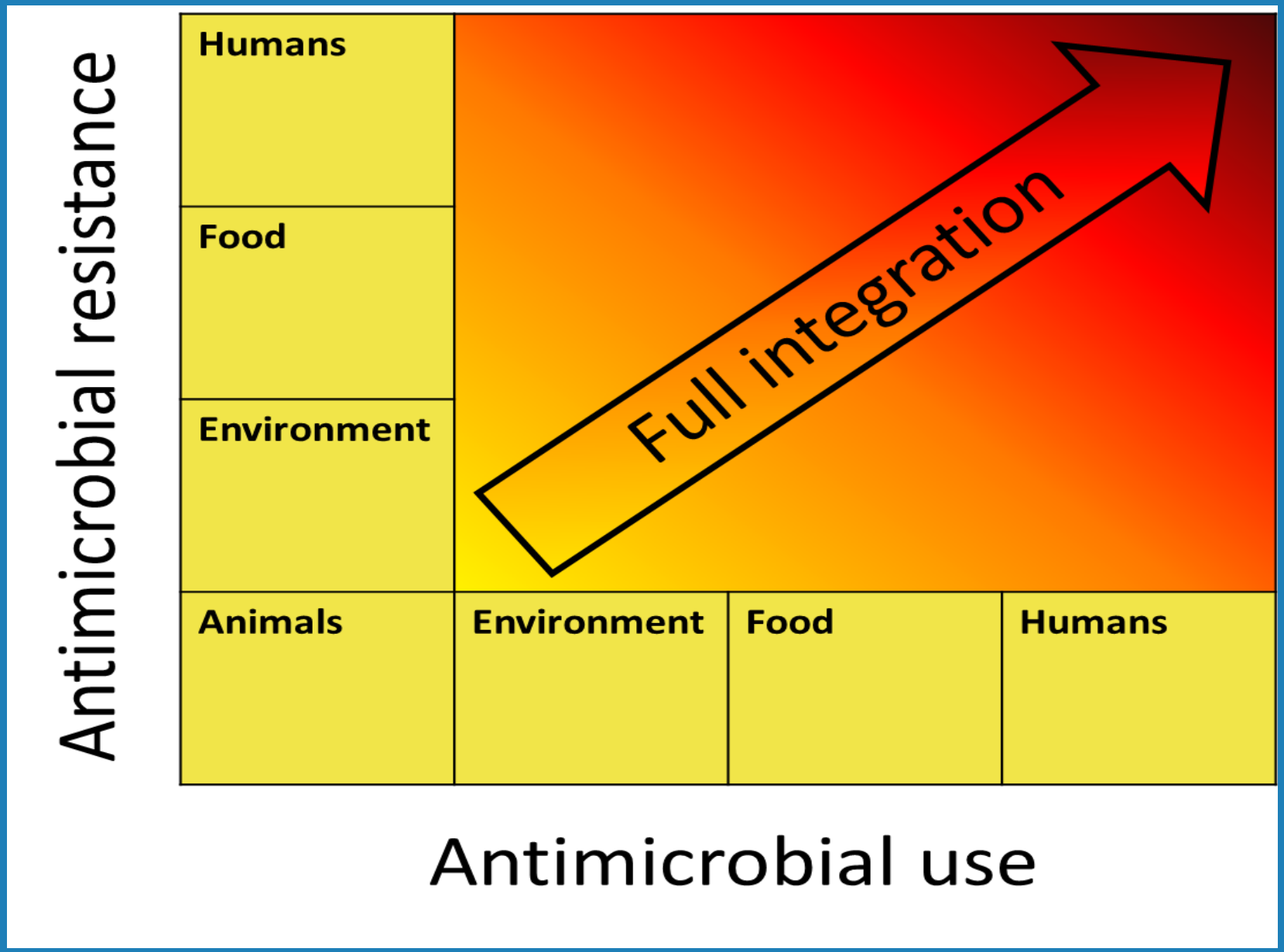
Integration of surveillance of antimicrobial use and antimicrobial resistance

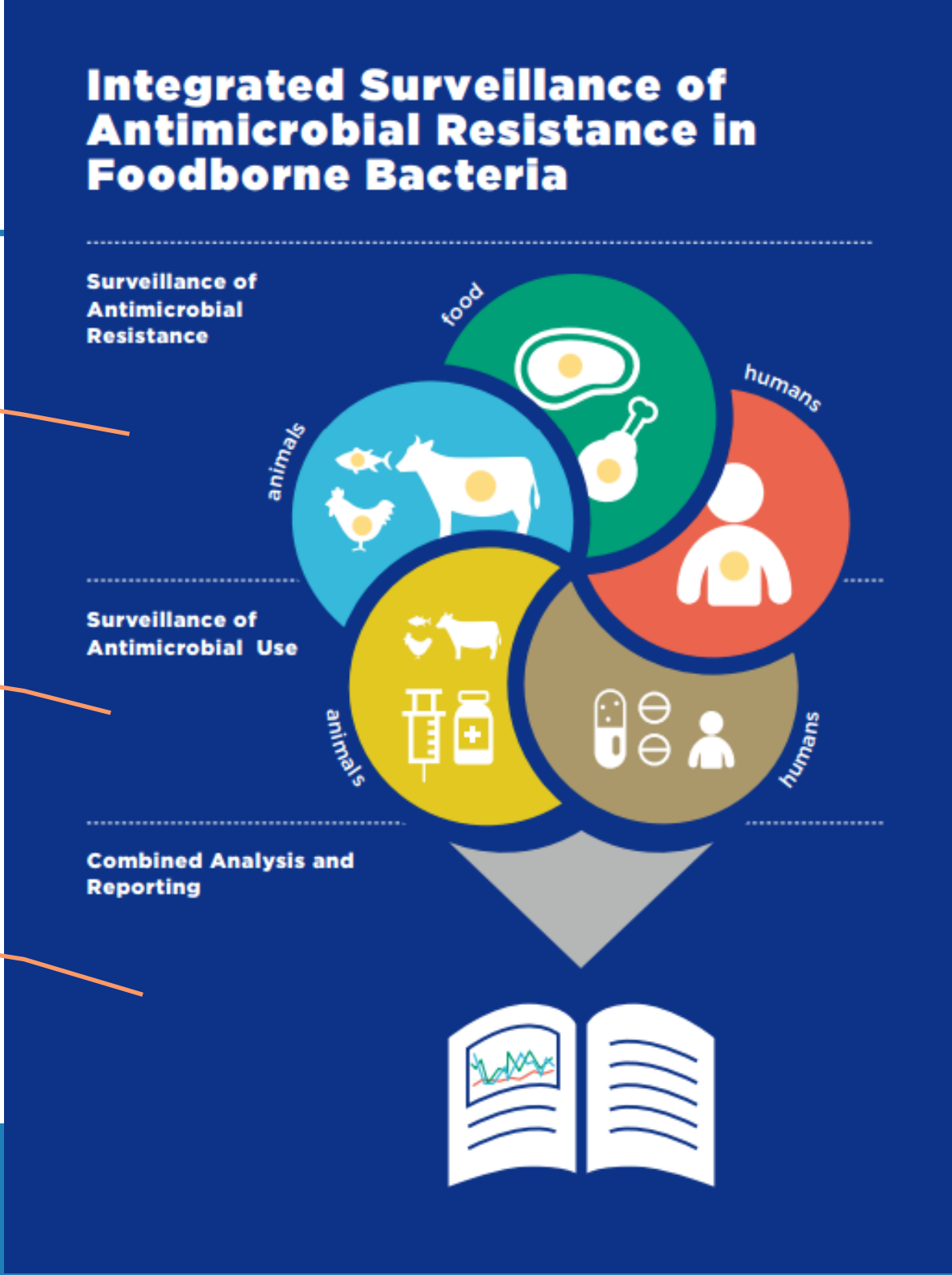


Released a guidance (June 2017)

Surveillance of resistance in animals, food, humans

Surveillance of use in animals, humans

Combined analysis and reporting



ESBL *E.coli*

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ESBL Ec Tricycle project: protocol development

Simple surveillance across the three main sectors

Simple microorganism and resistance mechanism as indicator

ESBL *E. coli*

Human

Food chain

Environment

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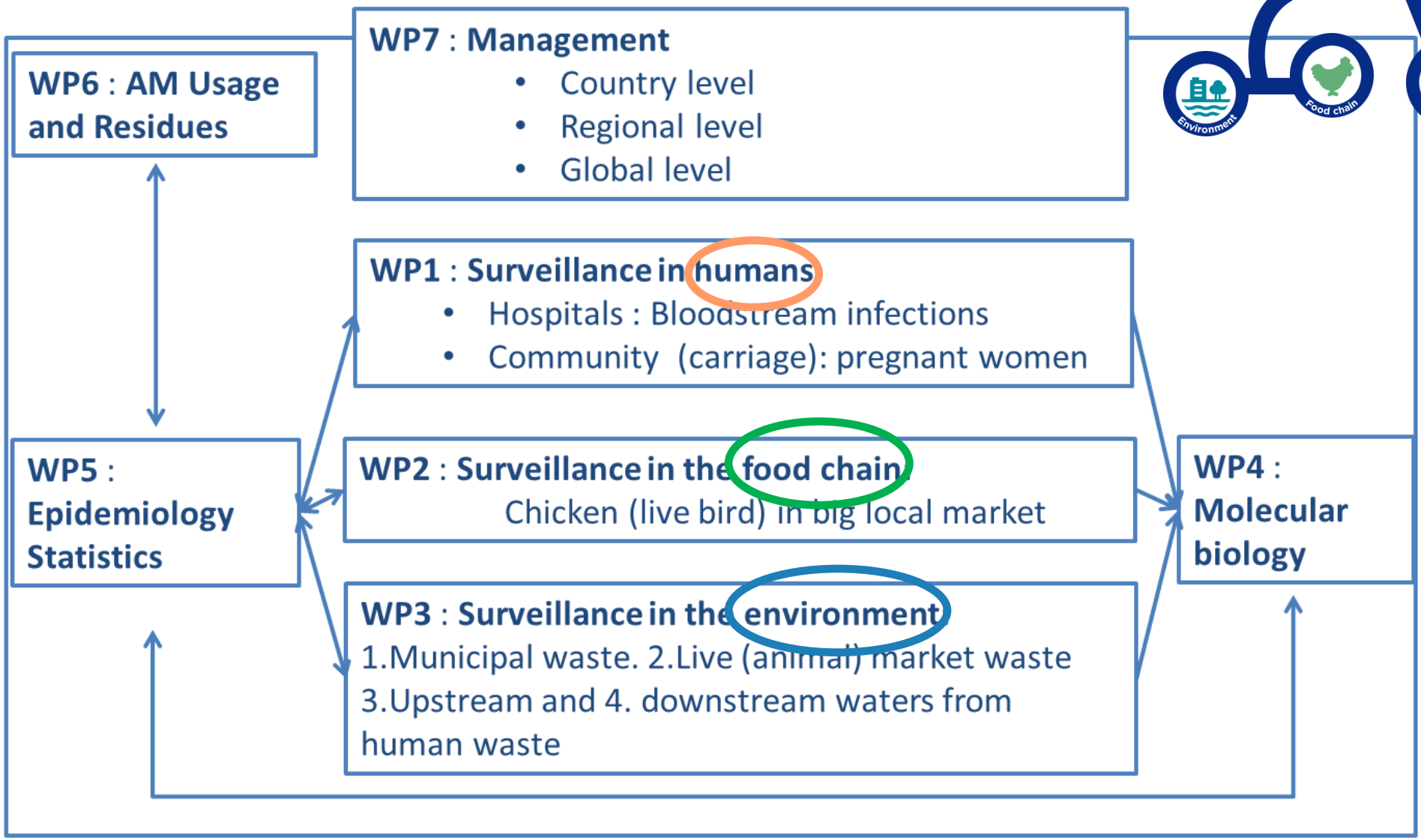

Figure 1. ESBL Ec Tricycle project.
WP Working Package

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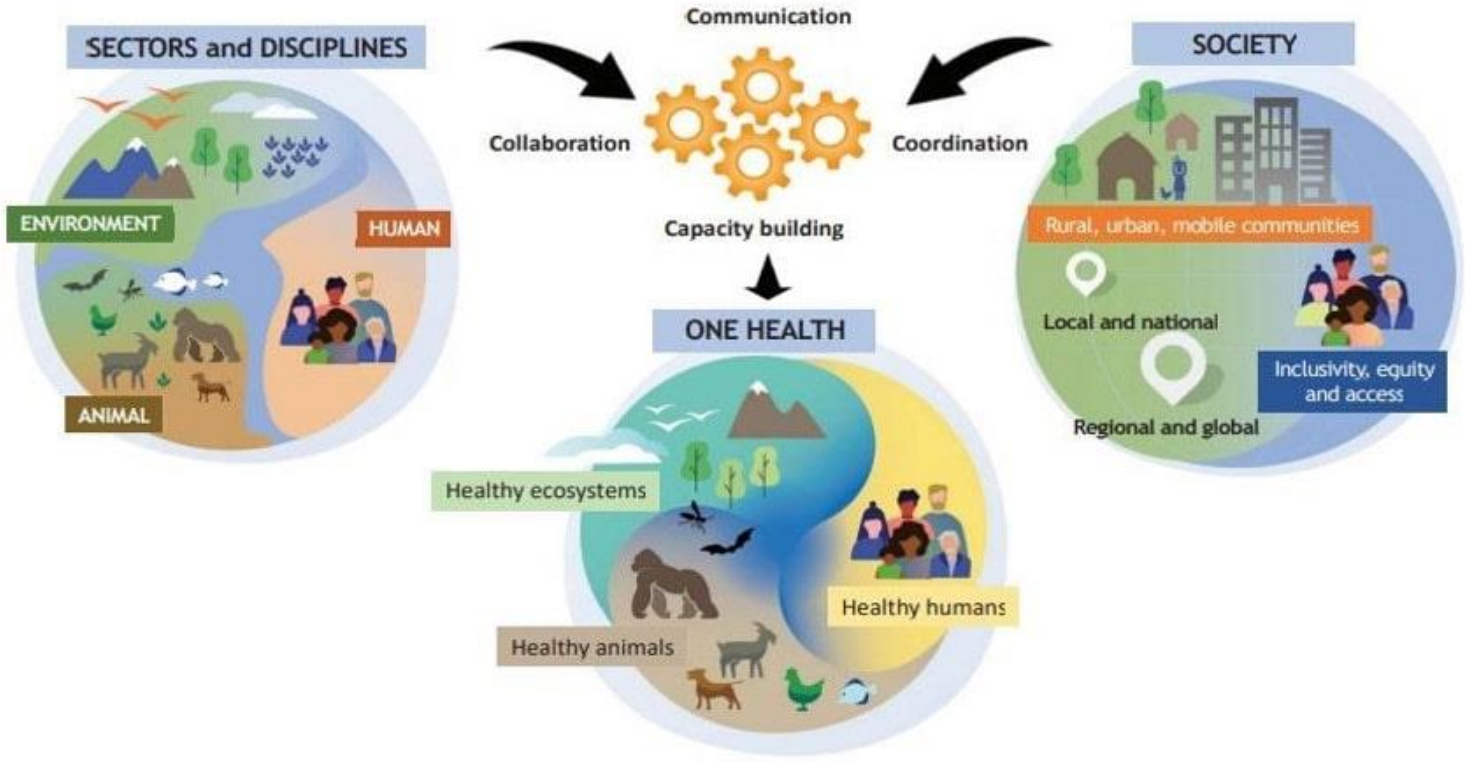
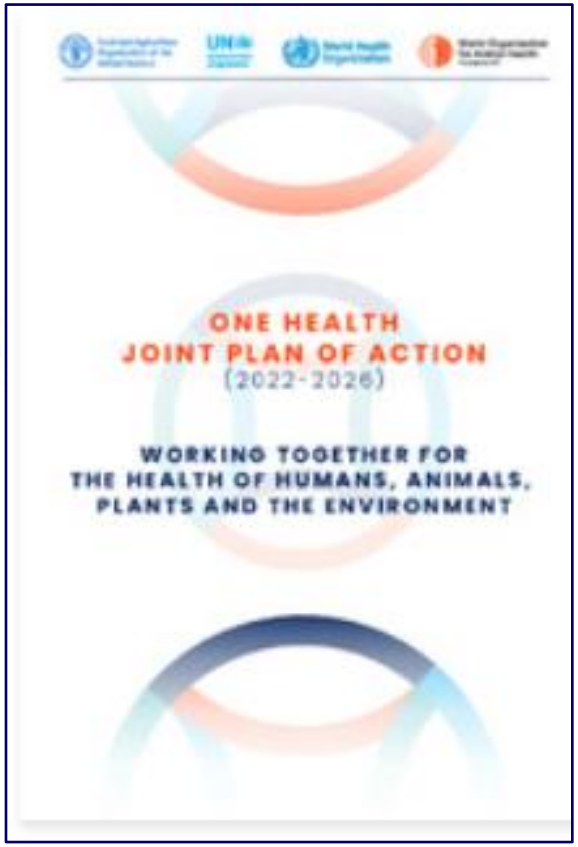
A Strengthened Quadripartite on One Health

- Joint vision and commitment
- Support countries
- Whole of society approach
- Synergies and overlaps
- Mobilize investment

One Health Joint Plan of Action (2022-2026) – Quadripartite
- An option to strengthen/establish a common strategy on One Health





Content

- A framework for action and proposes a set of activities that the four organizations can offer together to enable countries to advance and sustainably scale up One Health in managing health threats to humans, animals, plants, and the environment

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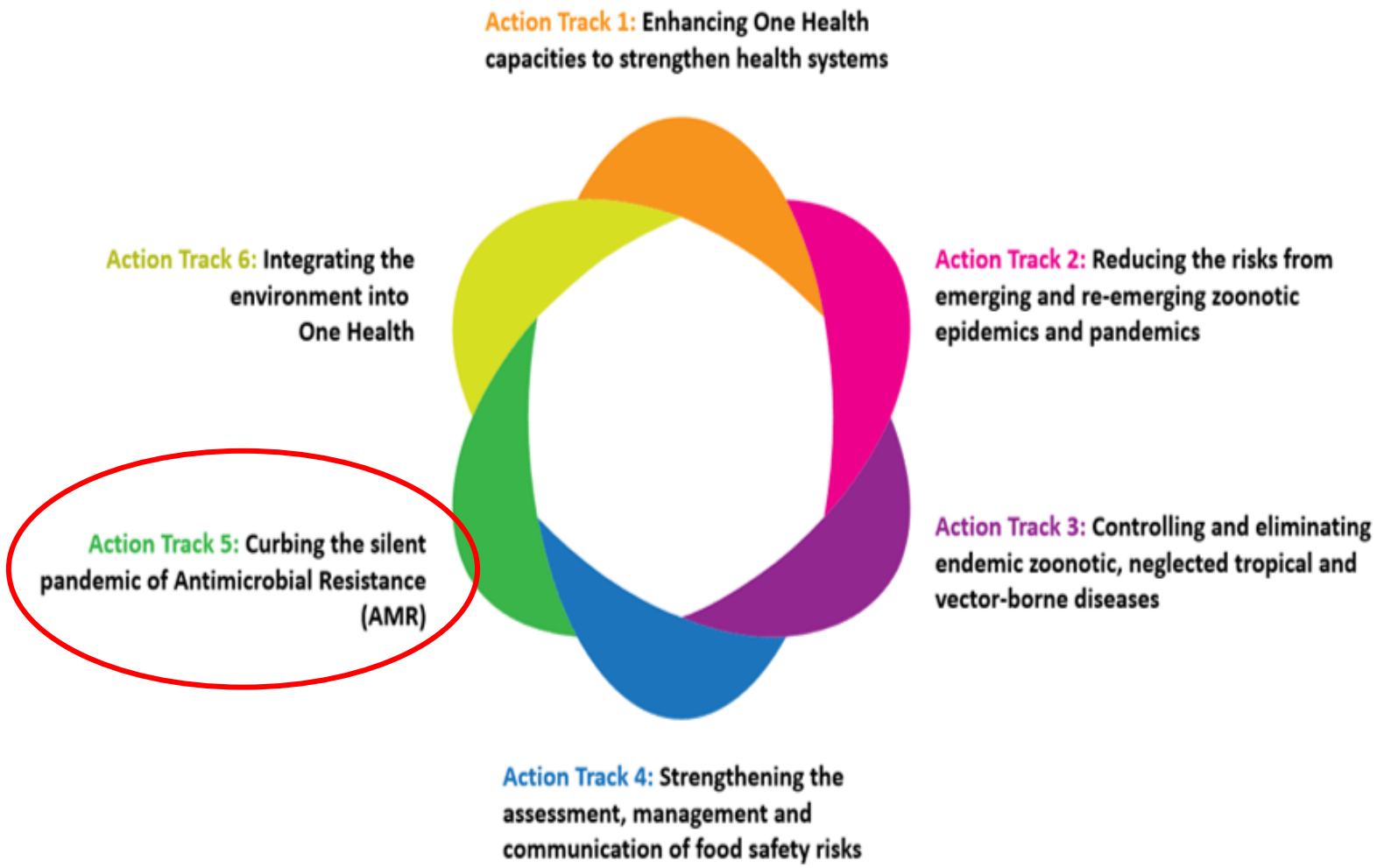
Six Action Tracks



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Action Track 5: Curbing the silent pandemic of AMR

Action 5.1. Strengthen the capacity and knowledge of countries to prioritize and implement context-specific collaborative work to control AMR in policies, legislation and practice

Action 5.2. Reinforce global and regional initiatives and programmes to influence and support One Health responses to AMR

Action 5.3. Strengthen global AMR governance structures

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Take home message

- Antimicrobial resistance is a complex problem at the human-animal-plant-environment interfaces that requires a multi-sectoral, "One Health" approach and sectoral stewardship
- There are window of opportunities and proof of concept;
  - Increased level of awareness and engagement
  - Global Action Plan galvanizes partners around common goals
- Think globally and act locally

Thank you

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