

# Prudent Use of Antimicrobials in Veterinary Medicine



**Yutaka Tamura**

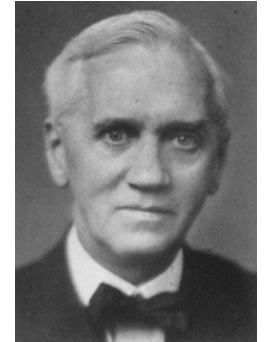
**Laboratory of Food Microbiology and Food Safety,  
School of Veterinary Medicine,  
Rakuno Gakuen University**



**Collaborating Center  
for Food Safety**

# Discovery of Penicillin and Emergence of Penicillin Resistant Bacteria

- 1928 Discovery of the penicillin by Fleming
- 1940 Purification of the penicillin by Florey & Chain
- 1940 Emergence of penicillin resistant bacteria
- 1941 Confirmation of clinical effects
- 1945 Start of the industrial production  
Awarded a Nobel Prize



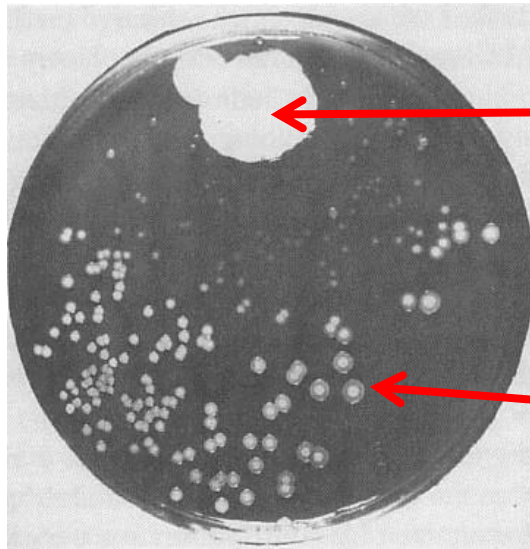
Alexander Fleming



Howard W Florey



Ernst B Chain



*Penicillium notatum*

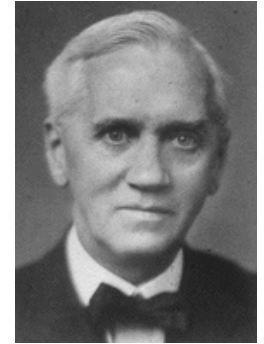
*Staphylococcus aureus*



Domestic Penicillin

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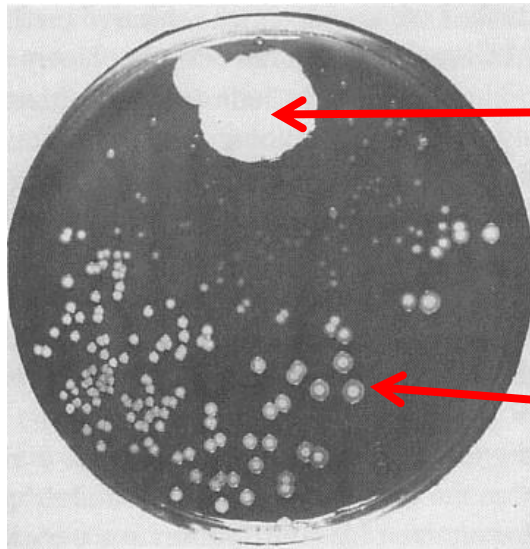
Howard W Florey



Domestic Penicillin



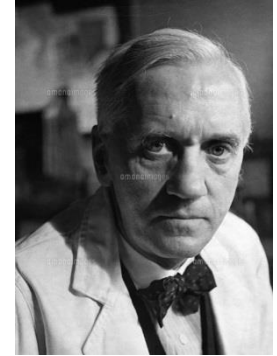
Ernst B Chain



*Penicillium notatum*

*Staphylococcus aureus*

**Predicted the spread of anti-microbial resistant bacteria !**



***The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.***



**In Alexander Fleming's speech accepting the 1945 Nobel Prize in Physiology or Medicine.**

# Antimicrobial Resistance Threats in USA



## NATIONAL SUMMARY DATA



Estimated minimum number of illnesses and deaths caused by antibiotic resistance\*:

At least  **2,049,442** illnesses,  
 **23,000** deaths

*\*bacteria and fungus included in this report*

**+**

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least  **250,000** illnesses,  
 **14,000** deaths

### WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.

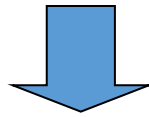
CS233559

U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

# History of Antimicrobials use in animal

**1928** Discovery of penicillin

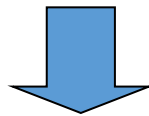
- antibiotics
- synthetic antimicrobials



**1946** Growth promotion effect of sulfa drugs and streptomycin as food additive in chicken

**1949** Practical use in USA

**1953** Practical use in UK



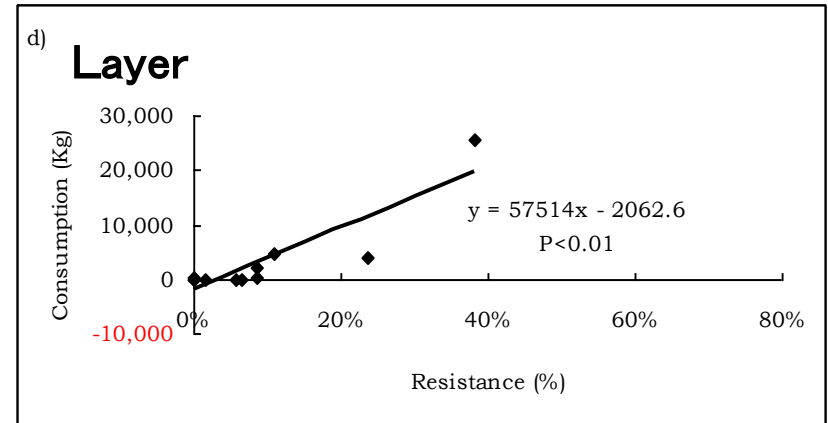
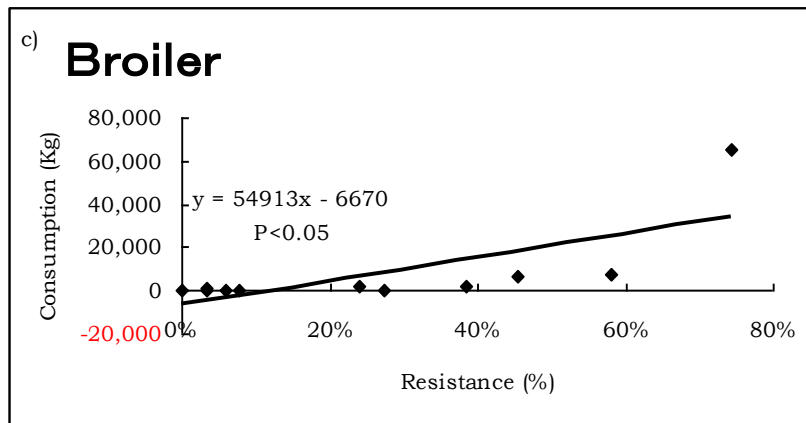
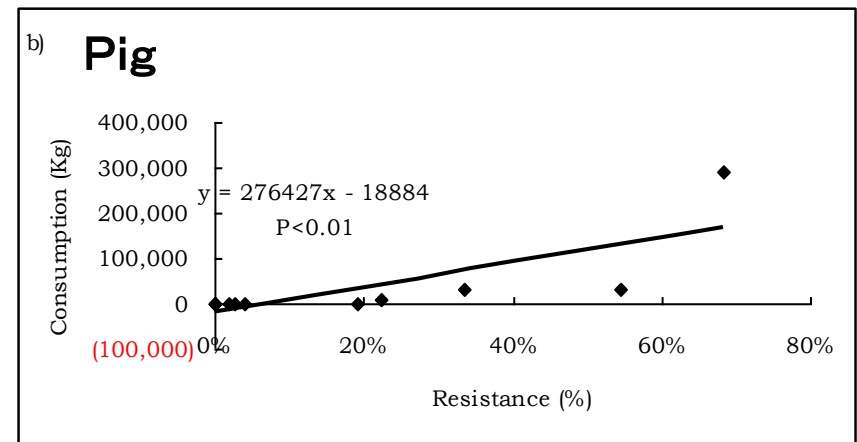
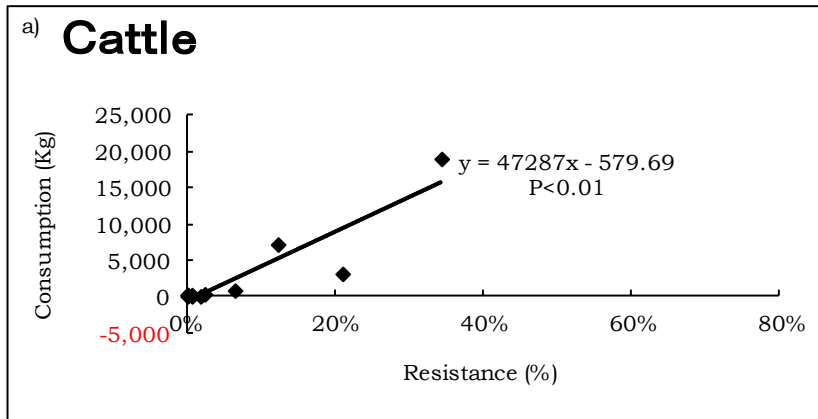
Contribution of stable supply of safe livestock products

**VS**



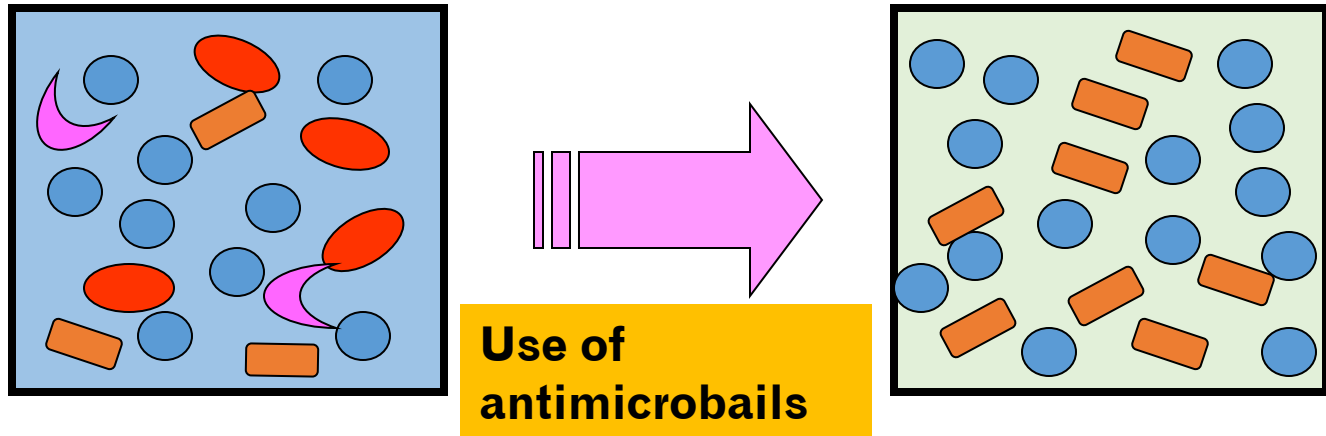
**Antimicrobial Resistnce**

# Relationship between quantity of antimicrobials use and prevalence of resistant *E.coli* in Japan



# Effect of antimicrobials use

## ● *Selection* of antimicrobial resistant bacteria



## ● *Dissemination* of antimicrobial resistant bacteria

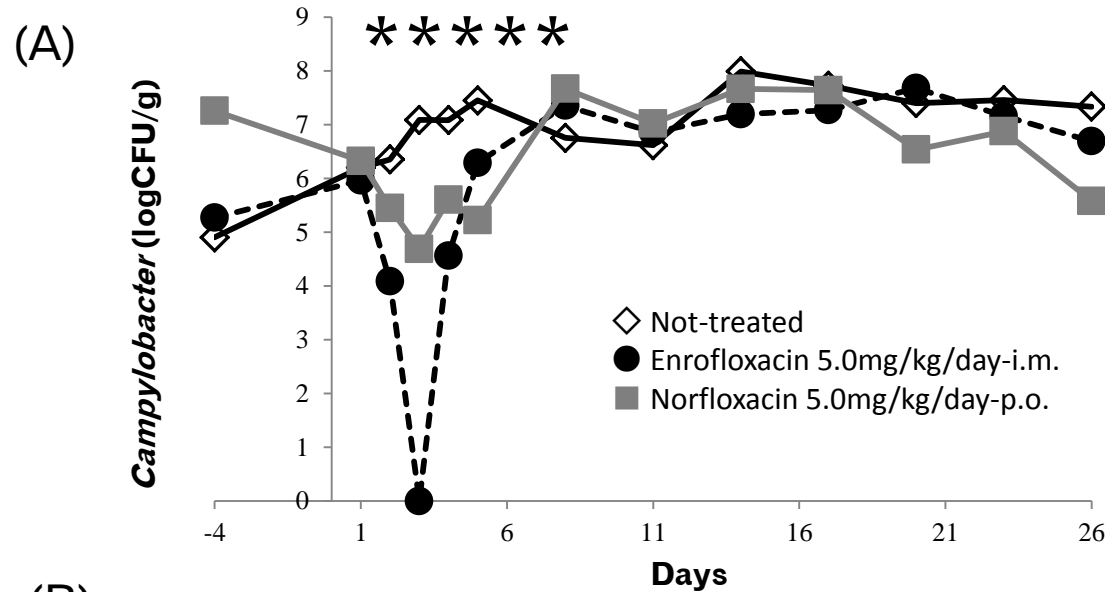
A big risk

Plasmid, transposon

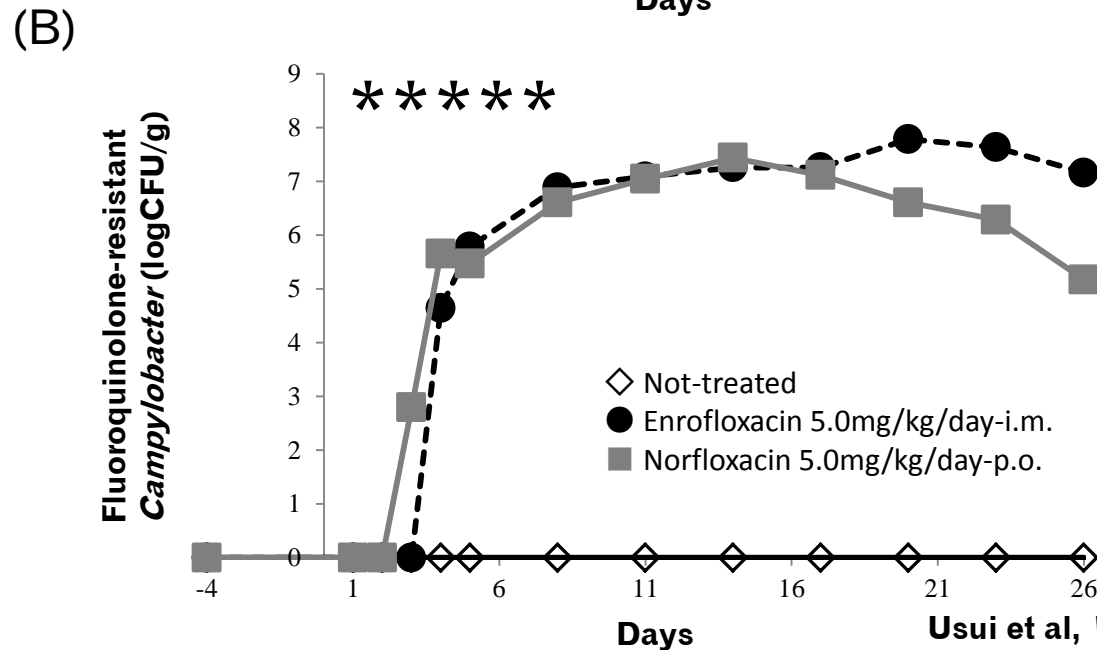
Pathogenic bacteria acquire antimicrobial resistance



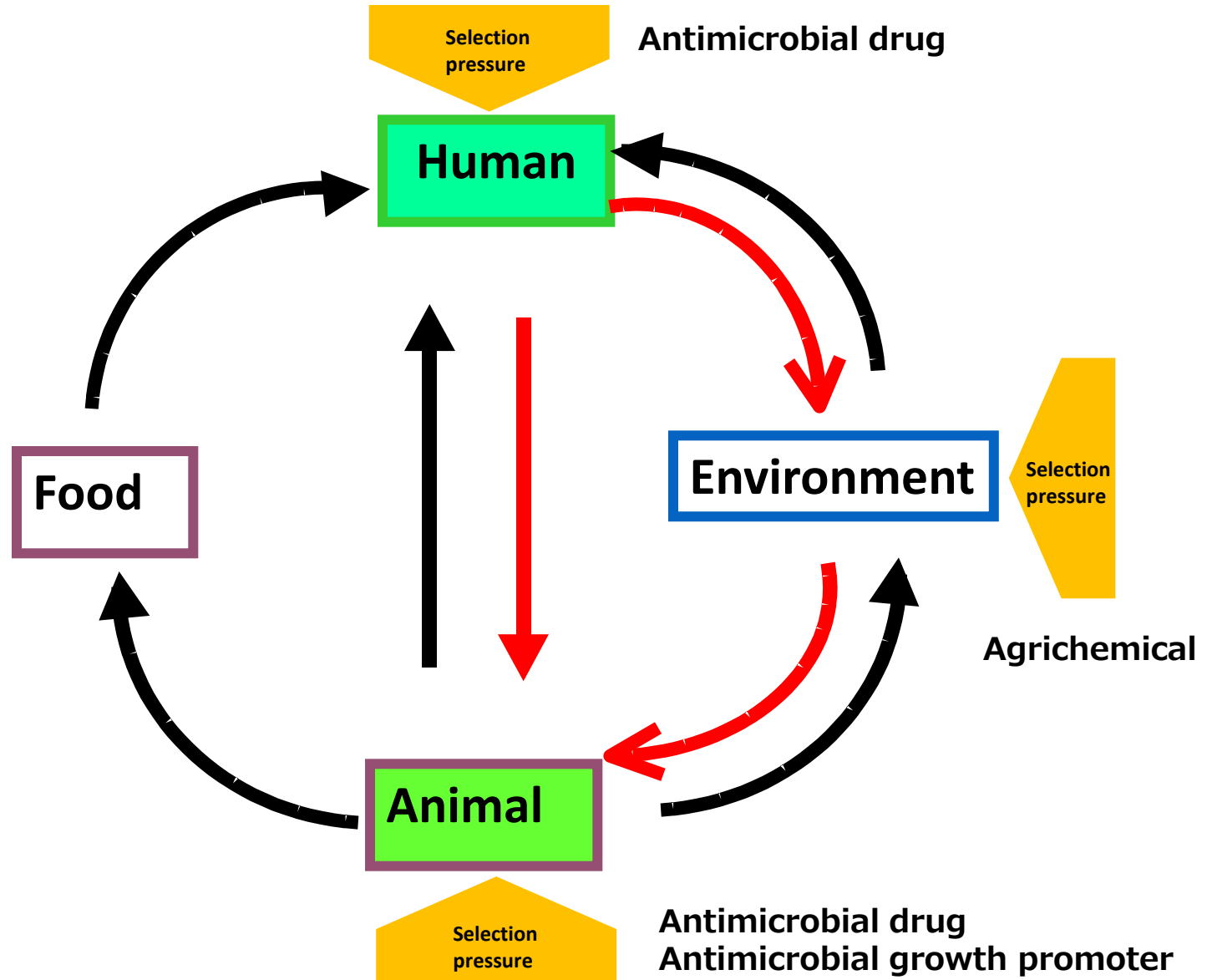
# Emergence of resistant *Campylobacter* in fecal samples of pigs by the administration of fluoroquinolone



The pigs were treated with fluoroquinolones on days 1-5 (asterisks).



# Transmission of Antimicrobial Resistant Bacteria between Animal and Human



# WHO Global Action Plan on Antimicrobial resistance

At the Sixty-eight World Health Assembly in May 2015, the World Health Assembly endorsed a global action plan to tackle antimicrobial resistance.

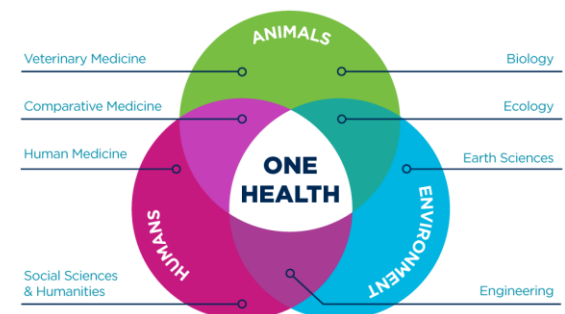


To achieve this goal, the global action plan sets out five strategic objectives:

1. to improve awareness and understanding of antimicrobial resistance;
2. to strengthen knowledge through surveillance and research;
3. to reduce the incidence of infection;
4. to optimize the use of antimicrobial agents
5. to increase investment in new medicines, diagnostic tools, vaccines and other interventions.



**One Health approach**



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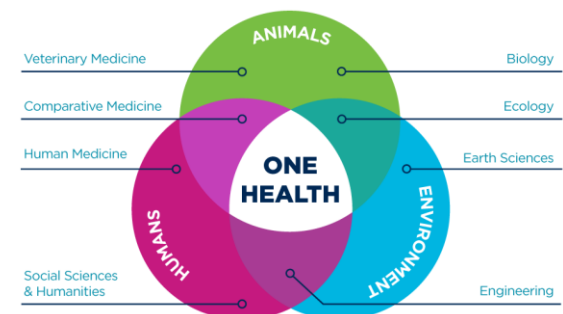


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**One Health approach**



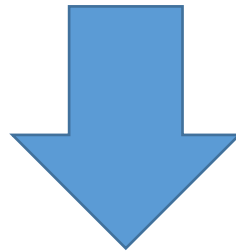
# **What is Prudent use of Antimicrobials ?**

**Prudent use of antimicrobials is an integral part of good veterinary practices. It is an attitude to maximise therapeutic efficacy and minimise selection of resistant micro-organisms.**

**Federation of Veterinarians of Europe**

# Emergence factor of Antimicrobial Resistant Bacteria

- ***Overuse*** of antimicrobials
- ***Misuse*** of antimicrobials



## Prudent Use of Antimicrobials

By veterinarian, herder, farmer, fisherman *etc.*

# Guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine

In OIE International Standards on Antimicrobial Resistance 2003

Guidelines provide guidance for the responsible and prudent use of antimicrobials in veterinary medicine with the aim of protecting both animal and human health.

- **Responsibilities of the regulatory authorities**
- the veterinary pharmaceutical industry**
- pharmacists**
- veterinarians**
- livestock producers**



Anthony F, Acar J, Franklin A, Gupta R, Nicholls T, Tamura Y, Thompson S, Threlfall EJ, Vose D, van Vuuren M, White DG: Antimicrobial resistance: responsible and prudent use of antimicrobial agents in veterinary medicine, *Rev. sci. tech. Off. Int. Epiz.*, 20(3):829-839, 2001.

# What can you do as veterinarians ?

We need to collectively ensure the responsible and prudent use of antibiotics in animals to preserve their effectiveness.

1. Only prescribe and dispense antibiotics for animal under your care and only if necessary.
2. Conduct antimicrobial sensitivity testing before prescribing or administering an antibiotics.
3. Educate animal owners on the risks associated with misuse of antibiotics.
4. Promote sound animal husbandry hygiene methods, vaccination strategies, and periodically review farm records to ensure compliance with your prescriptions.
5. Keep your knowledge on antibiotics use recommendations up to date.

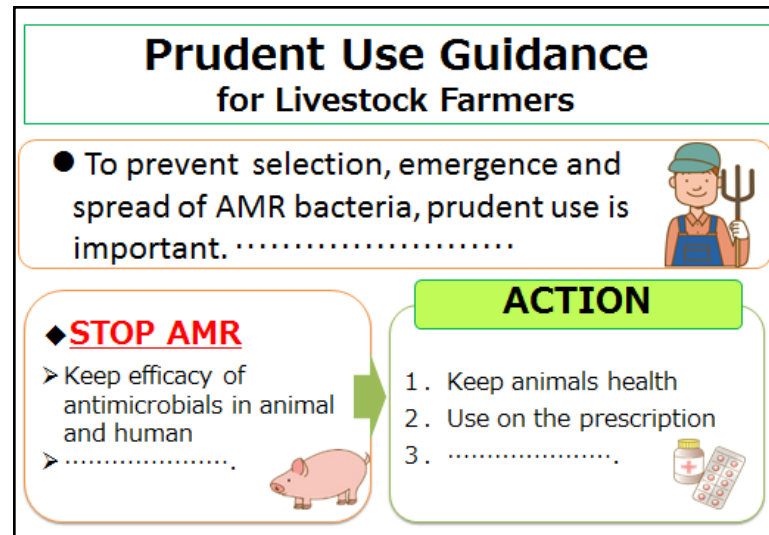
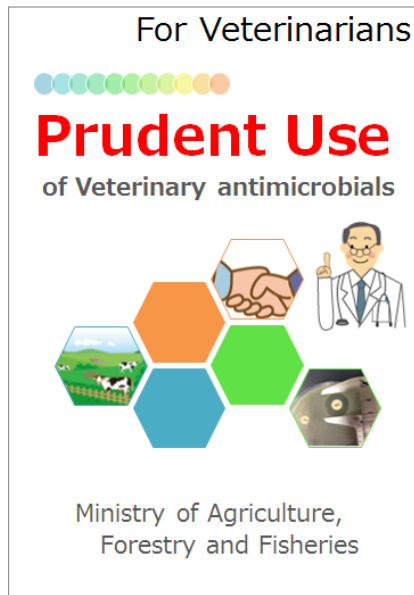


# Prudent Use Guidelines in the world

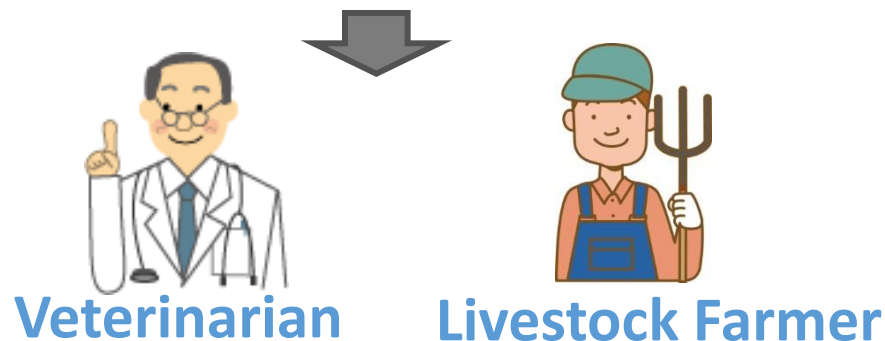
- **USDA/FDA(2012); Guidance for Industry # 209 The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals**
- **European Union(2015); Guidelines for the Prudent Use of Antimicrobials in Veterinary Medicine 2015/C 299/04**
- **Federation of Veterinary of Europe; Antibiotics Resistance & Prudent Use of Antibiotics in Veterinary Medicine**
- **American Veterinary Medical Association; Judicious use of Antimicrobials**
- **American Veterinary Medical Association(2008); Judicious Use of Antimicrobials for Treatment of Aquatic Animals**
- **American Association of Feline Practitioners(2009); Basic Guidelines of Judicious Therapeutic Use of Antimicrobials**
- **American Association Bovine Practitioners; Prudent Antimicrobial Use Guidelines for Cattle**
- **Canadian Food Inspection Agency; Prudent Use of Veterinary Drugs in Livestock Feeds**
- **Canadian Veterinary Medicine Association; Guidelines on the Prudent Use of Antimicrobial Drugs in Animals**
- **Alliance for the Prudent Use of Antibiotics: Antibiotics Use in Food Animals**
- **Bayer; Guidelines for the Use of Quinolones in Veterinary Medicine**

# Prudent Use Guidelines in Japan (1)

**“Prudent Use Guidelines” were established in 2013 and distributed to promote prudent use of antimicrobials**



Leaflets explaining prudent use guideline for veterinarians and livestock farmers.



# Prudent Use Guidelines in Japan (2)

## Main Points of Prudent Use Guidelines

### i) Prevention of infection

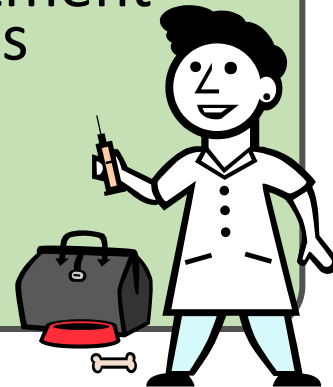
It is essential to prevent infection by appropriate management of feeding, sanitation and vaccines.

- The standards of Rearing Hygiene Management
- The guidelines on good hygienic practice



### ii) Definite diagnosis

Identify the cause of infection and determine treatment measures based on veterinarian's definite diagnosis



# Prudent Use Guidelines in Japan (3)

## Main Points of Prudent Use Guidelines

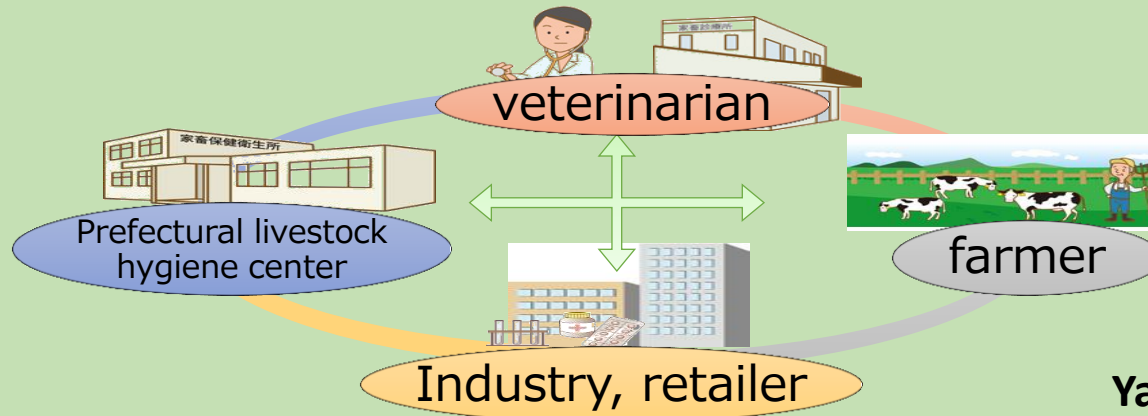


### iii) Effective use of antimicrobials

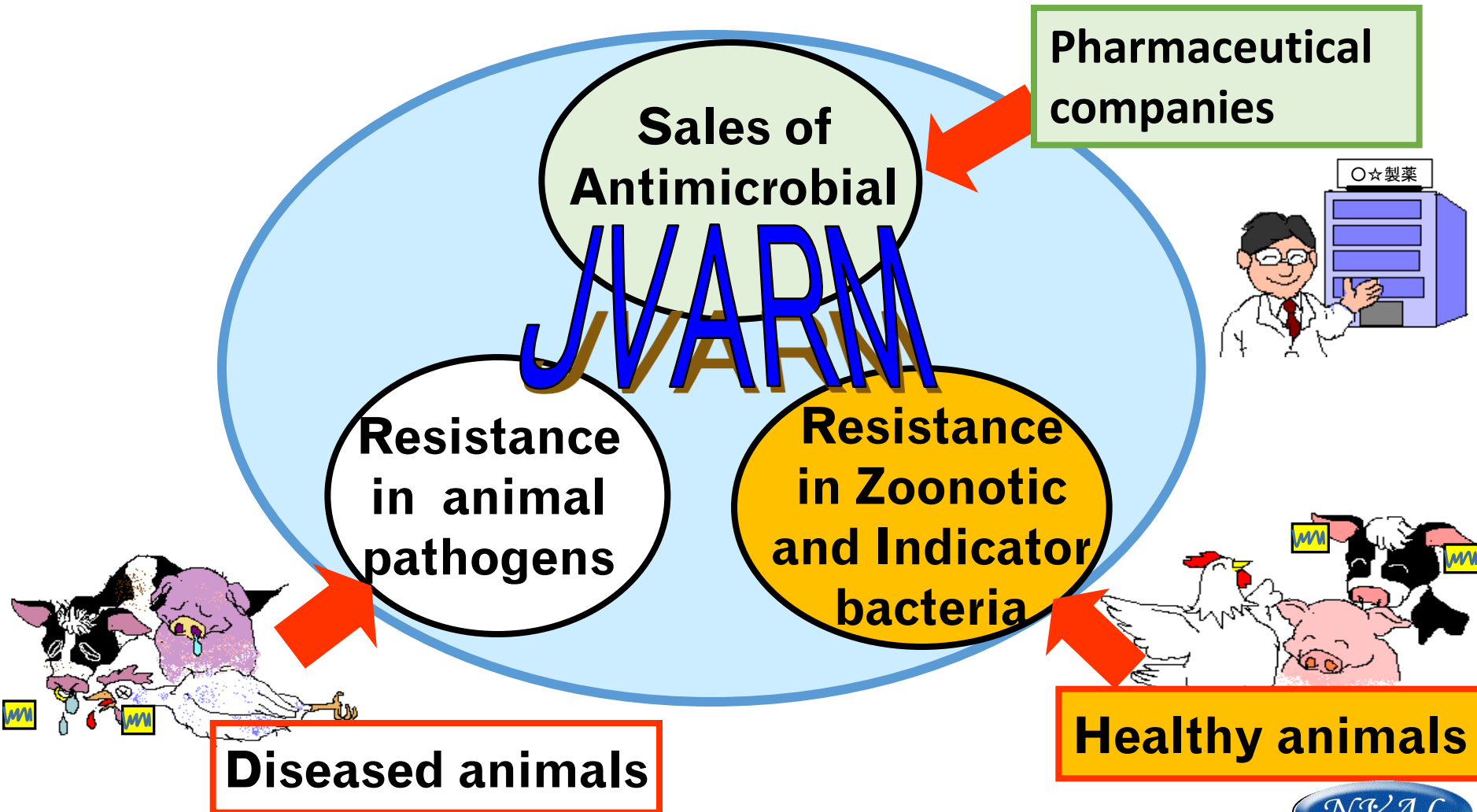
- Choose effective antimicrobial drugs with microbial sensitivity test
- Fluoroquinolones, 3<sup>rd</sup> generation cephalosporins, etc. should be used as the second choice drug, only if the first choice drug is not effective

### iv) Information sharing

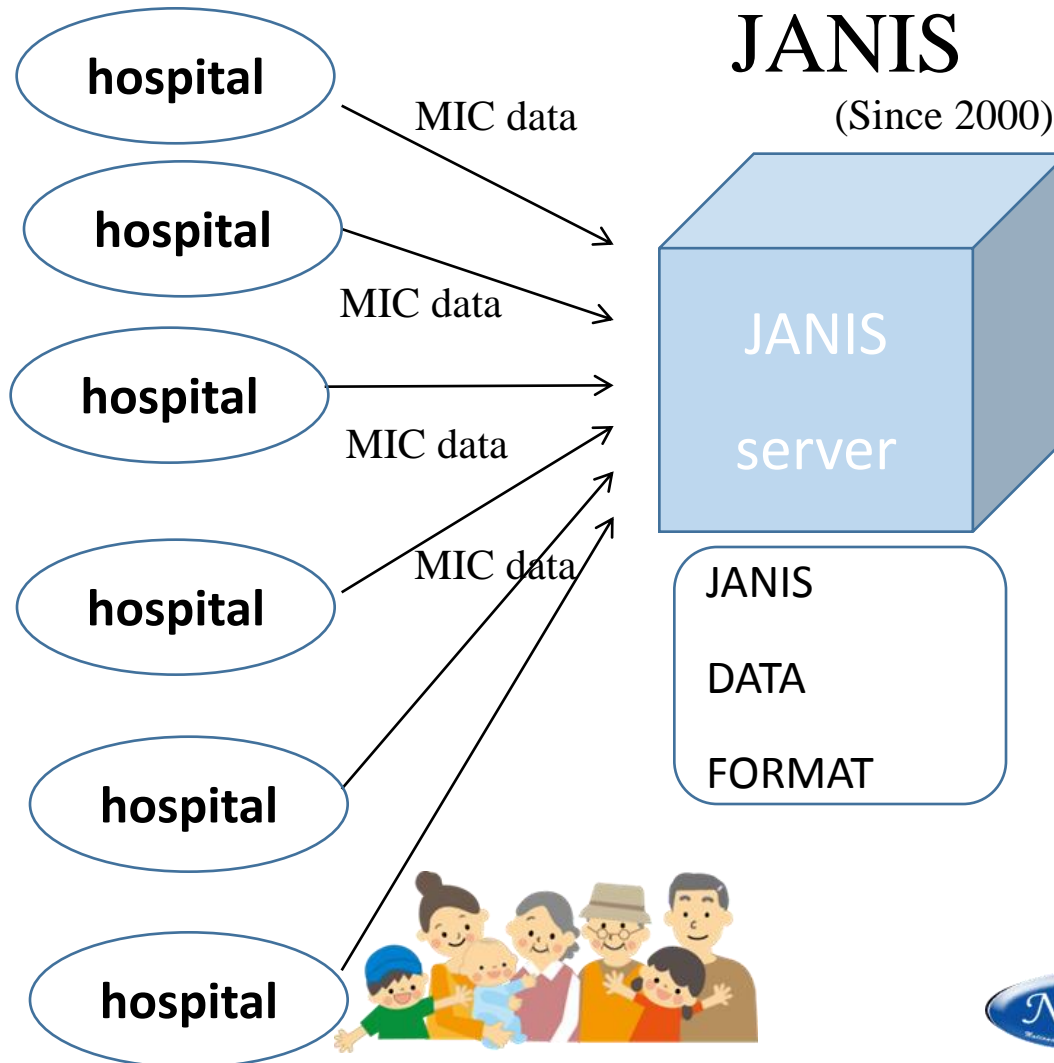
Share information about AMR bacteria among the relevant parties



# JVARM : Japanese Veterinary Antimicrobial Resistance Monitoring System



# JVARM has started collaboration with JANIS (Japan Nosocomial Infectious Surveillance: AMR surveillance in the human health sector) in order to establish the integrated surveillance system recommended by WHO based on One Health Approach.



Analyze and evaluate data, provide two types of information, Open Report and Feedback Report.



Japan Nosocomial Infections Surveillance  
Ministry of Health, Labour and Welfare

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About JANIS

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[JANIS Open Report](#)

Japan Nosocomial Infections Surveillance (JANIS) is a national surveillance system organized by the Ministry of Health, Labour and Welfare (MHLW) to provide basic information on the incidence and prevalence of antimicrobial-resistant bacteria in Japanese medical settings since 2000 with three divisions: the clinical laboratory (CL) division, the bacterial infection (ARBI) division, and intensive care unit (ICU) division. In 2002, two more divisions, the surgical site infection (SSI) and neonatal intensive care unit (NICU) divisions, were added. Further system renewal is being implemented, dealing with all surveillance data online.

Although participation in JANIS is on a voluntary basis, currently over 1,000 hospitals across Japan that are members of our surveillance system provide representative nation-level epidemiological data on antimicrobial-resistant bacteria.

● [The Five Divisions of JANIS](#)

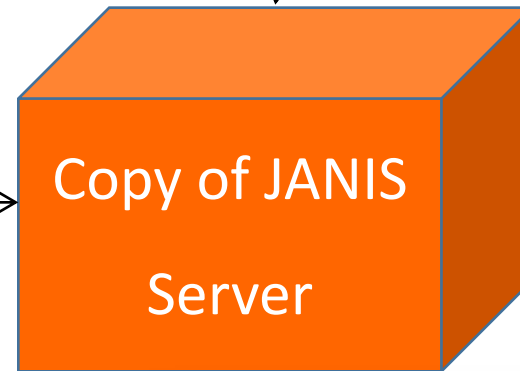
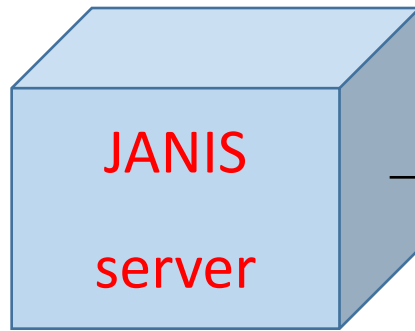


<http://www.nih-janis.jp>

# Integrate the JVARM data into the JANIS system

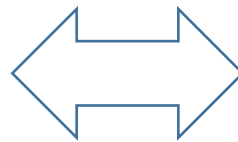
JANIS server program can calculate

- SIR judgement from MIC
- resistant rate
- multi-antimicrobial resistant rate

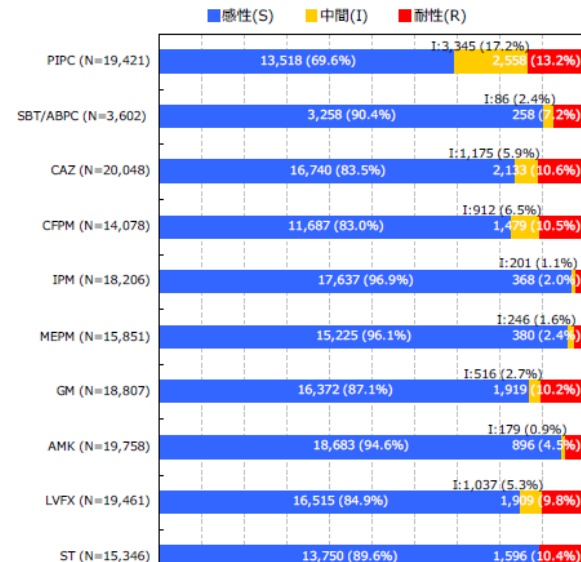
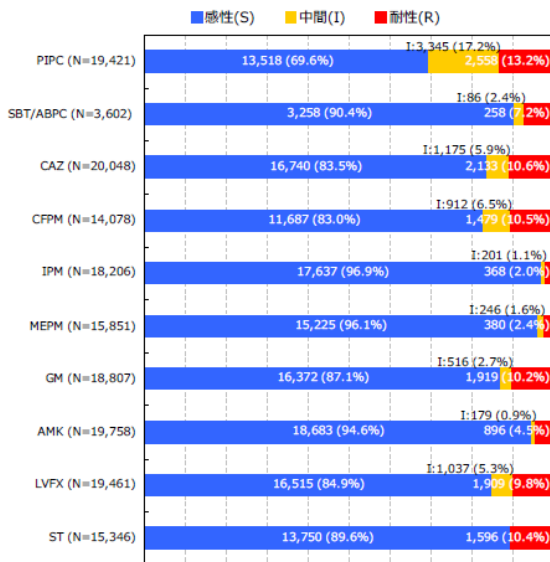


**JVARM data**

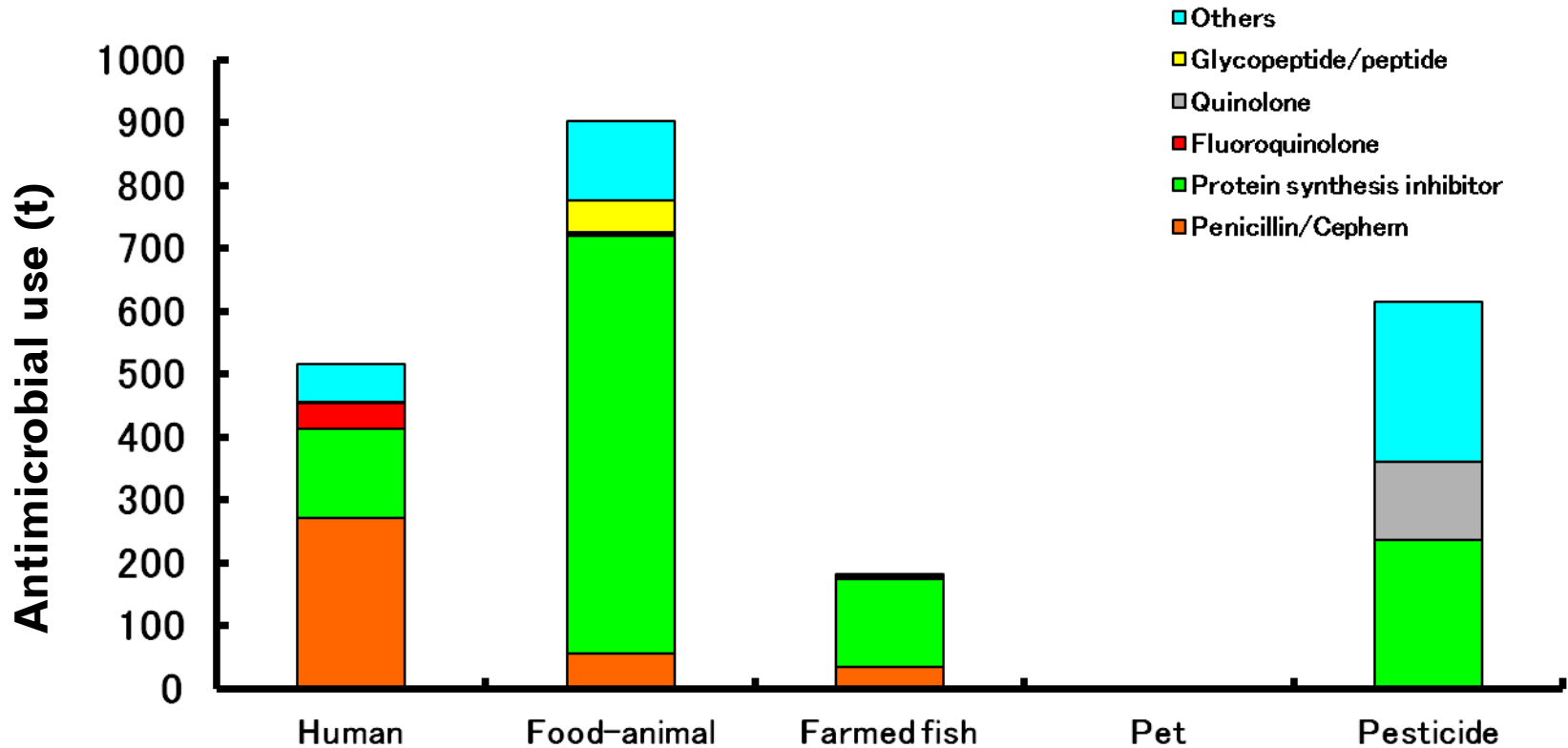
MIC data (*E. coli* :2003-2013)



**Annual report in same format**



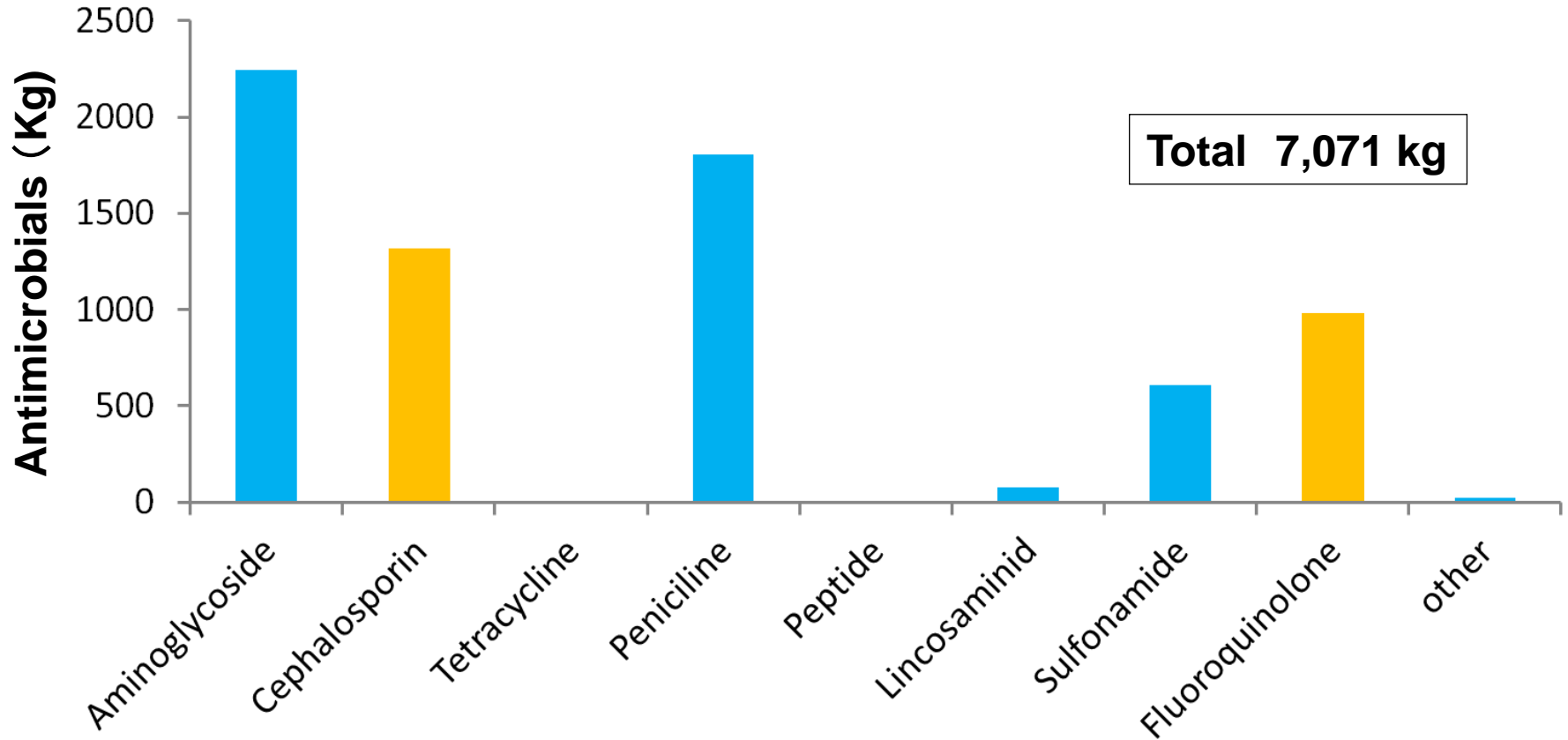
# Antimicrobial use in Japan



(MAFF and MHLW in 2002)

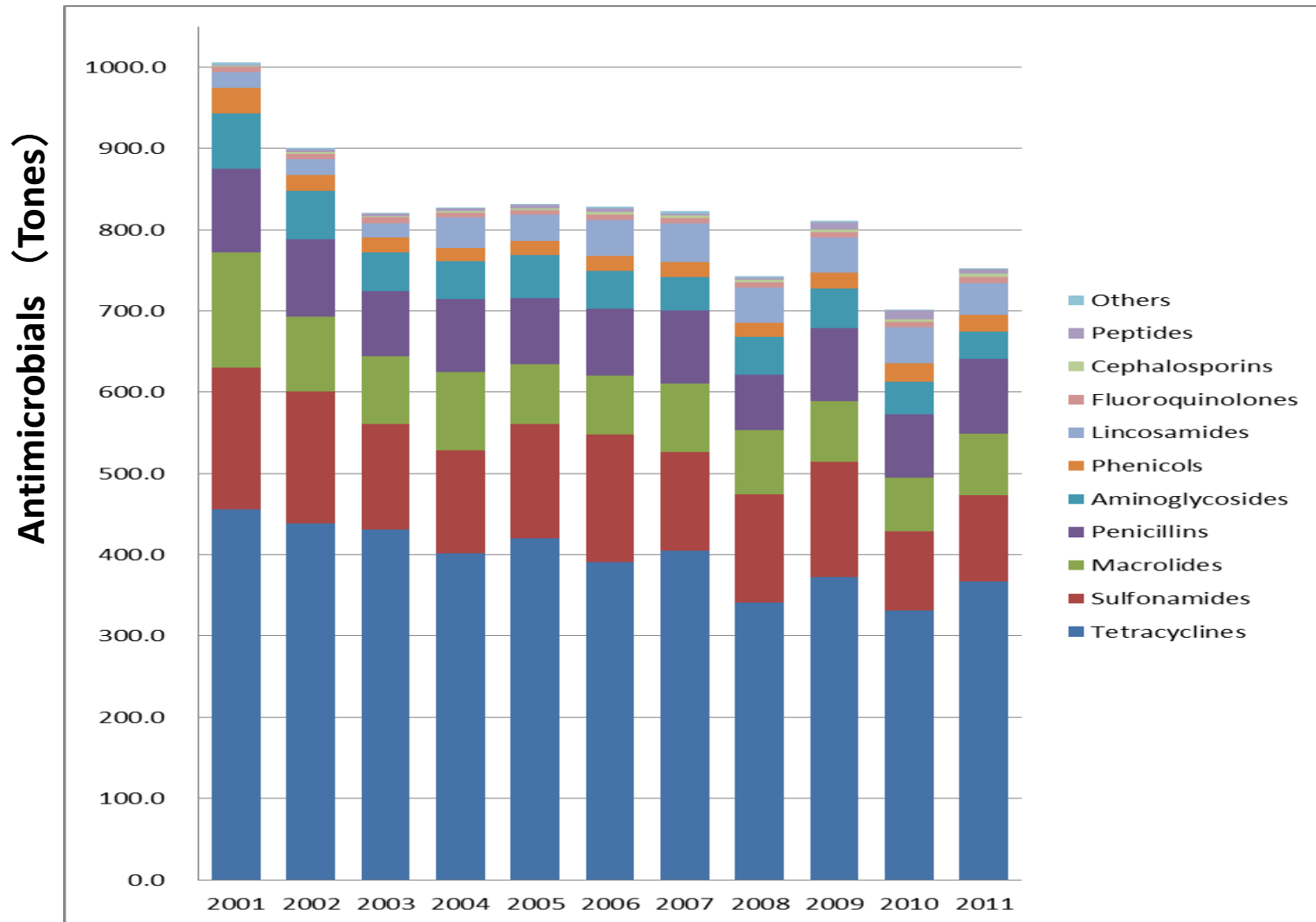


# Sale of Antimicrobials in Companion animals

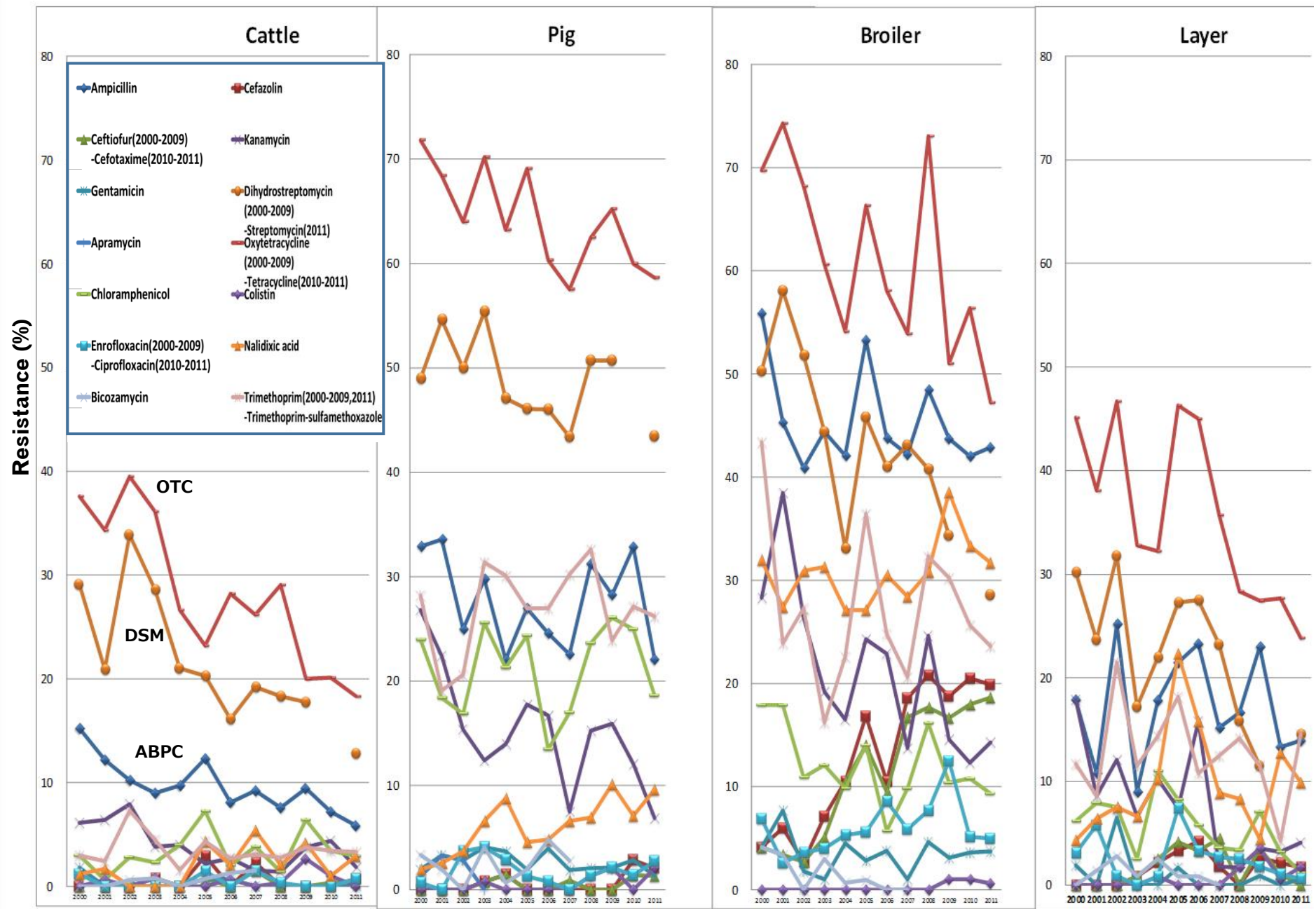


JVARM, 2012

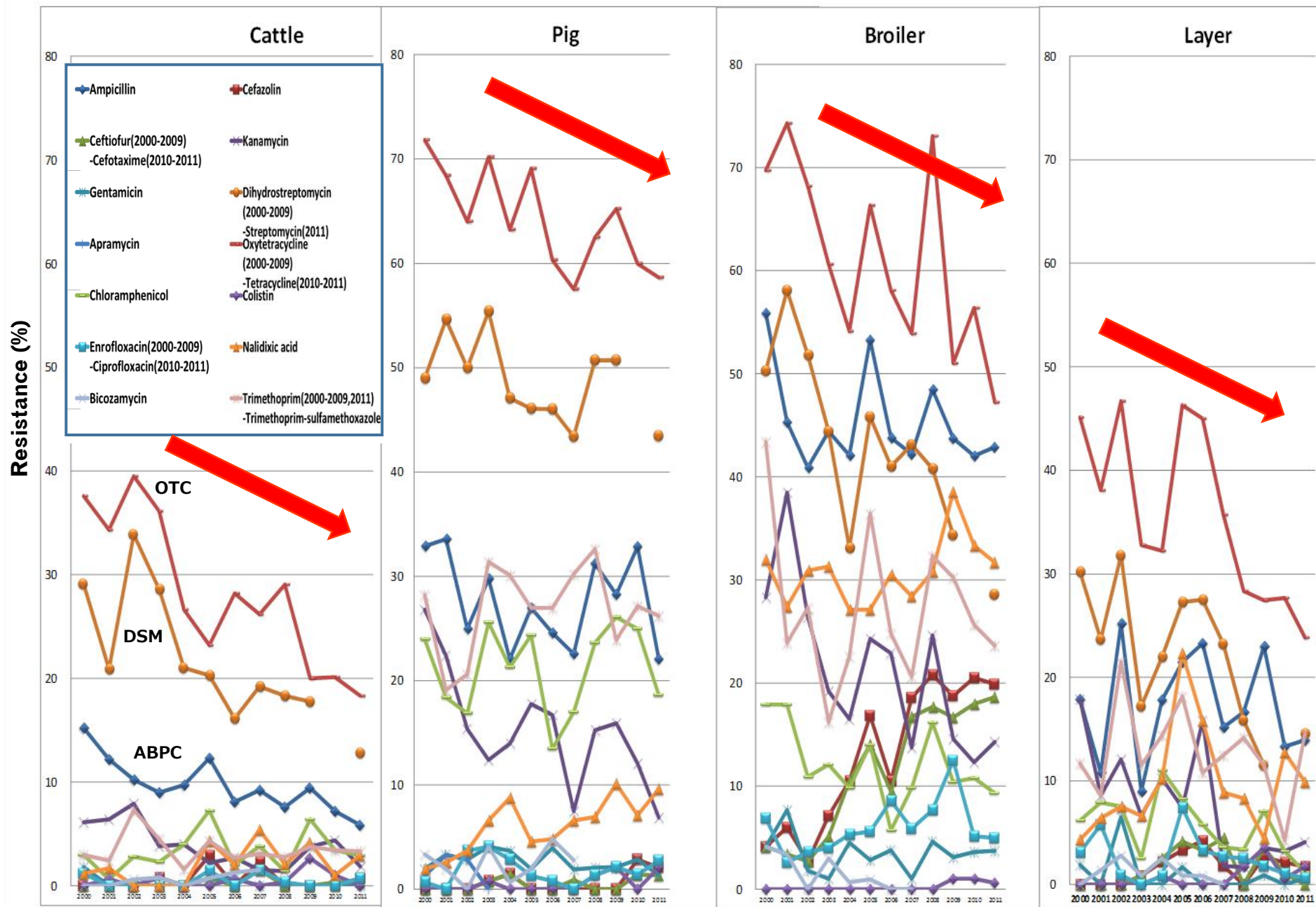
# Sale of Antimicrobials in animals as active compound in Japan



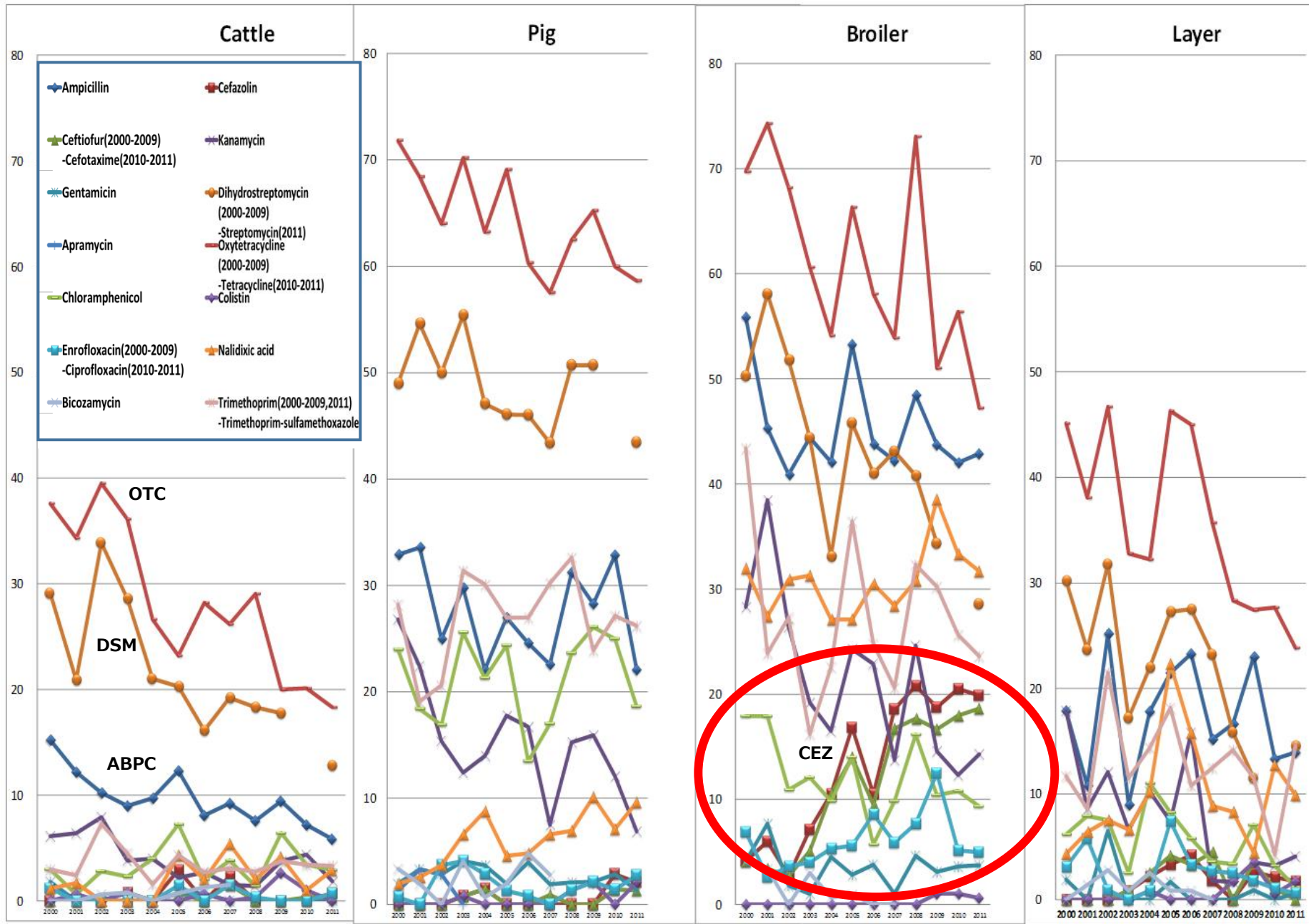
# Change of resistance(%) in *Escherichia coli* isolates from animals



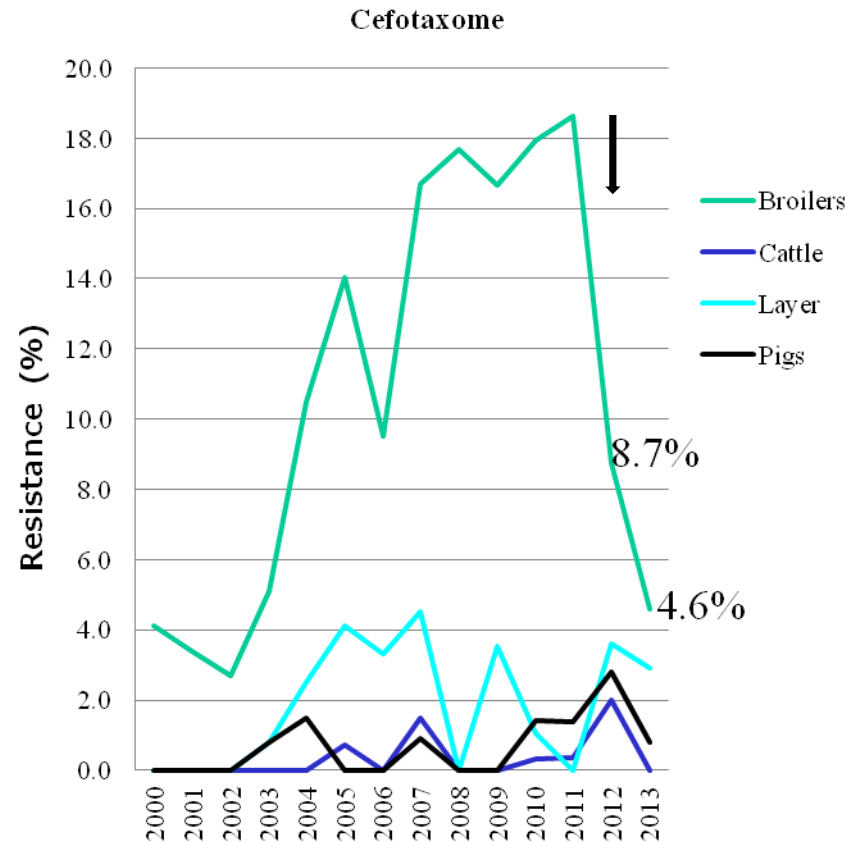
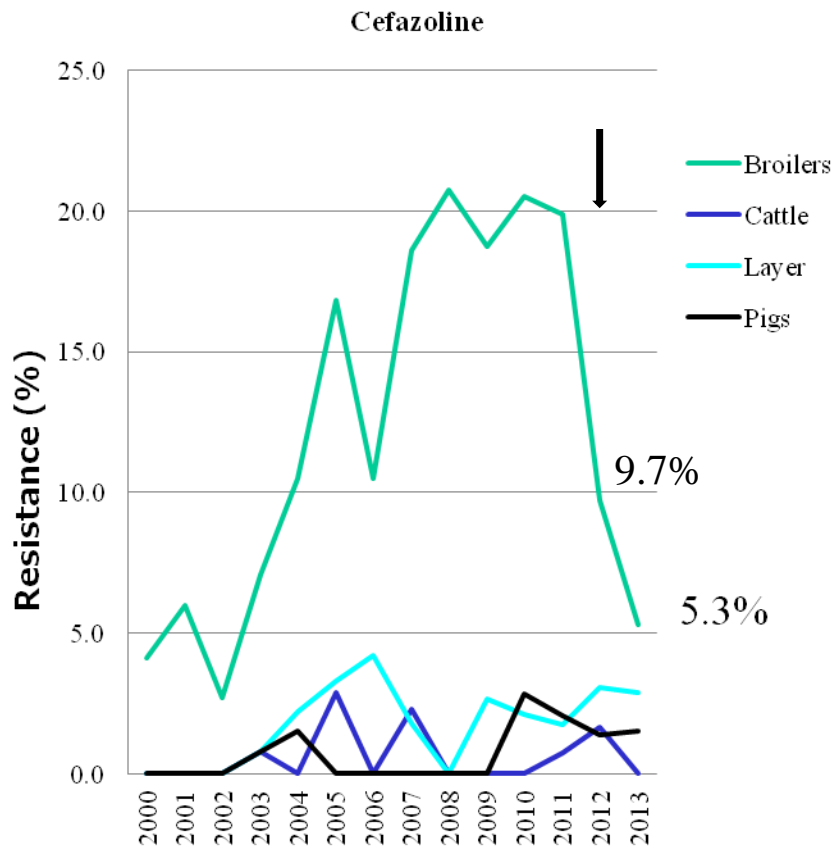
# Change of resistance(%) in *Escherichia coli* isolates from animals



# Change of resistance(%) in *Escherichia coli* isolates from animals



# Cephalosporin resistance rate in *E.coli* isolates from healthy broilers



↓ : Withdrawal of the off-label use of ceftiofur at hatcheries

# Conclusion

- 1. Antibiotic resistance has emerged as a very significant health care problem due to the overuse and misuse of antimicrobials in human and veterinary medicine and in agriculture.**
- 2. The spread and enlightenment of the prudent use guideline for the clinical veterinarian and farmer is insufficient.**
- 3. The antimicrobial in the field of aquaculture is not to appoint prescription legend drug.**
- 4. Antimicrobaial for human is empirically used in a companion animals, and the emergence of drug resistant bacteria and antimicrobial consumption is unclear.**
- 5. Because monitoring in the environment is not carried out, an effect of antimicrobial agrochemicals to the environmental microorganism is unclear.**



***Antimicrobial Resistance:  
No action today, no cure tomorrow !***

**WHO, 2011**



# Thank you for your attention !



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